INFECTIOUS DISEASE KAHOOT!

Dr. Shinar

PREVENTION: #1

Your 40 year-old patient was started on PJP prophylaxis after a diagnosis of AIDS one year ago. At that time, his CD4 count was 80/mm^3. He immediately began cART therapy and has been compliant with labs and follow up visits. His viral load has dropped to undetectable levels and his CD4 count has increased to 200/mm^3 3 months ago, and is 220/mm^3 at this current visit. This is when you can safely stop primary PJP prophylaxis in a patient with AIDS.

A. When CD4 count is > 200/mm^3 for 3 months

B. When CD4 count is > 200/mm^3 for 6 months

C. When CD4 count is > 200/mm^3 for 9 months

C. When CD4 count is > 200/mm^3 for 12 months

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PRIMARY PJP PROPHYLAXIS

- Pneumocystis is ubiquitous and infection is acquired through airborne route
- 66% of children aged 2-4 have antibodies to *P. jirovecii*
- 90% of PJP infection in HIV patients occurs when CD4 < 200
- Prophylaxis should start when CD4 < 200

- A1 recommendation
  TMP/SMX 1 ds tab q day
  TMP/SMX 1 ss tab q day
- B1 recommendation
  TMP/SMX 1 ds tab 3x/week
- Continue if feasible in patients with non-life threatening side effects
- Discontinue when CD4 count is > 200/mm^3 for 3 months

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PREVENTION: #2

This is the indication for life-long primary SBP prophylaxis in patients with ascites due to liver cirrhosis, according to the AASLD guidelines.

A. A history of SBP

B. Ascitic fluid protein < 1.5 g/dL and creatinine > 1.0 mg/dL

C. Ascitic fluid protein < 1.5 g/dL and bilirubin > 3 mg/dL

RECOMMENDATIONS

34. Intravenous ceftriaxone for 7 days or twicedaily norfloxacin for 7 days should be given to prevent bacterial infections in patients with cirrhosis and gastrointestinal hemorrhage. (Class I, Level A). Perhaps parenteral antibiotic, while the patient is bleeding and oral antibiotic after oral intake is resumed, for a total of 7 days, is a practical treatment regimen.

35. Patients who have survived an episode of SBP should receive long-term prophylaxis with daily norfloxacin (or trimethoprim/sulfamethoxazole). (Class I, Level A)

36. In patients with cirrhosis and ascites, longterm use of norfloxacin (or trimethoprim/sulfamethasoxazole) can be justified if the ascitic fluid protein <1.5 g/dL along with impaired renal function (creatinine ≥1.2, BUN ≥25 or serum Na ≤130) or liver failure (Child score ≥9 and bilirubin ≥3. (Class I, Level A)

37. Intermittent dosing of antibiotics to prevent bacterial infections may be inferior to daily dosing due to the development of bacterial resistance) and thus daily dosing should preferentially be used. (Class IIb, Level C)

2012 AASLD Guidelines for Prevention of SBP

PREVENTION: #3

According to the 2017 Focused Update for the Management of Patients with Valvular Heart Disease (and the AHA 2007 Recommendations) , this condition DOES NOT require endocarditis antibiotic prophylaxis.

A. Bioprosthetic heart valve

B. Valve regurgitation due to a structural valve problem in a heart transplant

C. Mechanical prosthetic heart valve

D. Bicuspid aortic valve

Table 2. Recommendations for IE Prophylaxis[4]

COR	LOE	Recommendation
IIa	C-LD	Prophylaxis against IE is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with the following: 1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts. 2. Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords. 3. Previous IE. 4. Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of, or adjacent to the site of, a prosthetic patch or prosthetic device. 5. Cardiac transplant with valve regurgitation attributed to a structurally abnormal valve.

From Nishimura et al.[4] Copyright 2017 American Heart Association, Inc. Used with permission. COR indicates class of recommendation; IE, infective endocarditis; LD, limited data; LOE, level of evidence.

