Infections without borders

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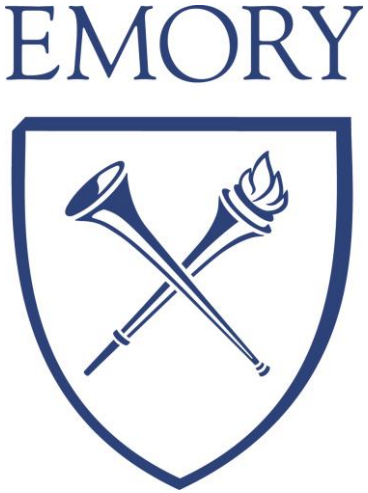


Financial Relationships

No relevant financial relationship(s) exist

- **I will not discuss off label use and/or investigational use in my presentation.**

But you need to know that:

- I am paid by The Emory Clinic
- I worked at CDC 1997-2007
- I was brought up in Mexico, thus funny accent, and worked in Mexico at the National Cancer Institute (INCan).

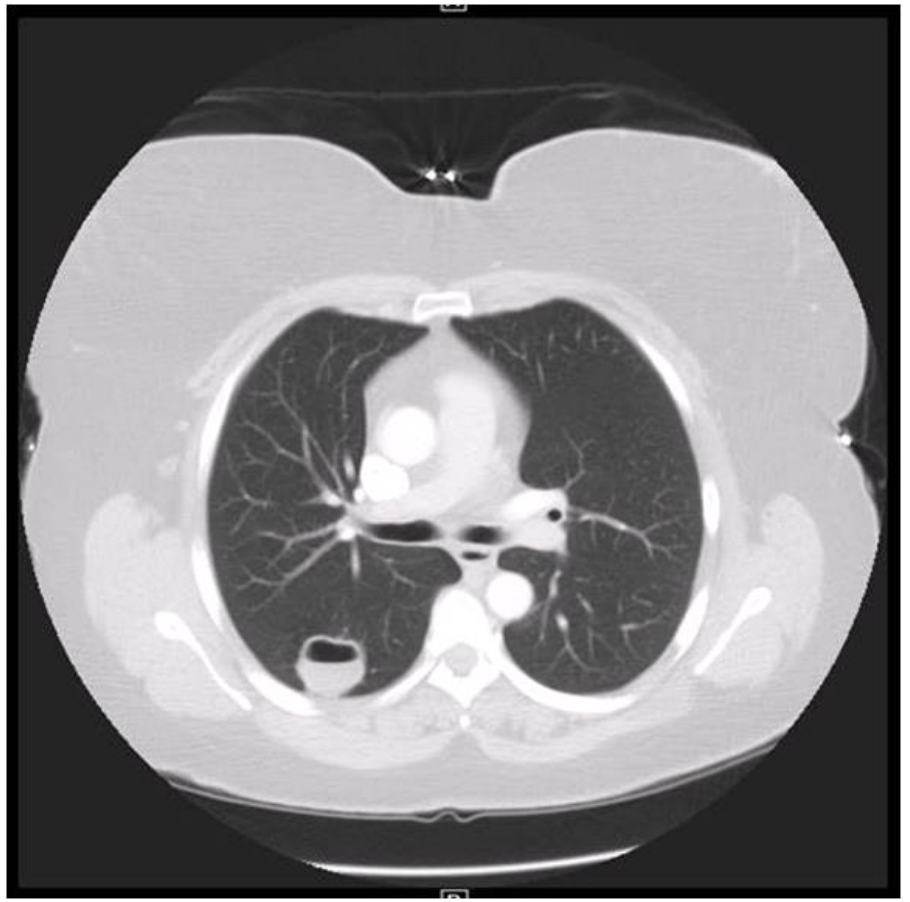
Objectives

We will use cases to:

- Explore infectious diseases in patients that have travelled or lived in other locations thus, the microorganism may not be suspected.
- Identify tests that can be used for diagnosis of the cases presented.
- Discover pitfalls in diagnoses of the cases presented.

Case 1

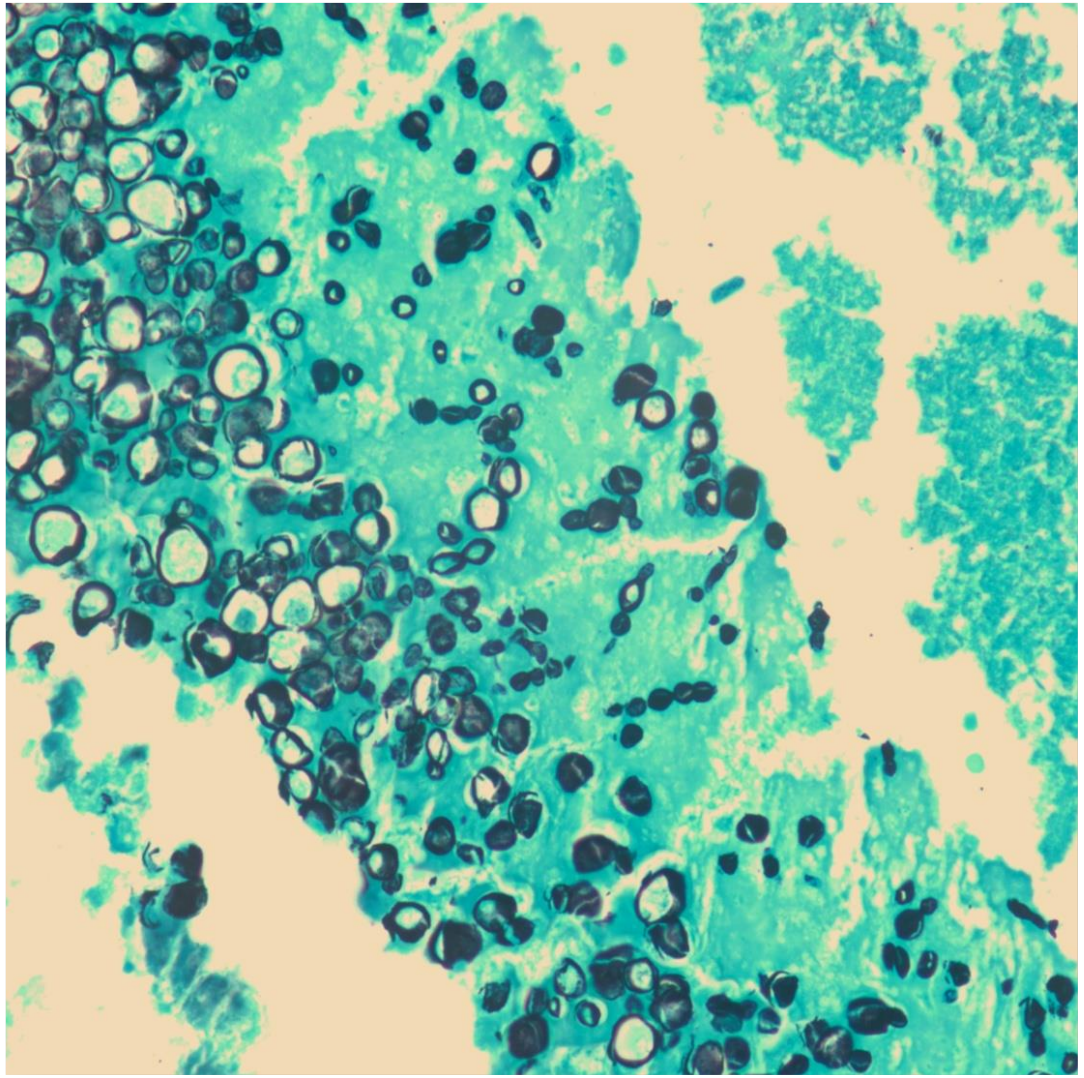
- 45 year old woman that is being worked up for severe persistent cough and shortness of breath, no fever
- She has a history of AML 7 years ago currently in remission.
- Imaging: right lung cavitary lesion
- She lived in Chihuahua, Mexico, while studying anthropology.
- She recently went to Arizona to do a train ride in Verde Canyon.

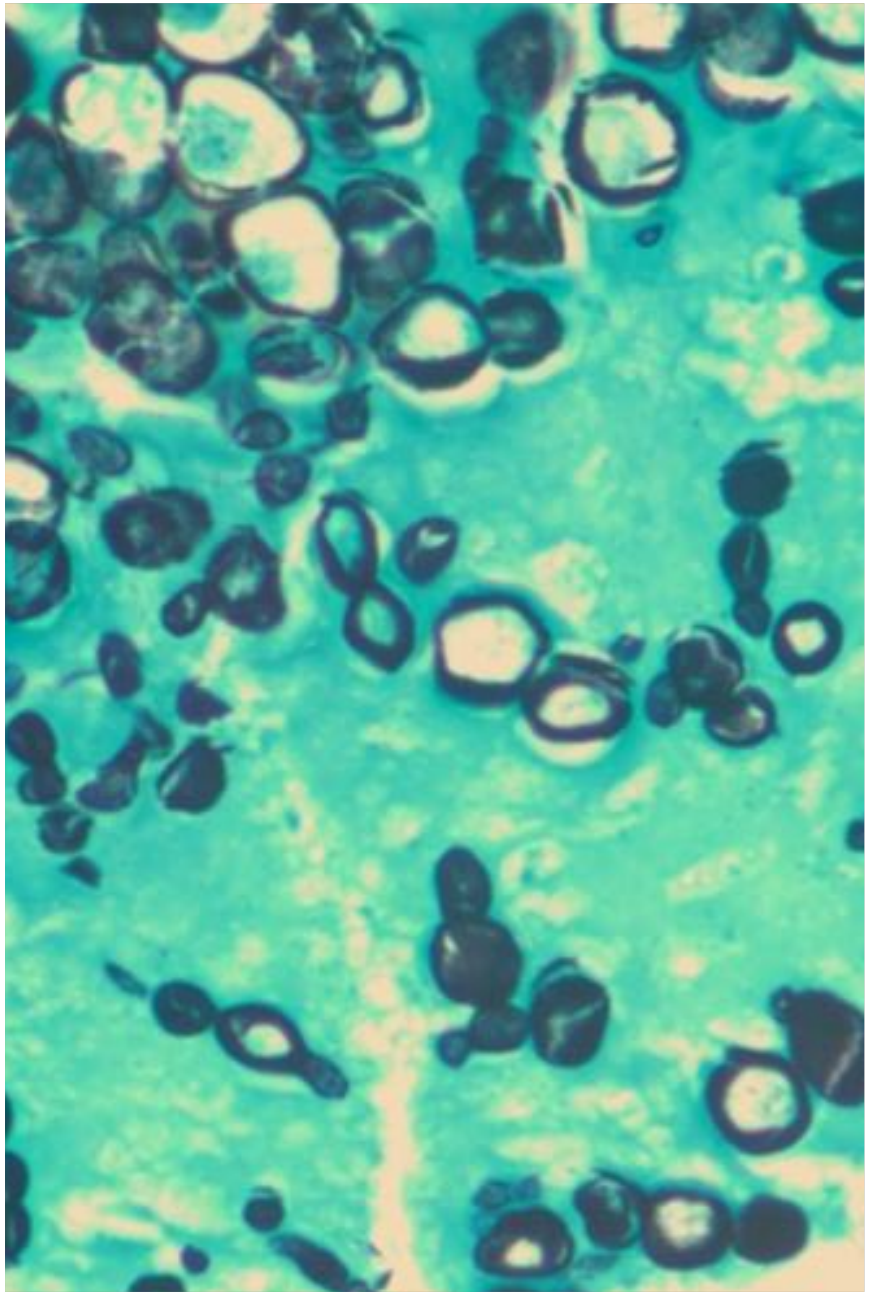


Case continues

- PPD negative, sputum PCR for Mtb negative
- Bronchoscopy with biopsies negative for neoplasia
- Wedge resection
- Operative report describes a large cavitary lesion and purulent material
- Material sent to pathology and microbiology

