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Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

Meridith Test
Webinar ID: 998-21-123
This session is being recorded.
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How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.

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MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.
THESE ANSWERS WILL BE REVIEWED.

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ACG Virtual Grand Rounds

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Week Number 36 – Thursday, September 8, 2022
Perianal Chron’s Disease – Evolutions in Management
 Faculty: Miguel D. Regueiro, MD, FACP
 Moderator: Jill K. J. Gaidos, MD, FACP
 Thursday, September 8th at Noon Eastern and **NEW! 8pm Eastern!**




Week Number 37 – Thursday, September 15, 2022
Pancreatic Cancer Palliation
 Faculty: Nalini Guda, MD, FACP
 Moderator: Prabhleen Chahal, MD, FACP
 Thursday, September 15th at Noon Eastern and **NEW! 8pm Eastern!**

Visit gi.org/ACGVGR to Register

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Disclosures



Mark S. Riddle, MD, DrPH
No relevant financial relationships



Freddy Caldera, DO, MS, FACG
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The presenter and moderator for this activity do not have any relevant financial relationships with ACCME ineligible companies.


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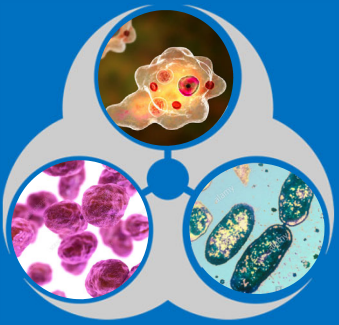
ID FOR THE GI - GI PRESENTATIONS OF UNUSUAL INFECTIONS (PARASITIC, RICKETTSIAL, AND ATYPICAL BACTERIAL INFECTIONS)

MARK S. RIDDLE, MD, DRPH
PROFESSOR OF INTERNAL MEDICINE & ASSOCIATE DEAN FOR CLINICAL RESEARCH





University of Nevada, Reno
School of Medicine



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CASE #1: THE WAITER FROM "ANYTOWN" USA

- A previously healthy 36-year-old man presented to the hospital with sudden-onset aphasia and right-sided hemiplegia secondary to a large ischemic left middle cerebral artery territory stroke with cortical swelling.
- His mental status declined following admission, along with development of new third cranial nerve palsy and uncal herniation with midline shift on repeat brain imaging, prompting emergent hemicraniectomy on hospital day 2.

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CASE #1: INITIAL PRESENTATION CONTINUED

- On hospital day 3, he had bright red blood per rectum evolving to bloody diarrhea and fever (39 °C), with worsening leukocytosis (white blood cell count increased from 14.6 to 30.0 × 10⁹/L).
- Computed tomography (CT) of his abdomen revealed pancolitis with reactive mesenteric lymphadenopathy suggestive of infection.
- Gastroenterology was consulted

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CASE #1: PERTINENT HISTORY

- no known gastrointestinal complaints before admission.
- native of Virginia and had no significant travel history.
- Worked in restaurant industry
- Father was in the military, formerly stationed in Asia.
- no pets and no reported sexual contact with males.
- drank bottled and municipal water but occasionally also drank water from a family well.
- HIV(-) and no history of fever, receiving corticosteroids or other immunosuppressant medications, including this hospitalization.

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CASE #1: DIAGNOSTIC WORK-UP

- Evaluation for cryptogenic stroke was unrevealing
- Infectious disease work-up
 - Chest X-ray: negative
 - Blood culture: negative
 - Stool:
 - *Clostridioides difficile* PCR: not detected in the stool by polymerase chain reaction (PCR), but a...
 - FilmArray GI panel (BioFire Diagnostics, UT): (+) *Entamoeba histolytica* (X 2), neg. for all other viral, bacterial pathogens
 - Ova & Parasites for microscopy X 2: negative

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CASE #1: TREATMENT & CLINICAL COURSE

- Treated for invasive amebiasis:
 - metronidazole 500 mg three times daily for 10 days followed by
 - luminal agent paromomycin 1,000 mg three times daily (35mg/kg/day) for an additional 7 days.
- His bloody diarrhea, fever, and leukocytosis improved with treatment.