2017 Focused Update for Management of Patients With Valvular Heart Disease: Summary of New Recommendations

Richard Matiasz and Vera H. Rigolin

EMPIRIC COVERAGE- #1

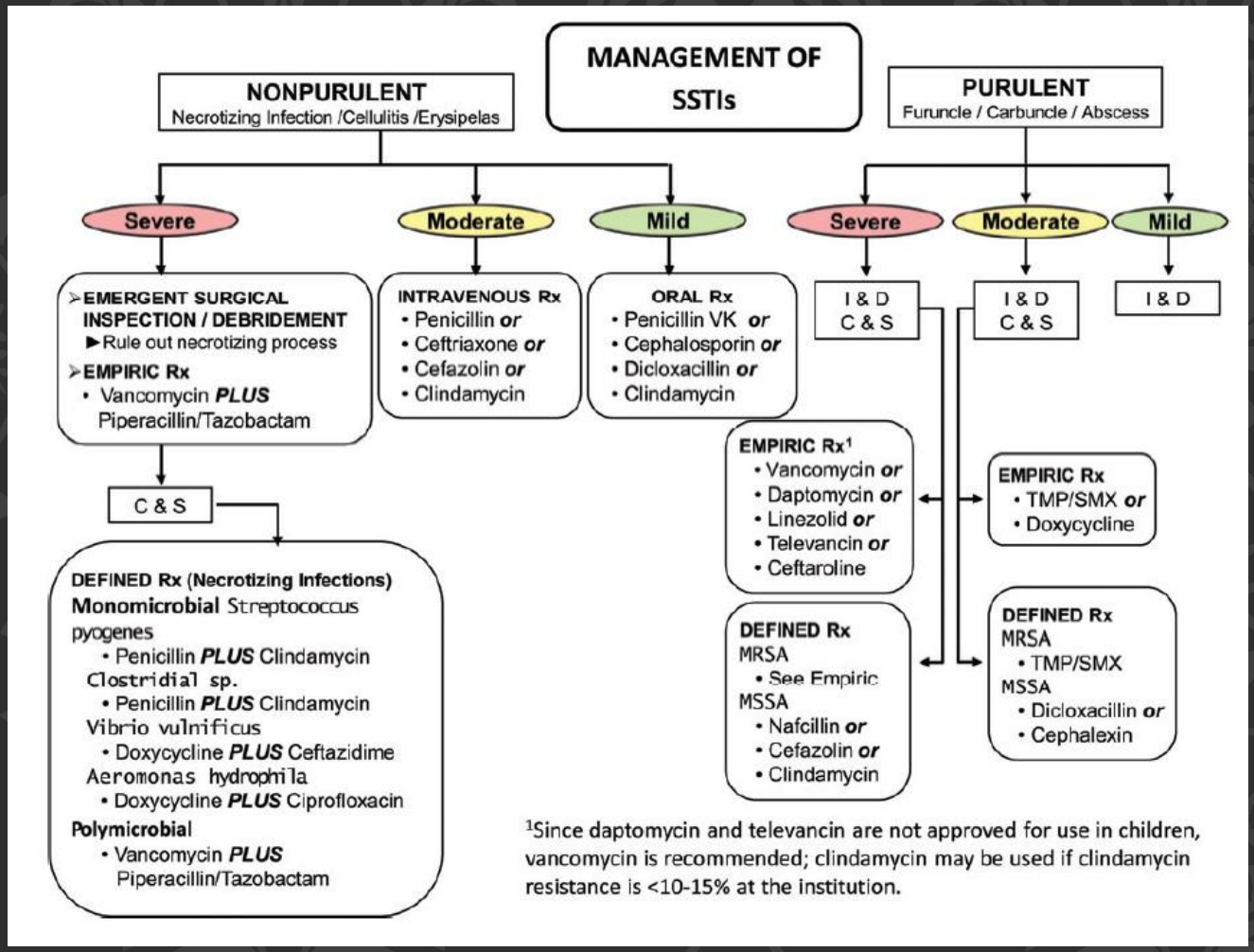
According to the 2014 IDSA guidelines, this is the most appropriate empiric antibiotic coverage for mild, non-purulent cellulitis in the outpatient setting.

A. Clindamycin

B. Doxycycline

C. Trimethoprim-sulfamethoxasole

D. Amoxicillin/clavulanic acid



2014 IDSA Guidelines for Skin and Soft Tissue Infections

Figure 1. Purulent skin and soft tissue infections (SSTIs). Mild infection: for purulent SSTI, incision and drainage is indicated. Moderate infection: patients with purulent infection with systemic signs of infection. Severe infection: patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection such as temperature >38°C, tachycardia (heart rate >90 beats per minute), tachypnea (respiratory rate >24 breaths per minute) or abnormal white blood cell count (<12 000 or <400 cells/μL), or immunocompromised patients. Nonpurulent SSTIs. Mild infection: typical cellulitis/erysipelas with no focus of purulence. Moderate infection: typical cellulitis/erysipelas with systemic signs of infection. Severe infection: patients who have failed oral antibiotic treatment or those with systemic signs of infection (as defined above under purulent infection), or those who are immunocompromised, or those with clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction. Two newer agents, tedizolid and dalbavancin, are also effective agents in SSTIs, including those caused by methicillin-resistant *Staphylococcus aureus*, and may be approved for this indication by June 2014. Abbreviations: C & S, culture and sensitivity; I & D, incision and drainage; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; Rx, treatment; TMP/SMX, trimethoprim-sulfamethoxazole.

EMPIRIC COVERAGE- #2

According to the 2010 IDSA guidelines, this is the appropriate empiric antibiotic coverage for a previously healthy 50 year- old woman who presents with left lower quadrant pain and a CT scan that is consistent with acute diverticulitis and abscess formation. Vitals are normal.