Resident shows me:





QUESTION: What do you think this should be called?

1. *Cryptococcus*
2. *Coccidioides*
3. *Blastomyces*
4. Broad-based budding yeasts
5. Large yeasts

Yeasts

Size
Grouping, budding
Epidemiology

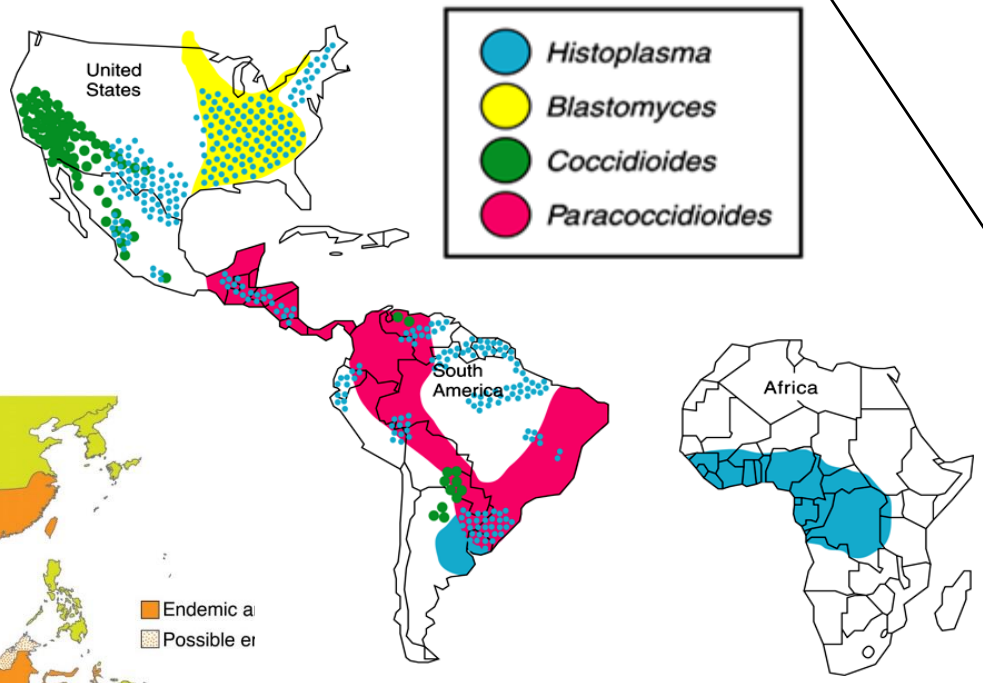
Small
(2 -10 µ)

Histoplasma
Talaromyces
Sporothrix
Emonsia
Cryptococcus
Candida glabrata
Pneumocystis

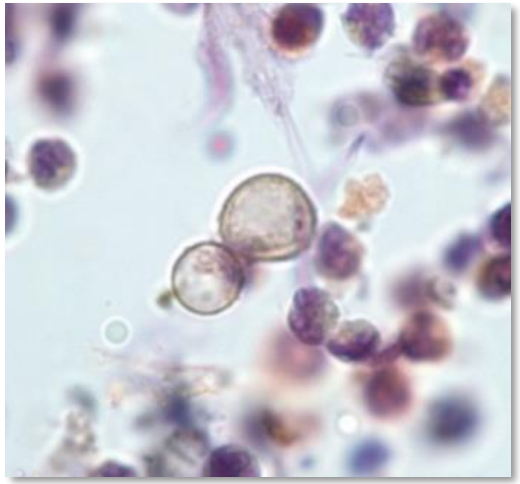
Large
(>10 µ)

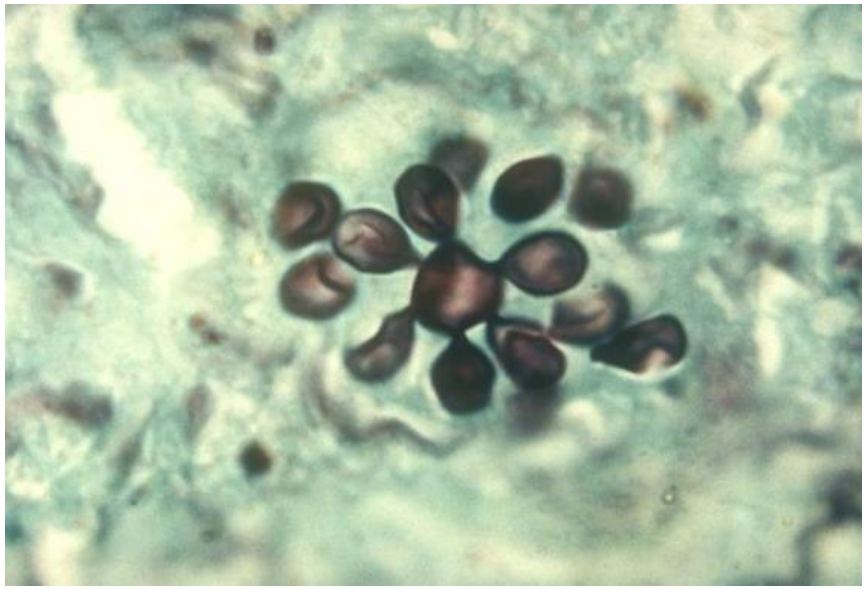
Blastomyces
Coccidioides
Paracoccidioides

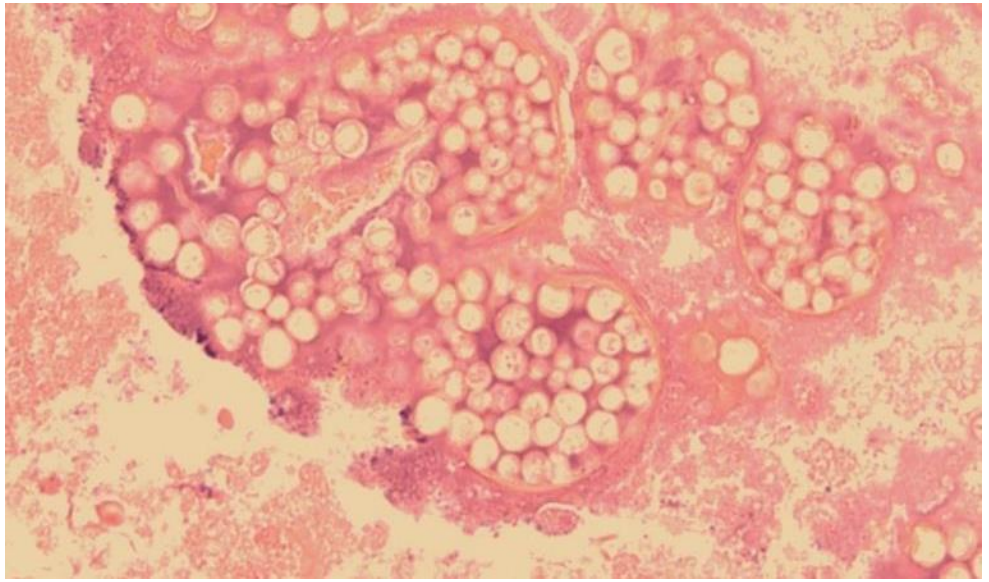
Parasites:
Toxoplasma,
Leishmania,
Trypanosome