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AMEBIASIS REFRESHER

Entamoeba histolytica: Category B Biodefense agent, low infectious dose, chlorine resistance, environmental stability

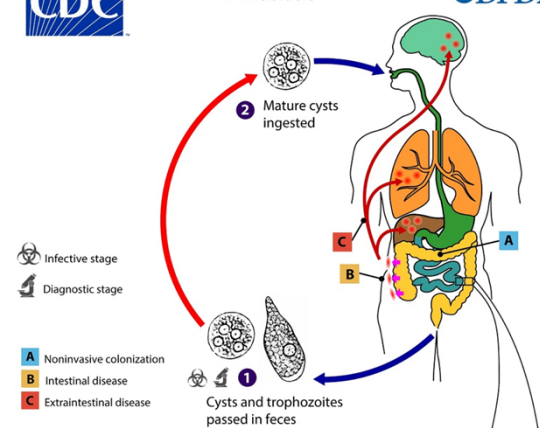
- Globally, millions of people are infected making amebic colitis a leading cause of diarrhea
 - ~55 000 deaths each year
- Amebiasis in the US is relatively rare and mainly seen in migrants and returning travelers
 - 14/1000 returning travelers seeking care with GI complaints
 - MSM is an increasingly recognized population at risk
- Clinical presentation is rarely severe, but...
 - Only 10-20% of people develop symptoms
 - Symptoms usually occur within weeks, but may develop years after infection (hepatic liver abscess)
 - Presentation may be acute or more gradual, present similarly to inflammatory bowel disease (IBD).
 - Can be indistinguishable from IBD even by imaging, inflammatory markers, or endoscopy

Life Cycle



Amebiasis

DPDx



Debbie-Ann T Shirley et al, *Open Forum Infectious Diseases*, 2018

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CASE #1: LEARNING POINTS

- History important, but...
 - In industrialized countries, most cases of amebiasis are imported, occurring primarily in the returning travelers or immigrants from endemic countries
 - Close contact with those from high endemic regions is also risk factor (?? Coworkers)
 - Invasive disease can develop even 20 years or more after exposure (?? Father)
 - Steroids can often unmask cryptic infections (but no steroids in this case)
- Given the potential case-fatality of ameba-associated severe colitis (40-89%), early diagnosis and treatment is key
- Sensitive, broad-coverage, PCR diagnostics are a valuable tool

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CASE #1: SUMMARY OF DIAGNOSTIC METHODS TO DETECT AMEBIASIS

Method	Sens (%)	Spec (%)	Attributes	Limitations
Stool microscopy	< 60	< 50	<ul style="list-style-type: none"> - Widely available - Other stool parasites may be visualized - Minimal equip./reagents 	<ul style="list-style-type: none"> - Poor sensitivity - Does not differentiate species - Skilled observer required - Needs multiple stools
Stool antigen detection	< 88	> 80	<ul style="list-style-type: none"> - Simple, rapid, easy - Some kits are multi-pathogen 	<ul style="list-style-type: none"> - Sensitivity may be reduced in non-endemic settings - Requires fresh stool
Stool PCR	> 92	> 89	<ul style="list-style-type: none"> - Preferred test, high sens/spec - Multiplex panels detect multiple etiol. - Can also test abscess fluid 	<ul style="list-style-type: none"> - More expensive - Requires specialized equipment, reagents, technicians
Serology	92	90	<ul style="list-style-type: none"> - Useful adjunct to stool studies, particularly in disseminated infections 	<ul style="list-style-type: none"> - Remains positive for years - May need to repeat if initial neg.