A. Ampicillin-sulbactam

B. Ciprofloxacin and metronidazole

D. Cefipime and clindamycin

E. Vancomycin and piperacillin-tazobactam

Table 2. Agents and Regimens that May Be Used for the Initial Empiric Treatment of Extra-biliary Complicated Intra-abdominal Infection

Regimen	Community-acquired infection in pediatric patients	Community-acquired infection in adults	
		Mild-to-moderate severity: perforated or abscessed appendicitis and other infections of mild-to-moderate severity	High risk or severity: severe physiologic disturbance, advanced age, or immunocompromised state
Single agent	Ertapenem, meropenem, imipenem-cilastatin, ticarcillin-clavulanate, and piperacillin-tazobactam	Cefoxitin, ertapenem, moxifloxacin, tigecycline, and ticarcillin-clavulanic acid	Imipenem-cilastatin, meropenem, doripenem, and piperacillin-tazobactam
Combination	Ceftriaxone, cefotaxime, cefepime, or ceftazidime, each in combination with metronidazole; gentamicin or tobramycin, each in combination with metronidazole or clindamycin, and with or without ampicillin	Cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin, or levofloxacin, each in combination with metronidazole[a]	Cefepime, ceftazidime, ciprofloxacin, or levofloxacin, each in combination with metronidazole[a]

[a] Because of increasing resistance of *Escherichia coli* to fluoroquinolones, local population susceptibility profiles and, if available, isolate susceptibility should be reviewed.

Community-Acquired Infection of Mild-to-Moderate Severity in Adults

28. Antibiotics used for empiric treatment of community-acquired intra-abdominal infection should be active against enteric gram-negative aerobic and facultative bacilli and enteric gram-positive streptococci (A-I).

29. Coverage for obligate anaerobic bacilli should be provided for distal small bowel, appendiceal, and colon-derived infection and for more proximal gastrointestinal perforations in the presence of obstruction or paralytic ileus (A-I).

30. For adult patients with mild-to-moderate community-acquired infection, the use of ticarcillin-clavulanate, cefoxitin, ertapenem, moxifloxacin, or tigecycline as single-agent therapy or combinations of metronidazole with cefazolin, cefuroxime, ceftriaxone, cefotaxime, levofloxacin, or ciprofloxacin are preferable to regimens with substantial anti-*Pseudomonal* activity (Table 2) (A-I).

31. Ampicillin-sulbactam is not recommended for use because of high rates of resistance to this agent among community-acquired *E. coli* (B-II).

32. Cefotetan and clindamycin are not recommended for use because of increasing prevalence of resistance to these agents among the *Bacteroides fragilis* group (B-II).

33. Because of the availability of less toxic agents demonstrated to be at least equally effective, aminoglycosides are not recommended for routine use in adults with community-acquired intra-abdominal infection (B-II).

34. Empiric coverage of *Enterococcus* is not necessary in patients with community-acquired intra-abdominal infection (A-I).

35. Empiric antifungal therapy for *Candida* is not recommended for adult and pediatric patients with community-acquired intra-abdominal infection (B-II).

36. The use of agents listed as appropriate for higher-severity community-acquired infection and health care–associated infection is not recommended for patients with mild-to-moderate community-acquired infection, because such regimens may carry a greater risk of toxicity and facilitate acquisition of more-resistant organisms (B-II).

37. For those patients with intra-abdominal infection of mild-to-moderate severity, including acute diverticulitis and various forms of appendicitis, who will not undergo a source control procedure, regimens listed for treatment of mild-to-moderate–severity infection are recommended, with a possibility of early oral therapy (B-III).

2010 IDSA Guidelines for Intra-Abdominal Infections

EMPIRIC COVERAGE- #3

A 65 year old man presented with sepsis due to a diabetic foot infection. The patient went to the OR on hospital day #2 and had an amputation of the affected limb and is clinically improved. This is the appropriate duration of antibiotic treatment for this patient according to the 2012 IDSA guidelines for diabetic foot infection.

A. IV antibiotics x 7 more days

B. IV antibiotics x 10 more days

C. PO antibiotics x 5 more days

D. PO antibiotics x 14 more days

Table 11. Suggested Route, Setting, and Duration of Antibiotic Therapy, by Clinical Syndrome

Site of Infection, by Severity or Extent	Route of Administration	Setting	Duration of Therapy
Soft-tissue only			
Mild	Topical or oral	Outpatient	1–2 wk; may extend up to 4 wk if slow to resolve
Moderate	Oral (or initial parenteral)	Outpatient/ inpatient	1–3 wk
Severe	Initial parenteral, switch to oral when possible	Inpatient, then outpatient	2–4 wk
Bone or joint			
No residual infected tissue (eg, postamputation)	Parenteral or oral	…	2–5 d
Residual infected soft tissue (but not bone)	Parenteral or oral	…	1–3 wk
Residual infected (but viable) bone	Initial parenteral, then consider oral switch	…	4–6 wk
No surgery, or residual dead bone postoperatively	Initial parenteral, then consider oral switch	…	≥3 mo