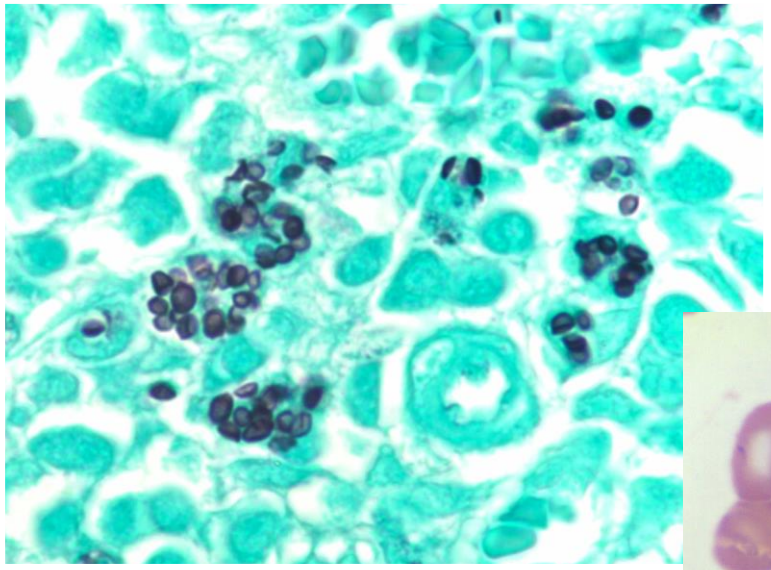
Large yeasts

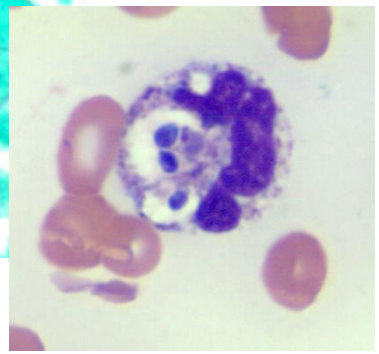


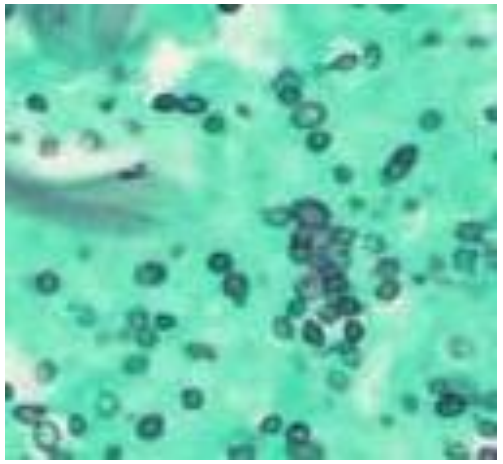


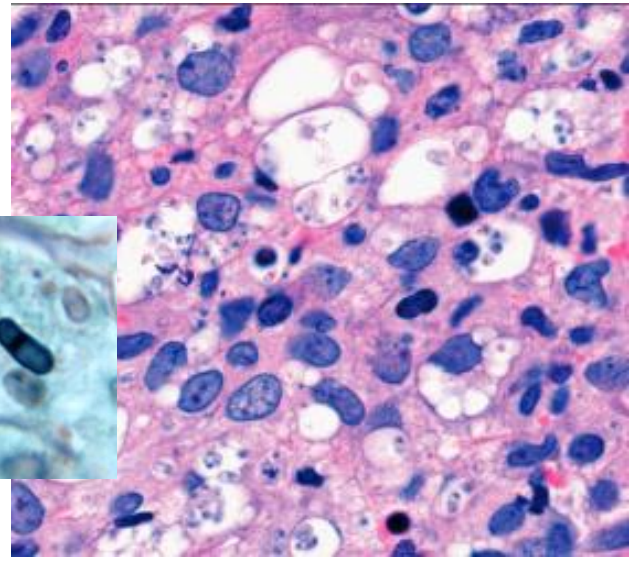


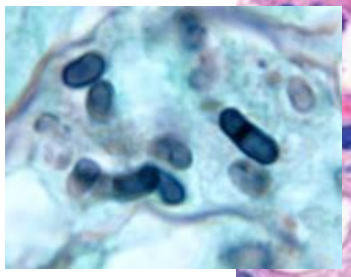
Small yeasts

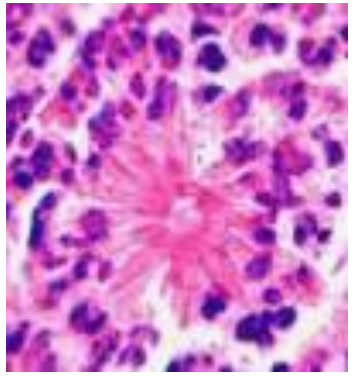


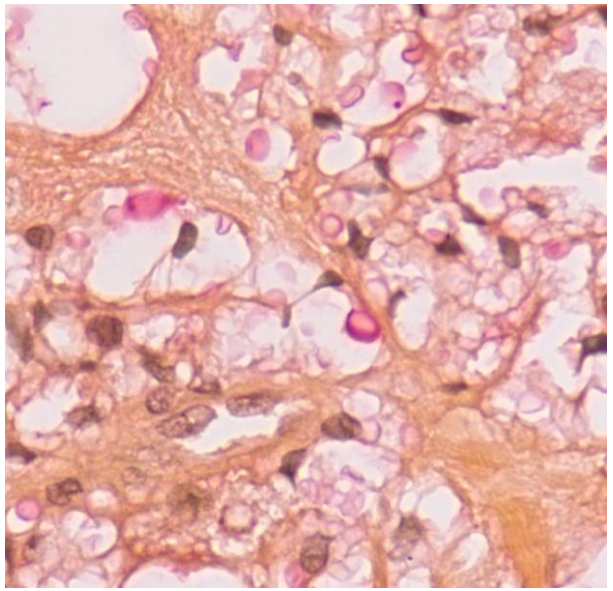












When broad-based budding yeast are seen in pathology, what have cultures shown:

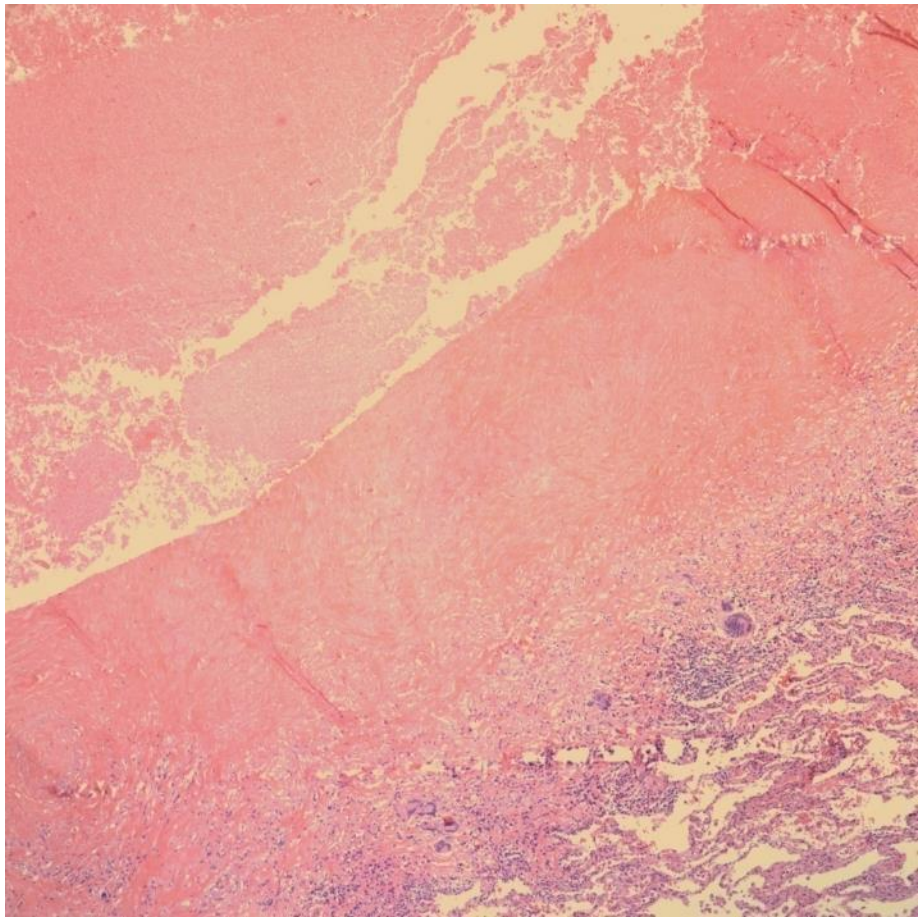
- High percent of cultures are overgrown with *Candida*.
- Retrospective study, 53 patients:
  - *Blastomyces* recovered in 67%
  - *Coccidioides immitis, Candida albicans* or *Aspergillus* from 4 (10%)
- Thus, not all broad based-budding yeasts in the 8 to 15 micron size range are *Blastomyces.*

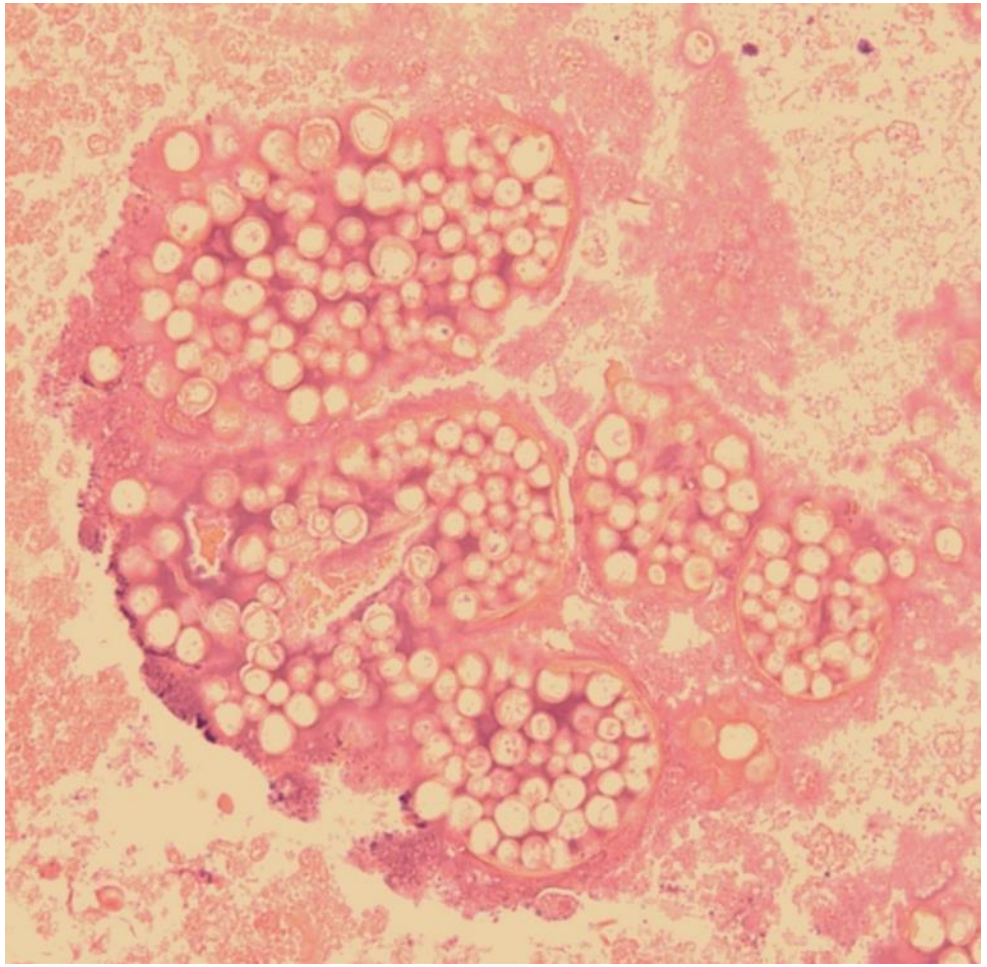
Lemos LB, et al. *Ann Diagn Pathol. 2000;*4:391-406.
Patel AJ, et al *Am J Surg Pathol. 2010;*34:256-261.