Madden GR et al. Am J Trop Med Hyg 2019

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CASE #2: THE FARMER FROM OKLAHOMA

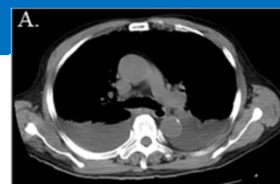
- A 67-year-old male presents to the Emergency Department after a 7 day history of severe fatigue, fever and chills, right lower abdominal pain, and mild diarrhea.
- His medical history includes hypertension and type 2 diabetes mellitus, well controlled on medications. On admission, his vital signs and physical exam were:
 - BP 128/53, HR 110, RR 16, SpO2 96% (room air) and temperature of 100.9 F
 - Auscultation revealed clear respiratory sounds. He exhibited right lower abdominal tenderness.
- His occupation is a farmer who lives in northeastern Oklahoma near the Lake of the Cherokees
- The patient owns the farm, and his habits included daily farm labor, followed by walks with his pet dog, Fido, around the farm.



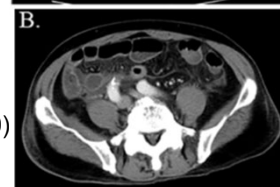
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CASE #2 DIAGNOSTIC WORK-UP

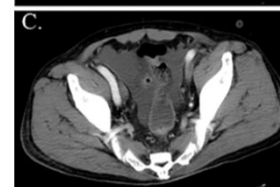
- A laboratory analysis revealed:
 - WBC 7600 cells/mL (NML 6-17K)
 - (N: 65.4%, L: 28.4%, E: 0.0%, M: 6.6%)
 - ESR 59 mm/h (NML <20), CRP 12.99 mg/dL (NML <8.2)
 - Chemistries:
 - glutamate oxaloacetate transaminase, 88 IU/L; (NML<50)
 - lactate dehydrogenase, 591 IU/L; (NML 135-214)
 - Total bilirubin, 1.5 mg/dL; (NML <1.2)
 - creatinine phosphokinase, 559 IU/L. (NML 15-105)
 - Three sets of blood cultures yielded negative results.



Bilateral pleural effusions



Inflammation of the ascending colon



Ascites

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CASE #2: INITIAL DIAGNOSIS AND TREATMENT

- Admitted to the hospital given complicated picture with presumptive diagnosis of bacterial diverticulitis of the ascending colon
- Parenteral antibiotic therapy with cefoperazone/sulbactam was initiated.
- However, his symptoms and blood tests had not improved 7 days after admission, and further deterioration of the bilateral pleural effusions and ascites were observed
- Your curious intern that started 2 weeks ago says,

"I'm not sure what's going on, but..."



Diverticulitis: An Update From the Age Old Paradigm

Hawkins AT et al. Curr Probl Surg. 2020

"..sigmoid colon involvement is considered the most common site of colonic diverticulitis in Western countries, [however]..in Asian countries, right-sided diverticulitis outnumbers the left."

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DOOGIE HOWSER, MD..."I THINK IT THIS COULD BE Q-FEVER..."

- Serological tests for Rickettsia group, Ehrlichiosis, tularemia, and Q fever were submitted.
- Doxycycline (200 mg/day) was initiated, and his clinical symptoms, blood test parameters, pleural fluid, and ascites rapidly improved.
- He received 14-day doxycycline treatment and was discharged 25 days after admission.
- Of these, a rapid slide agglutination test for *Francisella tularensis* was elevated by 320 (cutoff value: <40).
- A microhemagglutination test using *F. tularensis* polysaccharide yielded a result of 1280 (cut off value: <40), and a micro-agglutination test was 2560x (cut off value: <160).
 - These serological results were sufficient to diagnose a probable case of *F. tularensis* infection after a single round of testing (Brouqui et al., 2004; Sato et al., 1990).
- As the patient did not exhibit local ulcer formation, lymph node swelling, pneumonic infiltration, or ophthalmic and/or oropharyngeal lesions, he was diagnosed with typhoidal tularemia.