2012 IDSA Guidelines for Diabetic Foot Infections

OI- #1

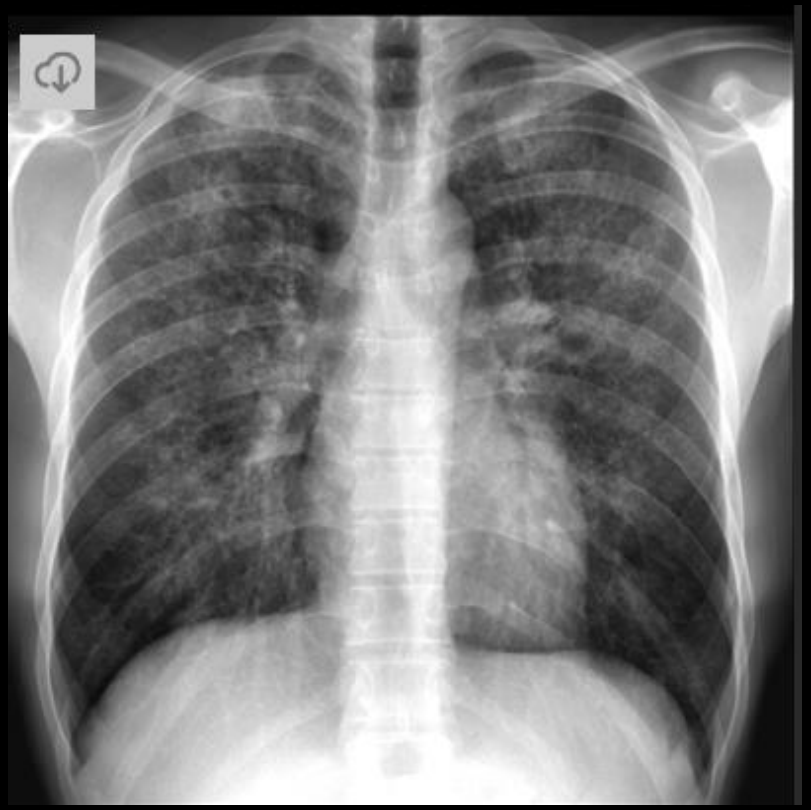
This is the appropriate treatment for a 28 year-old man with dyspnea x 3 weeks, dry cough, and fever. He has scattered white plaques on oral mucous membranes and is saturating 88% on RA. ABG reveals pH 7.48, pC02 30, and pa02 60. CXR is shown. Rapid HIV test is positive.

A. IV gancyclovir

B. IV ceftriaxone and azithromycin

C. IV TMP-SMX

D. IV TMP-SMX and prednisone



Treating PCP

Note—Patients who develop PCP despite TMP-SMX prophylaxis usually can be treated effectively with standard doses of TMP-SMX **(BIII)**.

For Moderate to Severe PCP—Total Duration = 21 Days (AII):

Preferred Therapy:

- TMP-SMX: (TMP 15–20 mg and SMX 75–100 mg)/kg/day IV given q6h or q8h **(AI)**, may switch to PO after clinical improvement **(AI)**.

Alternative Therapy:

- Pentamidine 4 mg/kg IV once daily infused over at least 60 minutes **(AI)**; may reduce the dose to 3 mg/kg IV once daily because of toxicities **(BI)** *or*
- Primaquine[b] 30 mg (base) PO once daily + (Clindamycin [IV 600 q6h or 900 mg q8h] or [PO 450 mg q6h or 600 mg q8h]) **(AI)**.

**Adjunctive corticosteroid may be indicated in some moderate to severe cases (see indications and dosage recommendations below)

For Mild to Moderate PCP—Total Duration = 21 days (AII):

Preferred Therapy:

- TMP-SMX: (TMP 15–20 mg/kg/day and SMX 75–100 mg/kg/day), given PO in 3 divided doses **(AI)** *or*
- TMP-SMX DS - 2 tablets TID **(AI)**.

Alternative Therapy:

- Dapsone[b] 100 mg PO daily + TMP 15 mg/kg/day PO (3 divided doses) **(BI)** *or*
- Primaquine[b] 30 mg (base) PO daily + Clindamycin PO (450 mg q6h or 600 mg q8h) **(BI)** *or*
- Atovaquone 750 mg PO BID with food **(BI)**

Adjunctive Corticosteroids:

*For Moderate to Severe PCP Based on the Following Criteria **(AI)**:*

- PaO_2 <70 mmHg at room air *or*
- Alveolar-arterial O_2 gradient ≥35 mmHg

Dosing Schedule:

Prednisone doses (beginning as early as possible and within 72 hours of PCP therapy) **(AI)**:

Days 1–5	40 mg PO BID
Days 6–10	40 mg PO daily
Days 11–21	20 mg PO daily

IV methylprednisolone can be given as 75% of prednisone dose

OI- PGY 2

A 33 year-old woman is evaluated for a 5 week history of whitish spots in the mouth and the back of the throat and pain in her chest with swallowing solid foods. She has never had these symptoms before. She has a 3 year history of HIV infection and also has moderately severe asthma that is well controlled on fluticasone and salmeterol. Her last CD4 count was 458 and her HIV RNA viral load is undetectable. This is the most appropriate management for this patient.