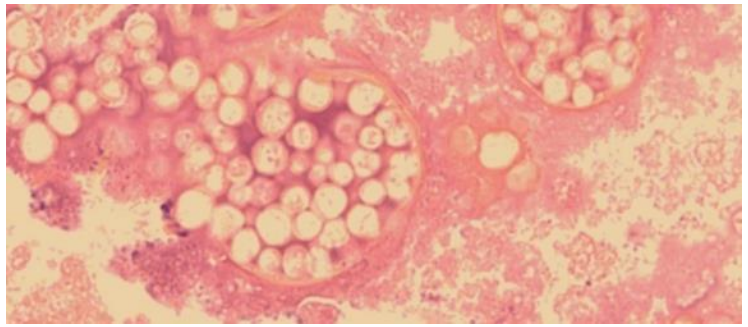
QUESTION: What should you do next?

1. See more material on the case
2. Wait for the culture results to report
3. Suggest urine antigen tests

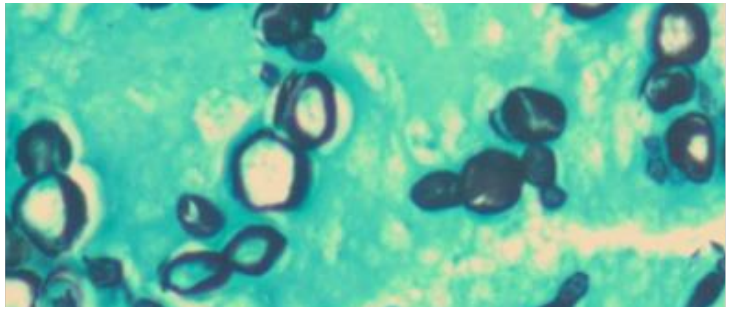
Review of more slides:







- **Description:** Spherules with multiple endospores (10 to 100µ in size).
- **Diagnosis:** Spherules with multiple endospores.
- **Comment:** The morphology is consistent with *Coccidioides* spp.
  - Differential diagnosis: *Rhinosporidium seeberi* which has sporangia with endospores but is much larger.



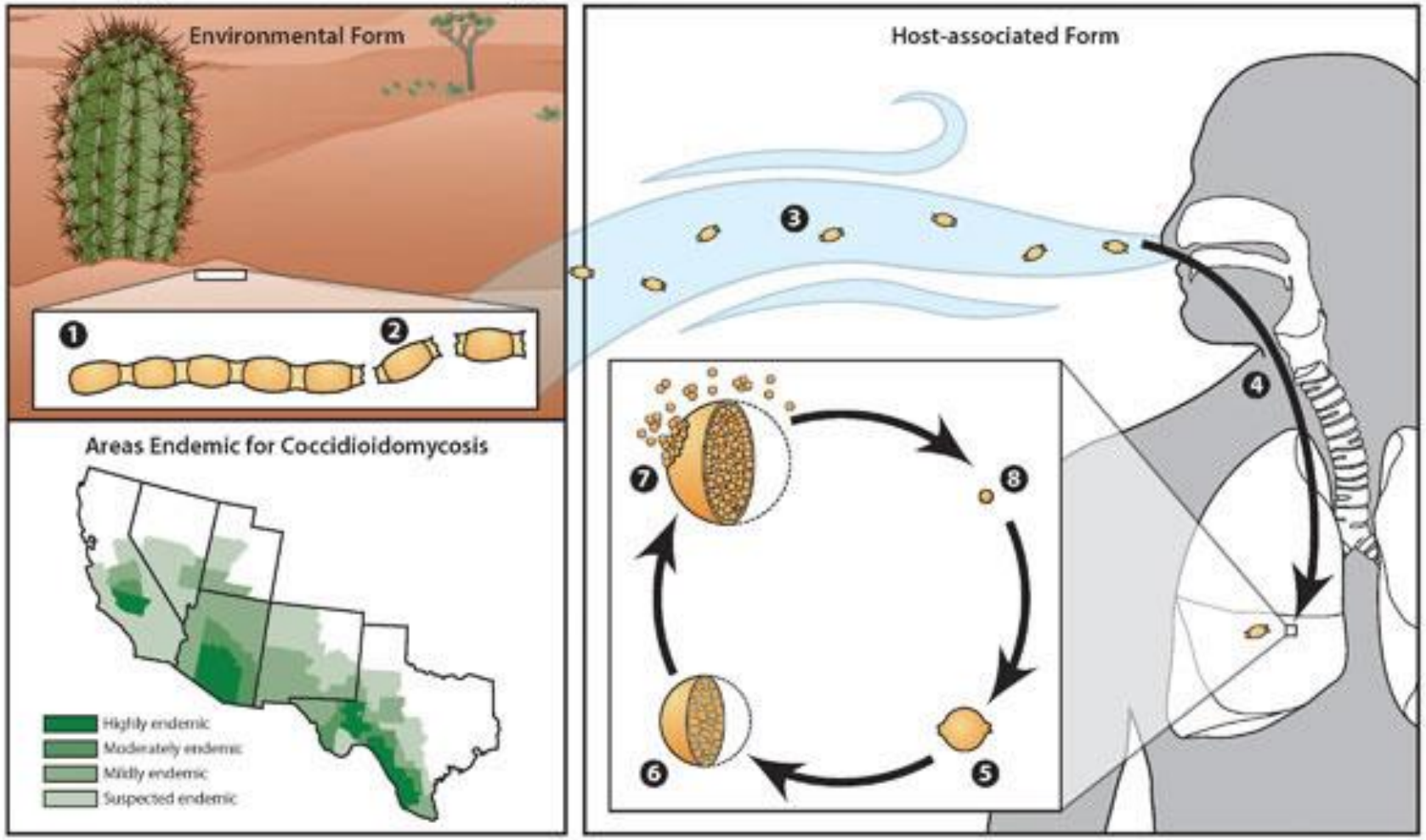
- **Description:** Yeast ranging in size from 10 to 20µ with broad-based budding.
- **Diagnosis:** Large budding yeasts
- **Comment:** The morphology is consistent with *Blastomyces* because broad based budding is noted, but other yeast can present with this morphology including *Histoplasma, Candida, Coccidiodes* and others.

Guarner J, Brandt ME. Histopathologic diagnosis of fungal infections in the 21st century. Clin Micro Rev 2011; 24:247-80

QUESTION: Which is an epidemiologic setting of coccidioidomycosis?

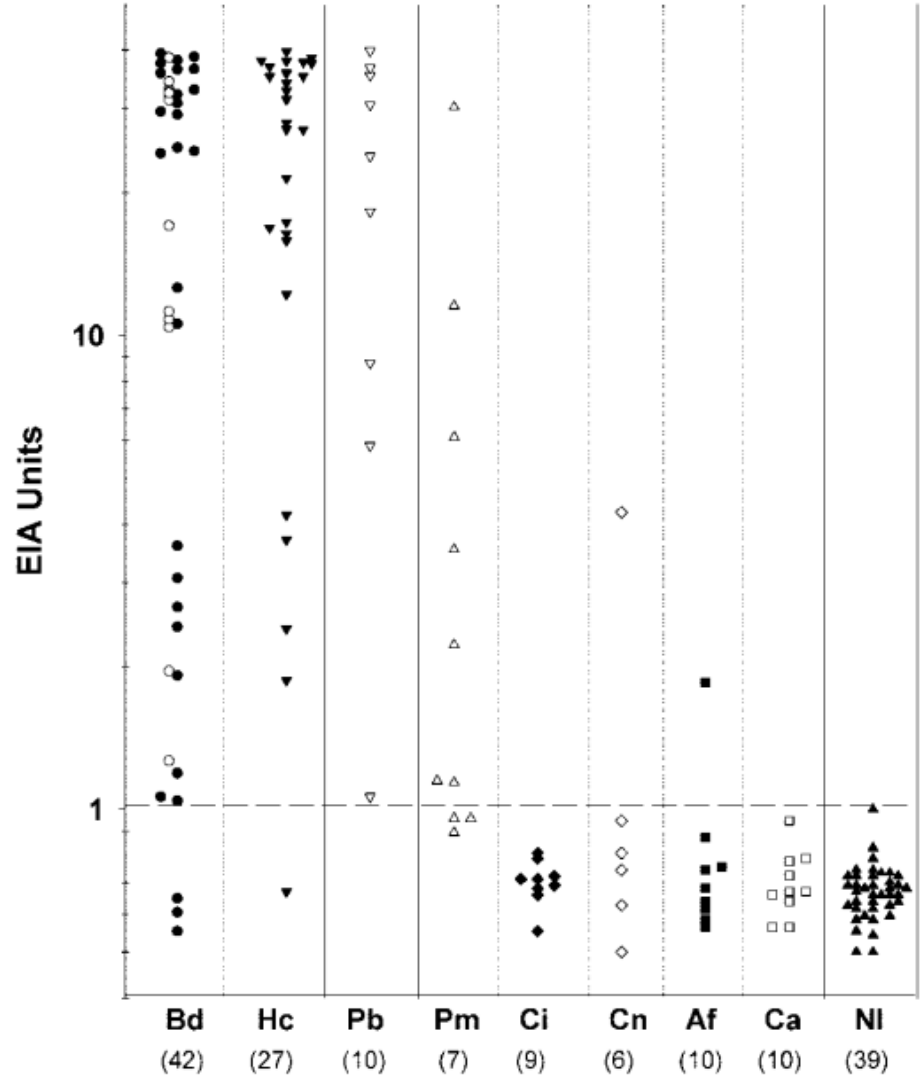
1. Having lived in Mississippi
2. Being a migrant from Vietnam
3. Travelled to South America for vacation
4. Going camping during the summer in the Colorado Rockies

Biology of Coccidioidomycosis



In the environment, *Coccioides ssp.* exists as a mold (1) with septate hyphae. The hyphae fragment into arthroconidia (2), which measure only 2-4 µm in diameter and are easily aerosolized when disturbed (3). Arthroconidia are inhaled by a susceptible host (4) and settle into the lungs. The new environment signals a morphologic change, and the arthroconidia become spherules (5). Spherules divide internally until they are filled with endospores (6). When a spherule ruptures (7) the endospores are released and disseminate within surrounding tissue. Endospores are then able to develop into new spherules (6) and repeat the cycle.