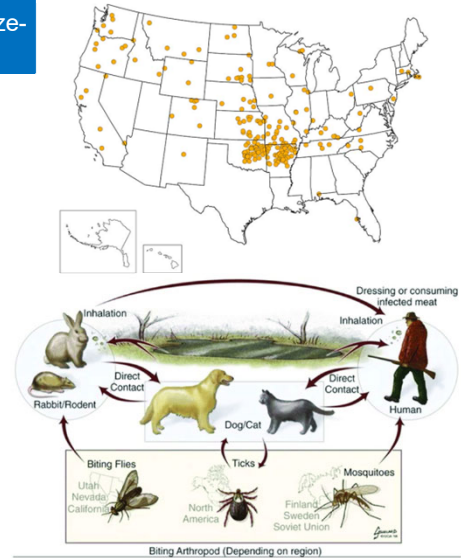
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CASE #2: TULAREMIA REFRESHER

Francisella tularensis: Category A agent due to potential for aerosolization, environmental contamination, fatal outcomes (respiratory)

- First reported in the United States (“Merica bacteria”)
- About 200 cases are diagnosed in the US each year, but on the rise over the last decade
- People can become infected in several ways, including:
 - Tick and deer fly bites
 - Skin contact with infected animals
 - Drinking contaminated water
 - Inhaling contaminated aerosols or agricultural and landscaping dust
- **Disease presentation varies depending how the person was infected.**
- Tularemia can be life-threatening, but most infections can be treated successfully with antibiotics.

Map of Reported Cases – US 2018
(<https://www.cdc.gov/tularemia/index.html>)



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TULAREMIA DIAGNOSIS: positive serologic tests should be interpreted in the context of a compatible clinical illness and exposure.

Confirmatory

- Isolation of *F. tularensis* from a clinical specimen (e.g. swabs or scrapings of ulcers, lymph node aspirates or biopsies, pharyngeal swabs, pleural fluid)
- Blood cultures may often be negative. Laboratory should be alerted if *F. tularensis* is suspected so cultures can be incubated for extended periods
 - Bug is slow-growing.
- Seroconversion from negative to positive IgM and/or IgG antibodies in paired sera.
 - the first serum sample would be collected during the acute phase of illness (within 1st week)
 - the second serum sample collected 2–3 weeks later.

Supportive

- Detection of *F. tularensis* in a clinical specimen by direct immunofluorescence assay (DFA), immunohistochemical staining, or polymerase chain reaction (PCR) assay.
- Detection of antibodies to *F. tularensis* through a single serologic test.
 - Ideally, serum would be collected at least 14 days after illness onset to ensure sufficient time for development and detection of an antibody response.

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Open Forum Infectious Diseases EDITOR'S CHOICE

Variation in Tularemia Clinical Manifestations—Arkansas, 2009–2013

Volume 4, Issue 1
Winter 2017

Laura K. Lester Rothfeldt, Richard F. Jacobs, J. Gary Wheeler, Susan Weinstein, Dirk T. Haselow

- Case series of all reportable suspected tularemia cases to the Arkansas Department of Health
- Standardized case report form completed based on interview and medical record reviews.
- Case Definition: Council of State and Territorial Epidemiologists
- Mean age: 47 years, predominantly male (67%)
- Typhoidal presentation most common overall, and 58% in age over 65
- Lymphadenopathy manifestations less common in this study

Manifestation of Tularemia at Initial Presentation (N=134)
(adapted from Table 1)

Manifestation	Percentage
Typhoidal	58%
Ulceroglandular	~15%
Glandular	~10%
Pneumonic	~5%
Intestinal	~5%
Oculoglandular	~5%
Oropharyngeal	~5%

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CASE #3: THE TUSCANY TROTS

A 59-year-old female whose only relevant history was primary hypothyroidism was referred to a gastroenterology outpatient clinic by her primary care doctor due to suffering from diarrhea for 15 days.

The patient complained of severe asthenia, headache, myalgia and 4-5 semi-solid stools without blood, mucus or pus for the past two weeks

She had no fever upon physical examination at the clinic, but said she felt cold (she had a fever of 38.5 °C for the first 3 days after the onset of symptoms).

She had traveled to Tuscany in the summer about a month prior to symptom onset.