A. Fluticasone cessation

B. Intravenous amphotericin B

C. Nystatin swish-and-swallow

D. Oral fluconazole

Recommendations for Treating Mucosal Candidiasis (page 1 of 2)

Treating Mucosal Candidiasis

Oropharyngeal Candidiasis: Initial Episodes (Duration of Therapy: 7–14 days)

Preferred Oral Therapy:

- Fluconazole 100 mg PO once daily **(AI)**, *or*

Preferred Topical Therapy:

- Clotrimazole troches 10 mg PO 5 times daily **(BI)**, *or*
- Miconazole mucoadhesive buccal tablet 50 mg: Apply to mucosal surface over the canine fossa once daily (do not swallow, chew, or crush tablet). Refer to product label for more detailed application instructions. **(BI)**

Alternative Oral Therapy:

- Itraconazole oral solution 200 mg PO daily **(BI)**, *or*
- Posaconazole oral suspension 400 mg PO BID for one day, then 400 mg daily **(BI)**

Alternative Topical Therapy:

- Nystatin suspension 4–6 mL QID or 1–2 flavored pastilles 4–5 times daily **(BII)**

Esophageal candidiasis (Duration of Therapy: 14–21 days)

Note: Systemic antifungals are required for effective treatment of esophageal candidiasis **(AI)**

Preferred Therapy:

- Fluconazole 100 mg (up to 400 mg) PO or IV daily **(AI)**, *or*
- Itraconazole oral solution 200 mg PO daily **(AI)**

Alternative Therapy:

- Voriconazole 200 mg PO or IV BID **(BI)**, *or*
- Caspofungin 50 mg IV daily **(BI)**, *or*
- Micafungin 150 mg IV daily **(BI)**, *or*
- Anidulafungin 100 mg IV for one dose, then 50 mg IV daily **(BI)**, *or*
- Amphotericin B deoxycholate 0.6 mg/kg IV daily **(BI)**, *or*
- Lipid formulation of amphotericin B 3-4 mg/kg IV daily **(BIII)**

Note: A higher rate of esophageal candidiasis relapse has been reported with echinocandins than with fluconazole.

SUMMARY AND RECOMMENDATIONS

Oropharyngeal candidiasis

- Oropharyngeal candidiasis is a local infection of older adults who wear dentures, patients treated with antibiotics, steroids, chemotherapy, or radiation therapy to the head and neck, and those with cellular immune deficiency states, such as AIDS. (See 'Introduction' above.)
- We recommend topical therapy for the treatment of oropharyngeal candidiasis in patients without AIDS (**Grade 1B**). (See 'HIV-seronegative patients' above.)
- We recommend topical therapy for the initial episode of oropharyngeal candidiasis in HIV-infected patients with mild disease (**Grade 1A**). For patients with recurrent infection, moderate to severe disease, or in those with advanced immunosuppression (CD4 <100 cells/microL) we recommend fluconazole (200 mg loading dose, followed by 100 to 200 mg daily for 7 to 14 days after clinical improvement) (**Grade 1A**). (See 'HIV-seropositive patients' above.)
- For patients with fluconazole-refractory disease (eg, those who clinically fail fluconazole therapy), we administer itraconazole solution, posaconazole suspension, or voriconazole for up to 28 days. (See 'Oropharyngeal candidiasis' above.)

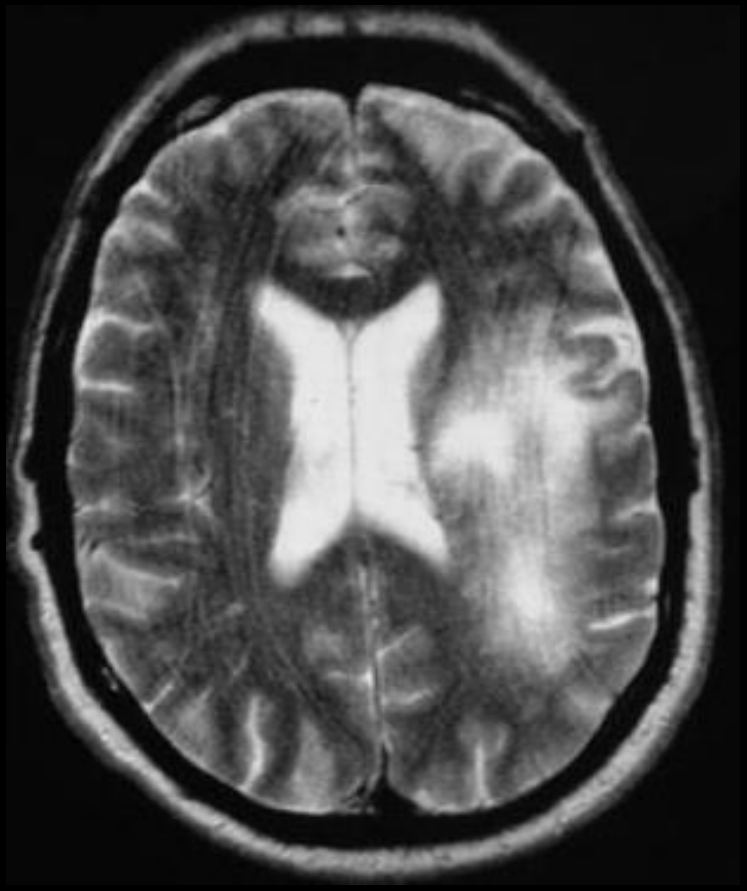
Esophageal candidiasis

- Esophageal candidiasis is most commonly seen in HIV-infected patients with advanced immunosuppression (CD4 <200 cells/microL). The presence of oropharyngeal candidiasis increases the risk of this disease; however, its absence does not eliminate the diagnosis. (See 'Esophageal candidiasis' above.)
- Empiric antifungal therapy can be initiated with careful follow-up. Endoscopy should be undertaken if the patient has no improvement of symptoms in 72 hours. (See 'Esophageal candidiasis' above.)
- We recommend systemic agents for the treatment of documented or suspected esophageal candidiasis (**Grade 1A**). (See 'Esophageal candidiasis' above.)