Mycology laboratory



Durkin M et al. J Clin Microbiol 2004; 42:4873
Measured *Blatomyces* antigen in urine.

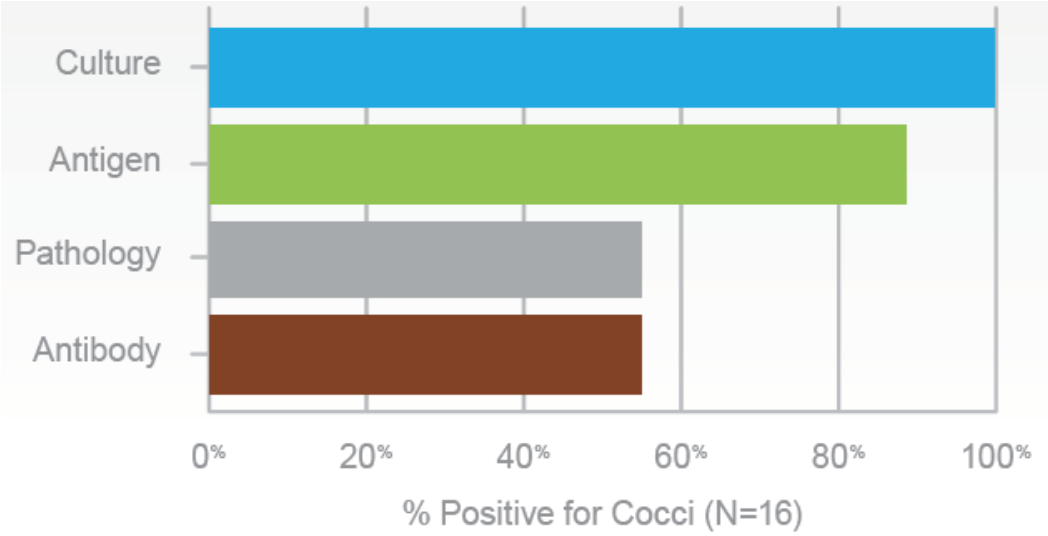
TABLE 1. Blastomyces antigen positivity blastomycosis cases and controls

Patient group	No. positive/no. tested	% positive (95% confidence interval)
Blastomycosis		
All	39/42	92.9 (80.5–98.5)
Pulmonary	14/14	
Disseminated	25/28	
Histoplasmosis	26/27	96.3 (81.0–99.9)
Paracoccidioidomycosis	10/10	100 (69.1–100.0)
Penicilliosis marneffei	7/10	70 (34.7–93.3)
Cryptococcosis		
All	2/68	2.9 (0.4–10.2)
Urine, initial cases	1/6	
Urine, additional cases	0/19	
Serum or CSF	1/43	
Aspergillosis		
All	1/88	1.1 (0.0–6.2)
Urine, initial cases	1/9	
Urine, additional cases	0/12	
Serum, additional cases	0/8	
Galactomannan positive serum	0/59	
Coccidioidomycosis	0/9	0 (0.0–33.6)
Candidiasis	0/10	0 (0.0–30.8)
Healthy volunteers	0/39	0 (0.0–9.0)

Bd, *B. dermatitidis*; Hc, *H. capsulatum*; Pb, *P. brasiliensis*; Pm, *P. marneffei*; Ci, *C. immitis*; Af, *A. fumigatus*; Ca, *C. albicans*; N1, normal controls.

Coccidioidomycosis: Alternative diagnostic methods

- IgM and IgG measured using EIA and/or immunodiffusion
  - False negative serology in up to 38% of patients with hematogenous infection and 46% of fatal cases
- Urine antigens using EIA present in 71% of patients
  - Cross-reaction in 10% of patients with other endemic mycosis



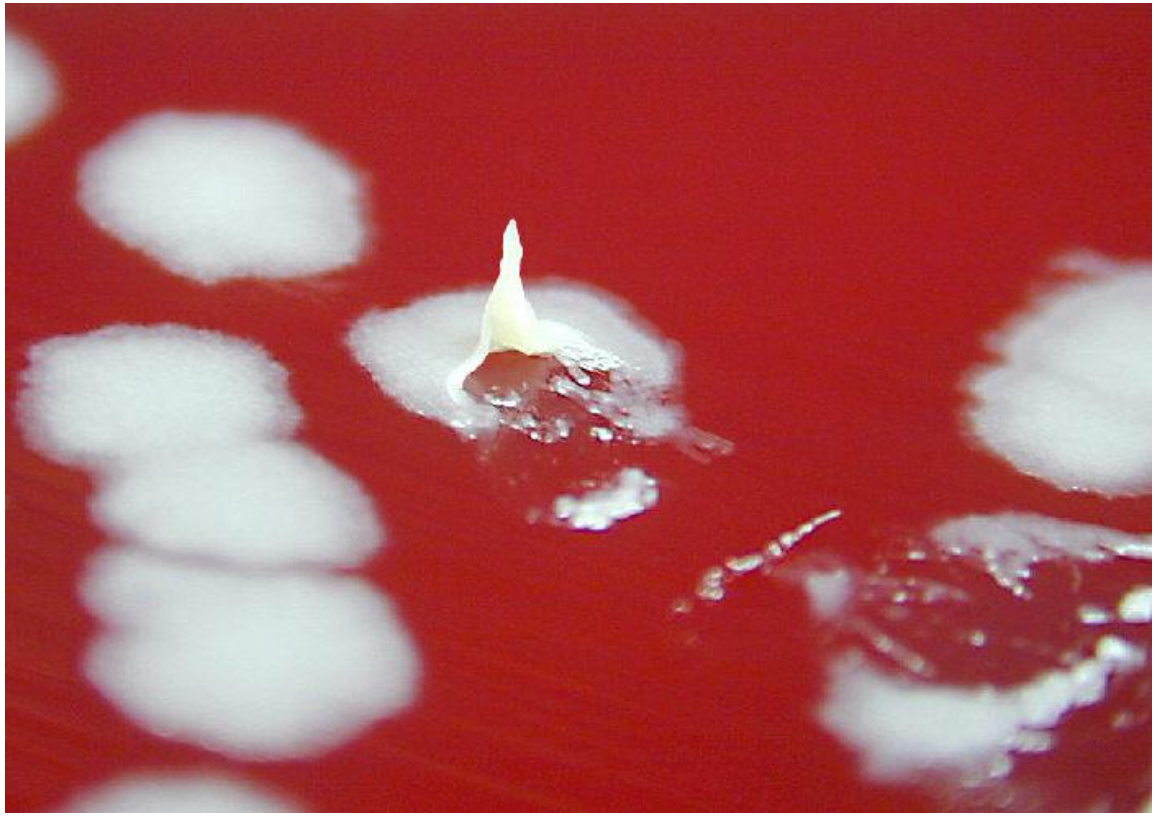
Case 2

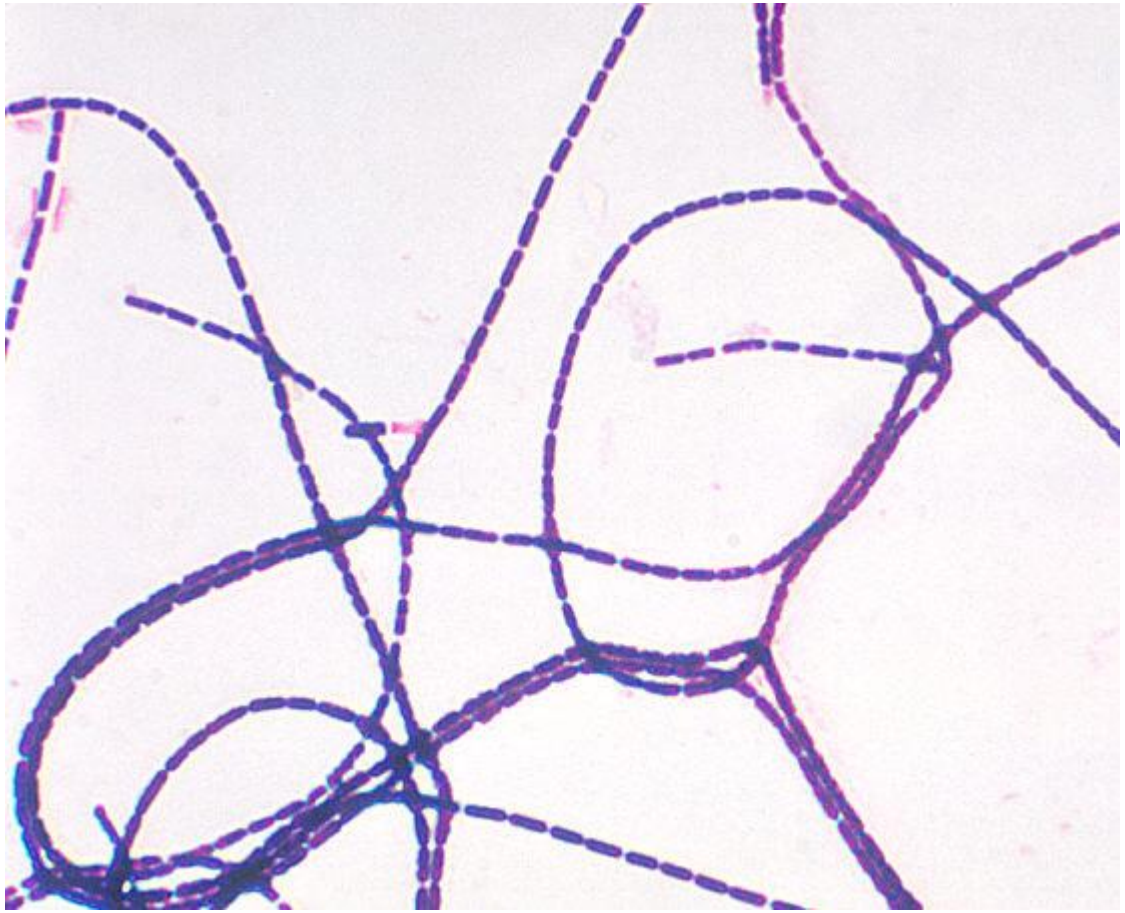
- 44-year-old male
- Presented with dyspnea, non-productive cough, pleuritic chest pain, profuse diaphoresis, and near syncopal event.
- Started symptoms 2–3 days prior to admission.
- Trip to Africa where he bought hides to make drums. He is a musician for an African dance troupe.