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CASE #3: FURTHER WORK-UP

A comprehensive stool culture was done with no relevant findings, and also an ileocolonoscopy was performed with no relevant gross findings, although biopsies showed mild nonspecific inflammation.

The following lab test results were obtained:

- negative celiac serologies
 - normal thyroid hormones
- An expanded history was taken to ask about travel to Italy:
 - She spent time in the Tuscany country-side and often went on hikes
 - She remembers having a tick one evening after returning from an excursion but didn't develop any rash that she was aware of.
 - She did reveal that she had a wound on her upper thigh that is new and hasn't gone away which she thought was an ingrown infected hair or something

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CASE #3: CONFIRMATION AND TREATMENT

- IgG/IgM anti-bodies for *Rickettsia typhi* (scrub typhus), *Rickettsia prowazekii* (epidemic typhus), and *Rickettsia rickettsii* (Rocky Mountain Spotted Fever)
 - RMSF (IgG) came back as 1:256 (positive)
 - RMSF (IgM) came back as 1:160 (positive)
- The patient lives in Washington State and there is no Rocky Mountain Spotted Fever in Italy
- Cross-reactivity within the spotted fever group precludes the speciation of the infecting rickettsia species.
- Antibody is variably absent for 1 to 2 weeks after onset of symptoms and an initial negative titer should not be used to exclude the diagnosis of rickettsial disease.
- Treatment was started with doxycycline 100mg bid x 7 days and the patient symptoms improved and became afebrile after 3 days

[SFGP - Clinical: Spotted Fever Group Antibody, IgG and IgM, Serum \(mayocliniclabs.com\)](https://www.mayocliniclabs.com)

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OXFORD
ACADEMIC

Clinical Infectious Diseases

Gastrointestinal and Hepatic Manifestations
of Tickborne Diseases in the United States

2002

Syed Ali Zaidi and Carol Singer

Table 1. Gastrointestinal and hepatic manifestations of tickborne diseases.

Manifestation	Lyme disease	Ehrlichiosis	RMSF	Tularemia	Colorado tick fever	TBRF	Q fever	Babesiosis
Anorexia	+	++	+	+	+	+	+	+
Nausea	+	++	++	++	++	+++	++	+
Vomiting	+	++	++	++	++	+++	++	+
Abdominal pain	+	++	++ to +++	++	+	++	+	+
Diarrhea	+	++	++	++ to +++	+	+ to ++	++	+
Hepatomegaly	R	+ to ++	+	+ to ++	R	+	+	+
Splenomegaly	+	+ to ++	+	+ to ++	R	R to +	+	+
Jaundice	+	+++	+	+	+	+	+	+ to ++
Elevated bilirubin level	+	+++	+ to ++	+	+	+	+ to ++	++ to +++
Elevated ALT level	++	++++	++ to +++	++	+	++	++ ^a	+

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TAKE HOME LESSONS

- Travel history is important, but endemic diseases causing atypical GI presentations occur in the United States
- **Ticks are bad**
- Invasive intestinal amebiasis should be considered as a differential diagnosis at the first clinical adult presentation of IBD-like symptoms despite suggestive endoscopic findings of Crohn's like ulcers (or absence of travel history).
- In febrile patients (particularly with protracted fever) with GI symptoms and high acute-phase reactants
 - Think about the rarer infectious causes of inflammatory gastrointestinal disorders may be the goal to earlier diagnosis and appropriate empiric therapy
- Rapid culture-independent diagnostics are particularly good for chronic diarrhea where you suspect an infectious cause.
- Consult infectious disease service (they like this stuff 😊)

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THANK YOU



Case presentation inspirations:

- Tularemia: Nakamura K. Int J Infect Dis 2018
- Rickettsia: Magaz Martinez M. Gastroenterol Hepatol 2018
- Amebiasis: Madden GR. Am J Trop Med Hyg 2019

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Questions and Answers



Mark S. Riddle, MD, DrPH



Freddy Caldera, DO, MS, FACG

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