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America.AUPappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, Zaoutis TE, Sobel JD SOClin Infect Dis. 2016;62(4):e1. Epub 2015 Dec 16.

OI- #3

A 37 year-old woman is evaluated for worsening multiple sclerosis. She has had 3 relapses in the past year treated with corticosteroids. A recent MRI showed additional ovoid lesions since diagnosis. The decision is made to change the patient's medication from glatiramer acetate to natalizumab. Six months after this medication is initiated, the patient develops altered mental status and ataxia. Her brain MRI is shown. This is the infectious etiology.



A. Creutzfeld-Jakob

B. Toxoplasmosis

C. JC Virus

D. Cryptococcus

Higher JCV Antibody Levels Precede PML Diagnosis

Patients who were diagnosed with PML (n = 71) had significantly higher JCV antibody index values more than 6 months before the diagnosis compared with patients without a PML diagnosis (n = 2522) ($P < .001$). Differences in antibody indices occurred only in comparison of patients with (n = 19) and those without (n = 176) a PML diagnosis who had not had prior immunosuppressive therapy; values were higher for patients later diagnosed with PML ($P < .001$).

For patients who had received immunosuppressive therapy earlier, there was no significant difference in antibody levels between those later diagnosed with PML and those without PML ($P = .87$).

For JCV antibody–positive patients with no prior immunosuppressant use, the risk for PML increased with longer natalizumab use. For 1 to 24 months of exposure to the drug, the risk was 0.6/1000. With 25 to 48 months of exposure, the risk increased to 5.2/1000, and with 49 to 72 months of natalizumab, the risk was 5.4/1000. Patients who were antibody negative had a risk of 0.07/1000.

For patients with no prior immunosuppressive exposure, antibody index values allowed estimation of PML risk according to the duration of exposure to natalizumab. Patients with lower antibody levels remained at substantially lower PML risk over the course of natalizumab therapy compared with patients with higher antibody levels.

Table. Estimation of PML Risk per 1000 Patients According to Antibody Index by Duration of Natalizumab Exposure

Antibody Index	1 to 24 Months	25 to 48 Months	49 to 72 Months
≤0.9	0.1	0.3	0.4
≤1.1	0.1	0.7	0.7
≤1.3	0.1	1.0	1.2
≤1.5	0.1	1.2	1.3
>1.5	1.0	8.1	8.5

Patients had no prior immunosuppressant exposure.

"We know that currently some physicians after 2 years of natalizumab treatment in their antibody-positive patients will take the patients off of drug because of a fear of PML," Dr. Ticho said. "Perhaps for patients who have lower antibody index levels there is another analysis of the benefit-risk that has to be made with respect to both the disease course that those patients have and the fact that their risk of PML may actually be lower than expected right now."

TRAVEL- #1

A 46 year-old woman travels to a rural area of Guatemala. Three days after arrival, she develops watery diarrhea with severe abdominal cramping. She reports two unformed stools daily for the past 2 days. She has noticed no blood in the stool and has not experienced a fever. This is the most likely cause of the patient's illness.

A. *Campylobacter jejuni*

B. Entertoxigenic Escherichia coli

C. Giardia lamblia

D. Norovirus

TRAVELERS' DIARRHEA

Bradley A. Connor

Travelers' diarrhea (TD) is the most predictable travel-related illness. Attack rates range from 30% to 70% of travelers, depending on the destination and season of travel. Traditionally, it was thought that TD could be prevented by following simple recommendations such as "boil it, cook it, peel it, or forget it," but studies have found that people who follow these rules may still become ill. Poor hygiene practice in local restaurants is likely the largest contributor to the risk for TD.

TD is a clinical syndrome that can result from a variety of intestinal pathogens. Bacterial pathogens are the predominant risk, thought to account for 80%–90% of TD. Intestinal viruses usually account for 5%–8% of illnesses, although increasing use of improved diagnostics may increase recognition of norovirus infections in the future. Infections with protozoal pathogens are slower to manifest symptoms and collectively account for approximately 10% of diagnoses in longer-term travelers. What is commonly known as "food poisoning" involves the ingestion of preformed toxins in food. In this syndrome, vomiting and diarrhea may both be present, but symptoms usually resolve spontaneously within 12 hours.

INFECTIOUS AGENTS

Bacteria are the most common cause of TD. Overall, the most common pathogen is enterotoxigenic *Escherichia coli*, followed by *Campylobacter jejuni*, *Shigella* spp., and *Salmonella* spp. Enteroadherent and other *E. coli* pathotypes are also common pathogens in TD. There is increasing discussion of *Aeromonas* spp. and *Plesiomonas* spp. as potential causes of TD as well. Viral diarrhea can be caused by a number of pathogens, including norovirus, rotavirus, and astrovirus.