Case continues

- Temperature 99.7◦F, blood pressure 111/77 mm Hg, pulse 92/min, and respirations of 24/min.
- Decreased breath sounds in the left lung & end-expiratory wheezing at the base.
- Chest X Rays: cardiomegaly, left upper lobe infiltrate or atelectasis, small right lower lobe infiltrate, & bilateral pleural effusions.
- Laboratory: WBC 8.28 (63% neutrophils, 24% lymphocytes, 11% monocytes), normal hematocrit and platelets.

- Admitted to the intensive care unit, started on ceftriaxone and zithromax for presumed community acquired pneumonia.
- BacT/Alert System grew gram-positive rods

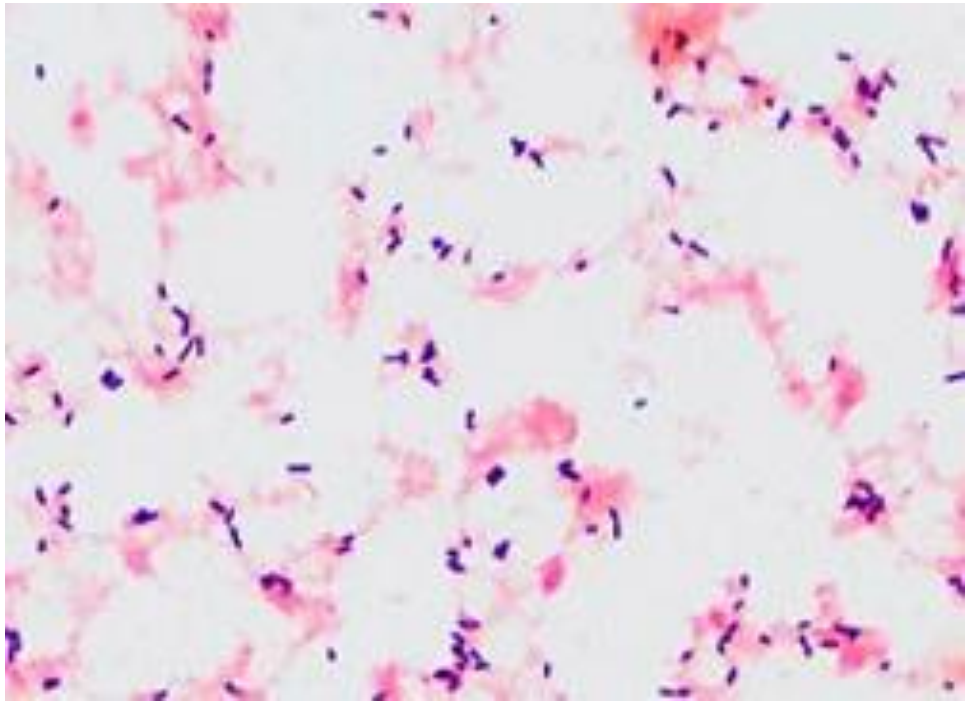




The organism has a capsule

QUESTION: Diagnosis?

1. *Listeria monocytogenes*
2. *Corynebacterium diphtheriae*
3. *Tropheryma whipplei*
4. *Bacillus anthracis*



QUESTION: Once you suspect or know you have anthrax growing, who should you contact?

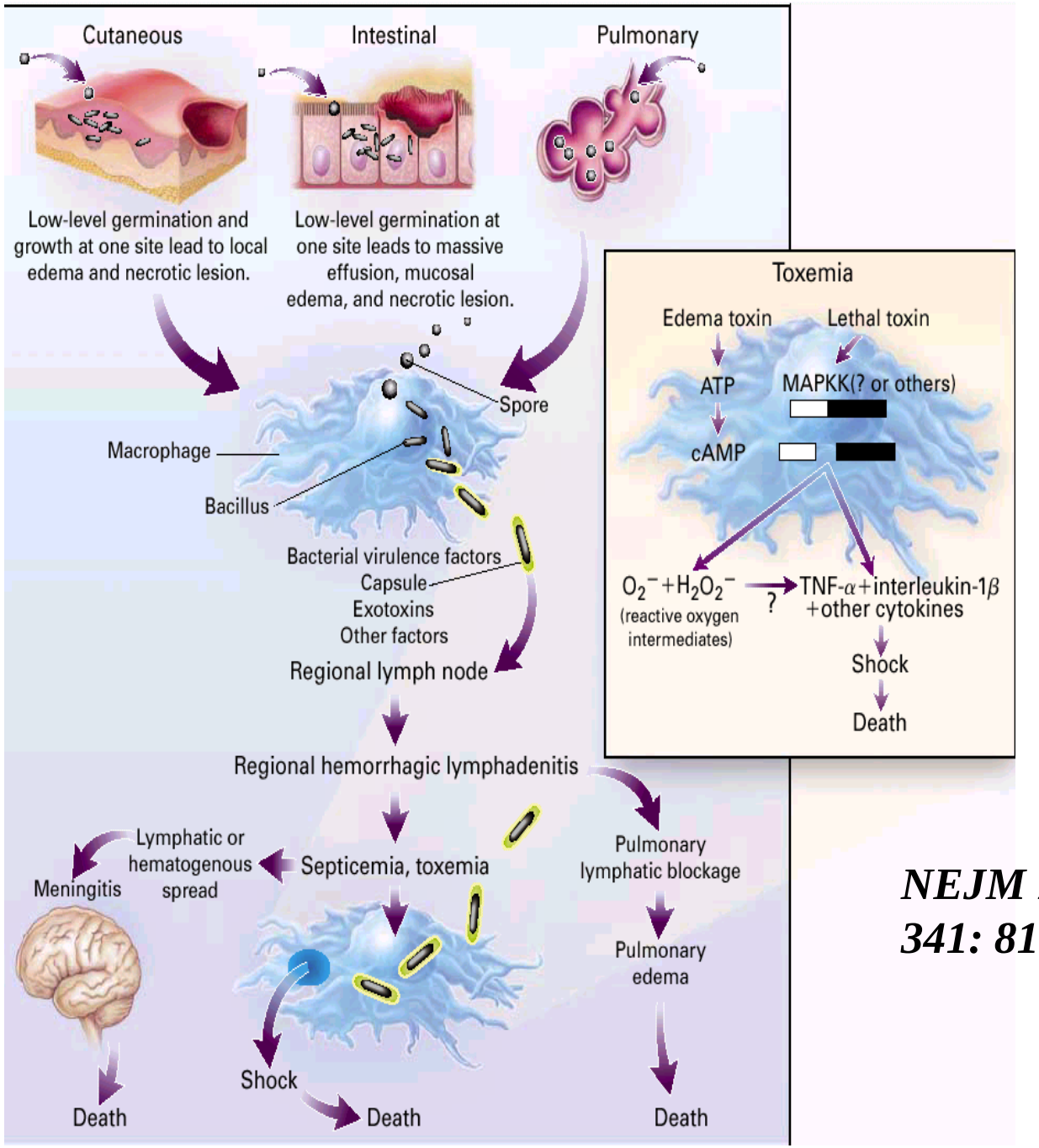
1. Centers for Disease Control and Prevention
2. Department of Defense
3. State Health
4. Local Police Department

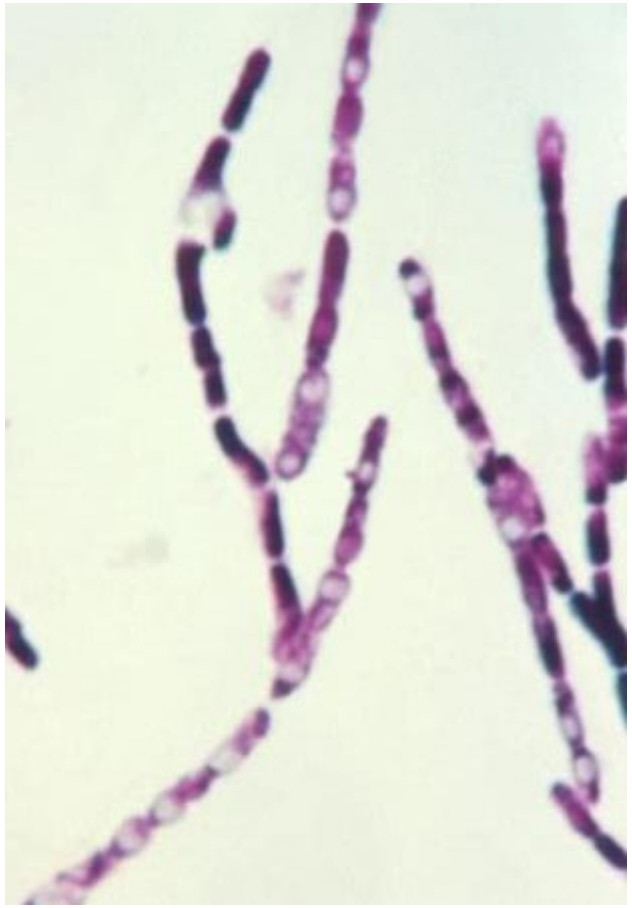
QUESTION: Which of the following is true?