Giardia is the main protozoal pathogen found in TD. *Entamoeba histolytica* is a relatively uncommon pathogen in travelers. *Cryptosporidium* is also relatively uncommon. The risk for *Cyclospora* is highly geographic and seasonal: the most well-known risks are in Nepal, Peru, Haiti, and Guatemala. *Dientamoeba fragilis* is a low-grade but persistent pathogen that is occasionally diagnosed in travelers. The individual pathogens are each discussed in their own sections in Chapter 3, and persistent diarrhea in returned travelers is discussed in Chapter 5.

TRAVEL- #2

A 19 year-old man is evaluated for a sore throat, daily fever, frontal headache, myalgia, and arthralgia of 5 days' duration. He also has severe low back pain and a rash on his trunk and extremities. He returned from a 7 day trip to the Caribbean 8 days ago. On physical examination, temperature is 38.3 (100.9), blood pressure is 104/72 mm Hg, HR is 102/min, and RR is 16/min. His pharynx is erythematous without exudate. He has a diffuse maculopapular rash on arms, legs, and chest that spares the palms and soles. There is no LAD. WBC is 3.1, platelet 85K, ALT 114 U/L, AST 154 U/L, total bilirubin 1.2 mg/dL. **This is the likely diagnosis.**

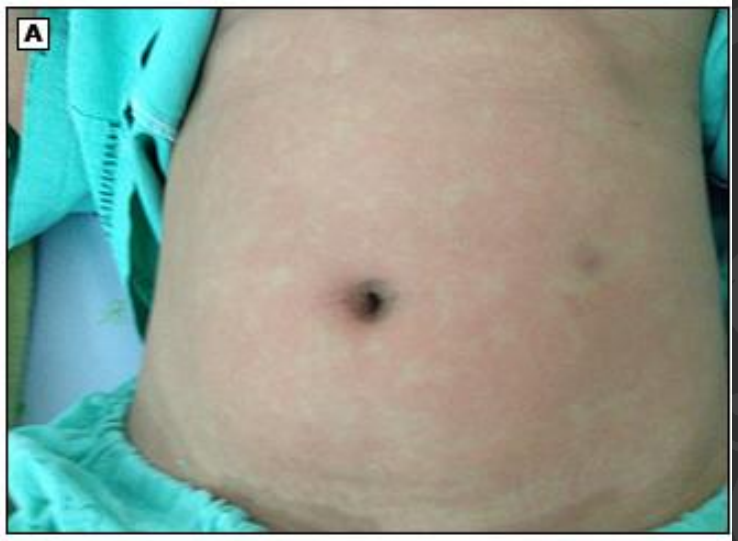
A. Denge fever

B. Leptospirosis

C. Malaria

D. Syphilis

Rash in dengue fever



Other symptoms — Acute dengue virus infection often presents without the full picture of classical DF, especially in children. Gastrointestinal or respiratory tract symptoms may dominate the clinical picture in some patients. Among 3926 patients with laboratory-diagnosed dengue virus infections in Puerto Rico during 1990 and 1991 (one-third of whom were <15 years of age), the frequency of specific symptoms was as follows [12]:

- Constitutional symptoms, including fever (90 percent)
- Headache, eye pain, body pain, and joint pain (63 to 78 percent)
- Rash (slightly more than 50 percent)
- Gastrointestinal symptoms including nausea or vomiting (more than 50 percent) and diarrhea (30 percent)
- Respiratory tract symptoms including cough, sore throat, and nasal congestion (each observed in approximately one-third of patients)

Physical examination — The physical examination in patients with DF is generally nonspecific. Conjunctival injection, pharyngeal erythema, lymphadenopathy, and hepatomegaly are observed in 20 to 50 percent of patients [13]. The rash is typically macular or maculopapular and may be associated with pruritus (picture 1).

Laboratory findings — Laboratory findings typical of DF include the following:

- Leukopenia is common in both adults and children with DF and is a useful diagnostic feature [13,15,16].
- Thrombocytopenia is noted in most patients with DF [17]. In several studies, platelet counts <100,000 cells/mm^3 were observed in 16 to 55 percent of patients [11,15].
- Serum aspartate transaminase (AST) levels are frequently elevated in both adults and children with DF; the elevations are usually modest (2 to 5 times the upper limit of normal values), but marked elevations (5 to 15 times the upper limit of normal) are occasionally noted [11,15].

TRAVEL- #3

A 27 year-old man is evaluated in the ED for a 2-day history of fever, weakness, and dark-colored urine. The patient returned yesterday from a 2 week camping trip to Cape Cod, Massachusetts. While there, he developed a target-shaped lesion on his thigh. He was seen at a walk-in clinic and early-stage Lyme disease was diagnosed. He was given a 14 day course of doxycycline of which he is on day #10. He is now jaundiced with normal BP and HR of 118. The liver is enlarged and tender. Hemoglobin is 8.4 g/dL, Retic count is 10%, Leukocyte count is 12.6 K, Platelet count is 110 K, LDH is 675 U/L, and total bilirubin is 8.3 mg/dL.