1. Can work up the organism in the clinical laboratory
2. Caretakers should take respiratory precautions
3. If the patient dies we should not do an autopsy
4. An epidemiological investigation is not necessary

List of biological agents considered bioterrorism threats:

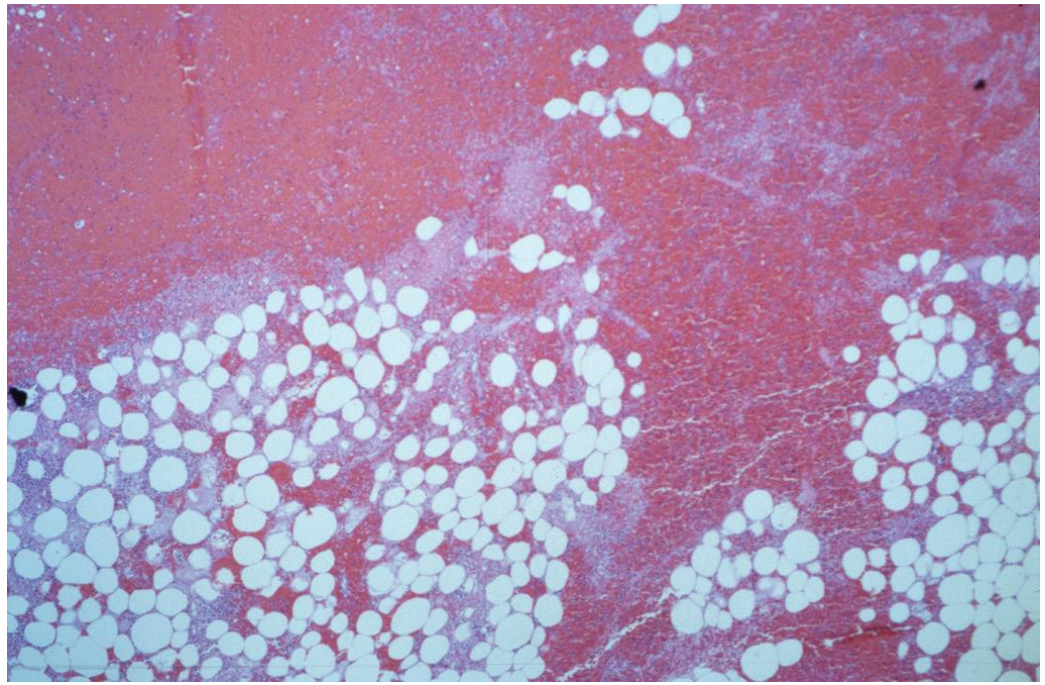
- Category A agents
  - bacteria (*Bacillus anthracis, Yersinia pestis,* and *Francisella tularensis*),
  - bacterial toxins (*Clostridim botulinum*),
  - viruses (Smallpox and organisms that can cause hemorrhagic fevers such as Ebola, Marburg, Lassa, Junin).

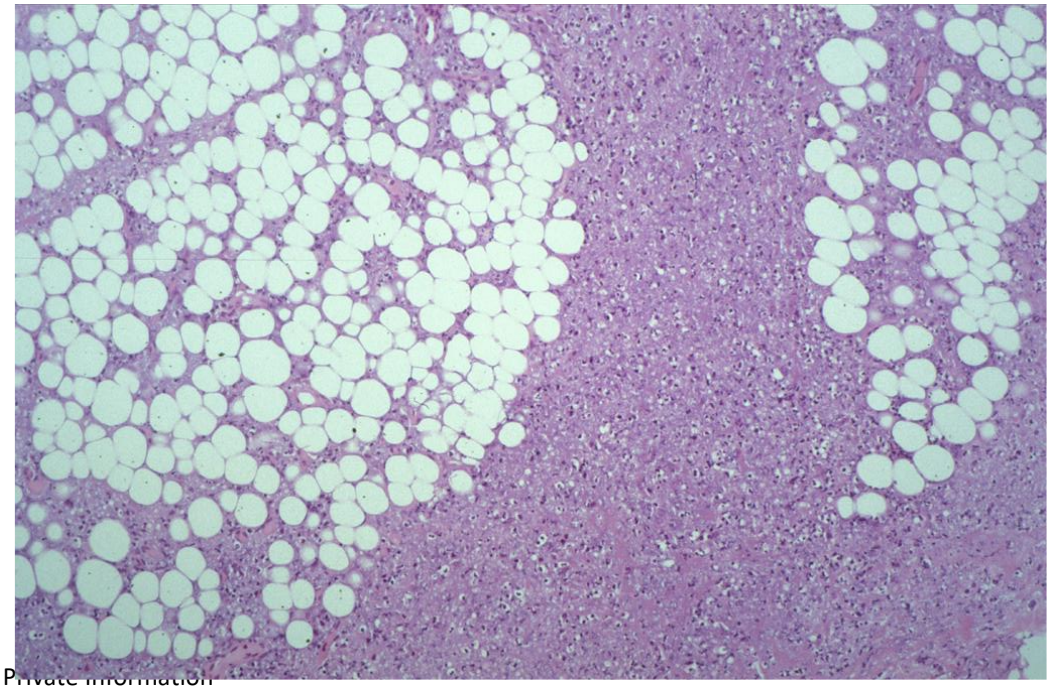


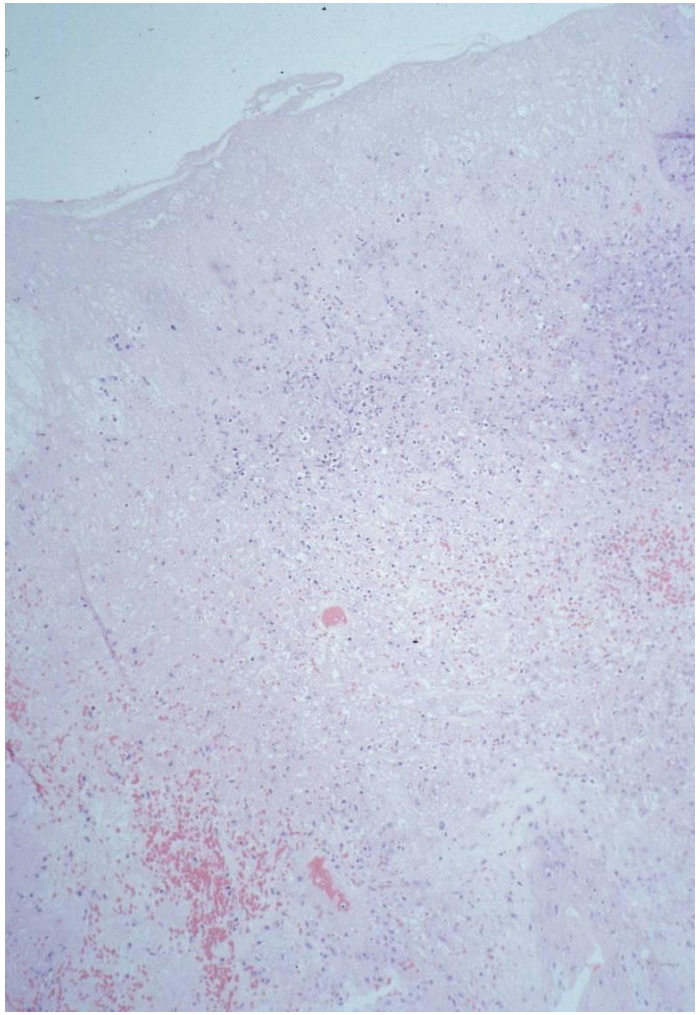


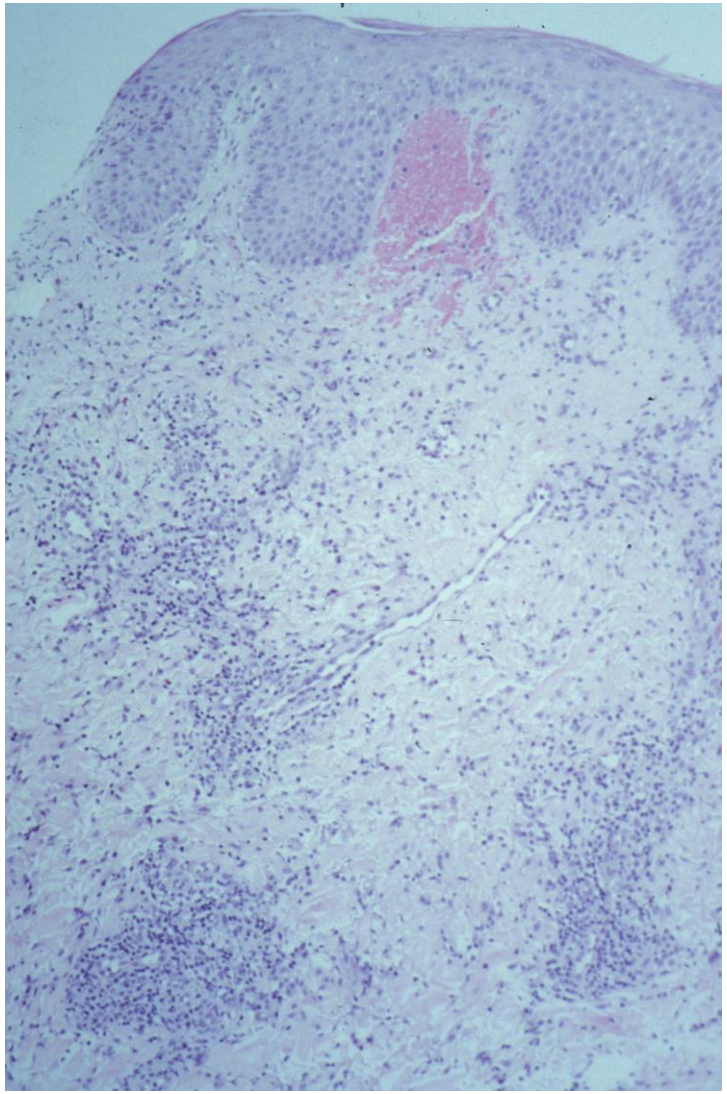
NEJM 1999; 341: 815- 826

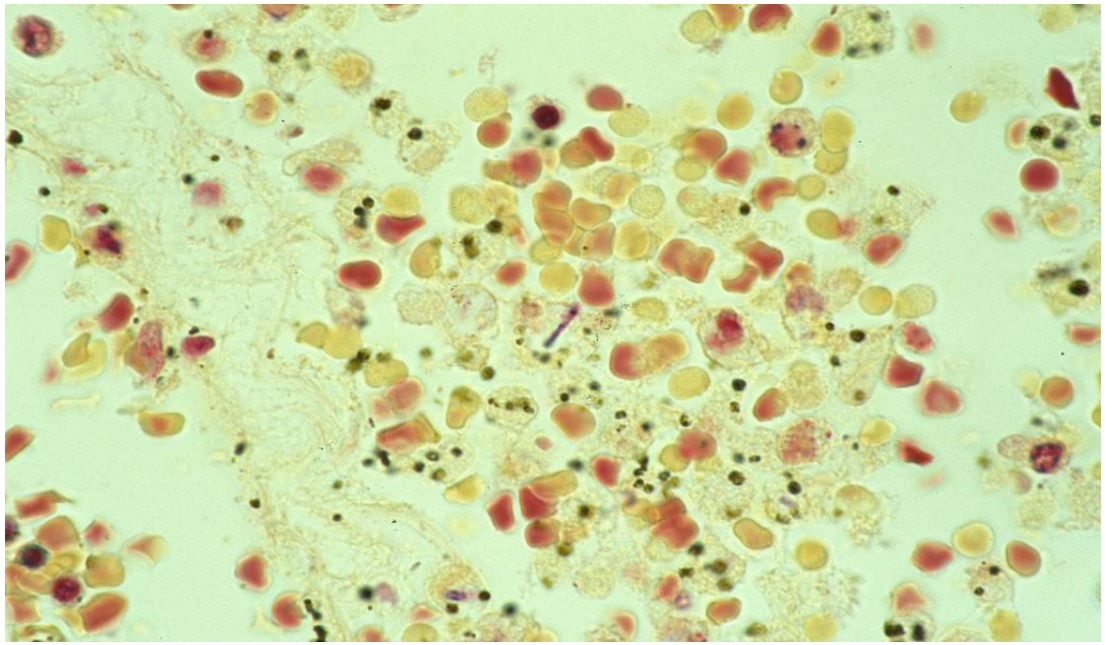
Abramova FA et al. Proc Natl Acad Scie. 1993; 90:2291