This is the pathogen most likely to cause the patient's current findings.

A. Anaplasma phagocytophilum

B. Babesia microti

C. Borrelia burgdorferi

D. Rickettsia rickettsii

SUMMARY AND RECOMMENDATIONS

- Babesiosis is an infectious disease caused by protozoa of the genus *Babesia*. *Babesia* protozoa infect vertebrate animals and cause lysis of host red blood cells. The zoonotic cycle is maintained by tick vectors. Human infection is accidental; humans are not definitive reservoir hosts. (See 'Introduction' above.)
- Clinical manifestations of *Babesia* infection range from asymptomatic to severe infection (sometimes fatal). Symptoms of mild illness typically include fever, chills, sweats, headache, myalgia, arthralgia, and anorexia. Severe illness may include manifestations of brisk hemolysis (jaundice, hemoglobinuria) as well as multiorgan system failure (acute respiratory distress syndrome, disseminated intravascular coagulation, congestive heart failure, and renal failure). (See 'Clinical manifestations' above.)
- The severity of infection depends on the *Babesia* species and the immune status of the host. *B. microti* is the predominant species in North America; manifestations of infection due to this species range from mild (in young healthy individuals) to severe (in immunocompromised patients and in older adults). *B. divergens* is the predominant species in Europe; nearly all symptomatic cases attributed to *B. divergens* were severe and occurred in asplenic individuals. (See 'Clinical manifestations' above.)
- Definitive diagnosis of babesiosis should be made by microscopic examination of a thin blood smear. Polymerase chain reaction (PCR) is useful in the setting of low parasitemia, (eg, at the onset of symptoms and during convalescence). Serology alone is not diagnostic but may help determine whether the infection is acute, active, or recent. (See 'Diagnosis' above.)
- For patients with mild *B. microti* infection, we recommend treatment with atovaquone-azithromycin (**Grade 1B**). For asymptomatic patients with babesiosis, we recommend not administering antibiotic therapy (**Grade 1C**). Treatment should be considered if parasites persist for ≥3 months. (See 'Treatment of mild illness due to B. microti' above.)
- For patients with severe *B. microti* infection, we recommend initial antimicrobial therapy with clindamycin-quinine (**Grade 1B**). Indications for red blood cell exchange transfusion include high-grade parasitemia (≥10 percent) and severe anemia (hemoglobin <10 g/dL), particularly if the patient is likely to develop pulmonary, renal, or hepatic compromise. Exchange transfusion may be lifesaving and should not be withheld in cases of severe disease, even if parasitemia is less than 10 percent. Exchange transfusion should be performed in consultation with experts in hematology and pheresis. Severe anemia alone (hemoglobin <10 g/dL) should be addressed with transfusion of packed red blood cells. (See 'Treatment of severe illness due to B. microti' above.)
- *B. divergens* frequently causes fulminant illness and should be considered a medical emergency. We recommend exchange transfusion in consultation with hematology and pheresis expertise (**Grade 1C**), followed by antimicrobial therapy with clindamycin (and quinine when tolerated) (**Grade 1B**).
- Administration of antimicrobial therapy for 7 to 10 days is usually sufficient for curative treatment of mild disease. Longer duration of antimicrobial therapy may be needed in cases of persistent and relapsing babesiosis. Immunocompromised patients should be treated for at least six weeks, including two weeks after parasites are no longer detectable on blood smear. (See 'Persistent and relapsing babesiosis' above.)

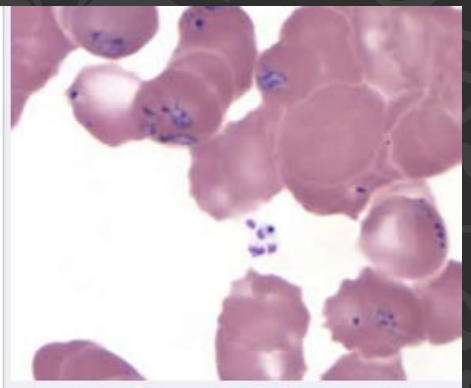


Figure G: Babesia MO-1 in a thin blood smear stained with Giemsa. *Babesia* sp. cannot be identified to the species level by morphology alone; additional testing, such as PCR, is always recommended.

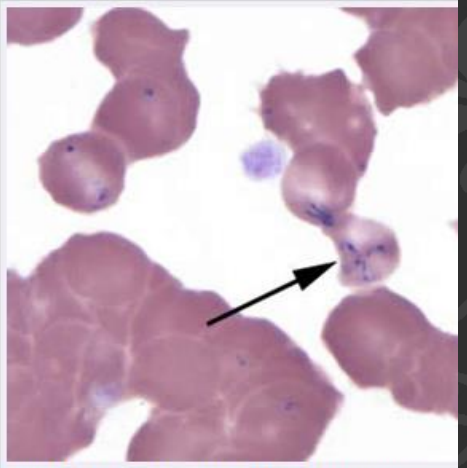


Figure J: Babesia MO-1 in a thin blood smear stained with Giemsa. Note the tetrad (black arrow).