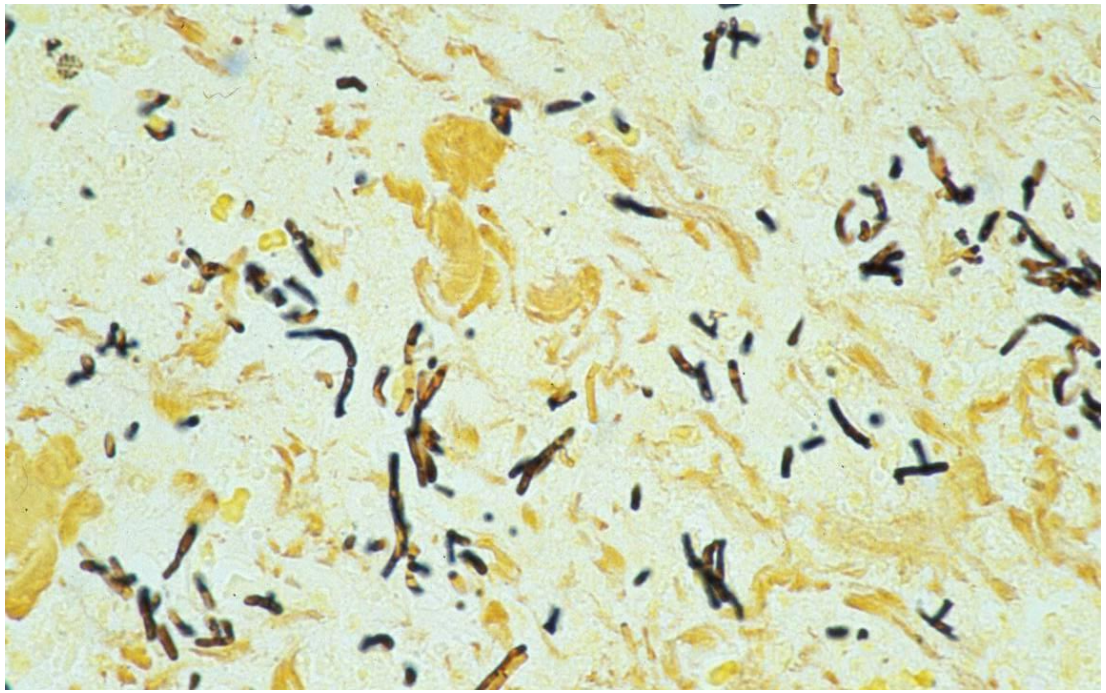


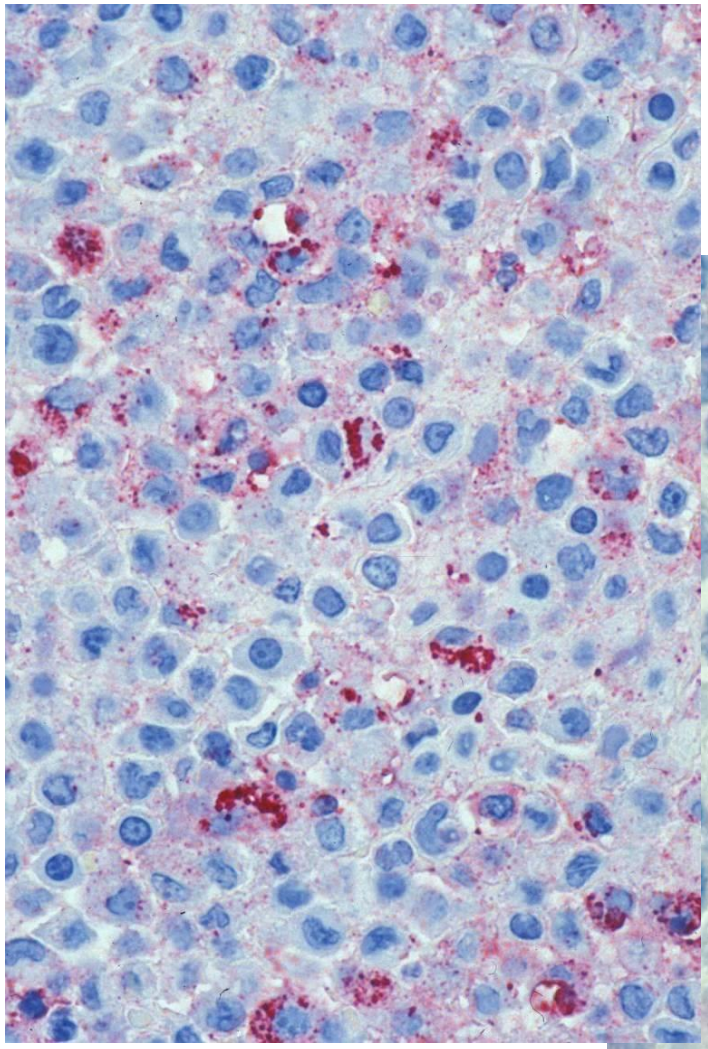


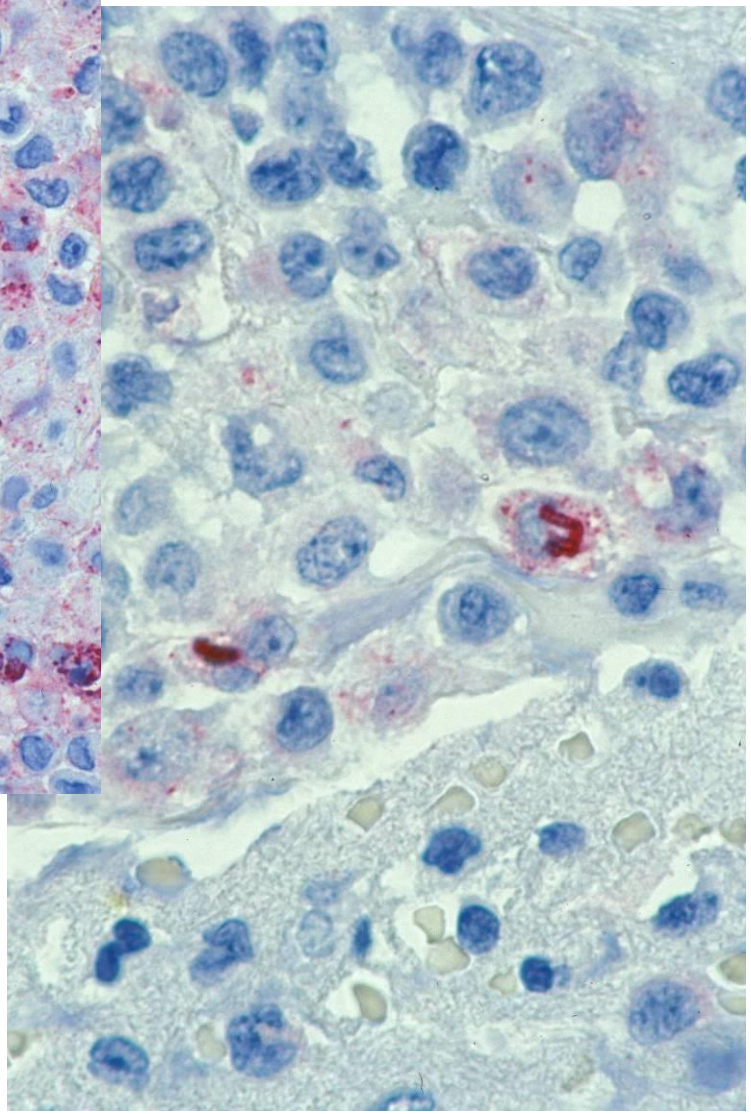








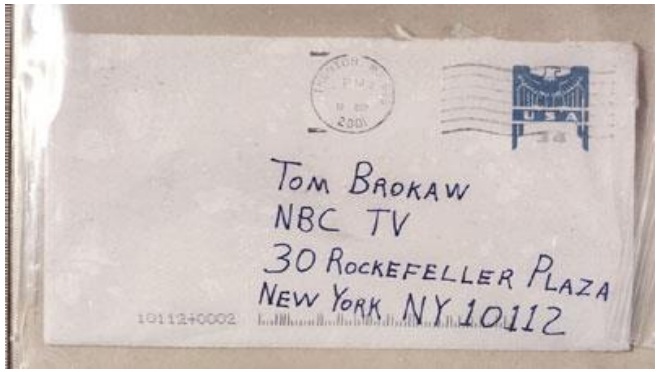


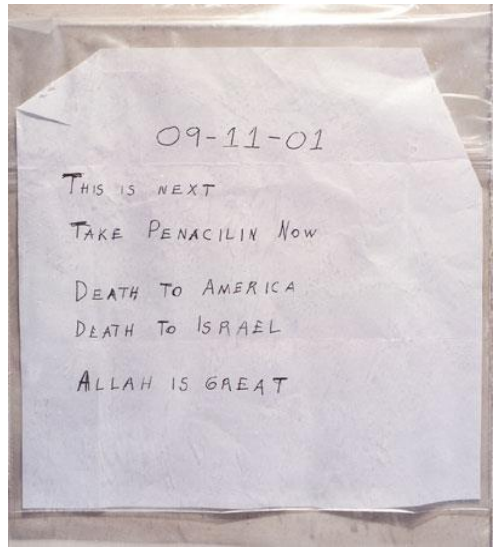


QUESTION: How do you think our patient got infected?

1. Travel to Africa
2. Drumming on hides
3. Sorting wool
4. Picking rags

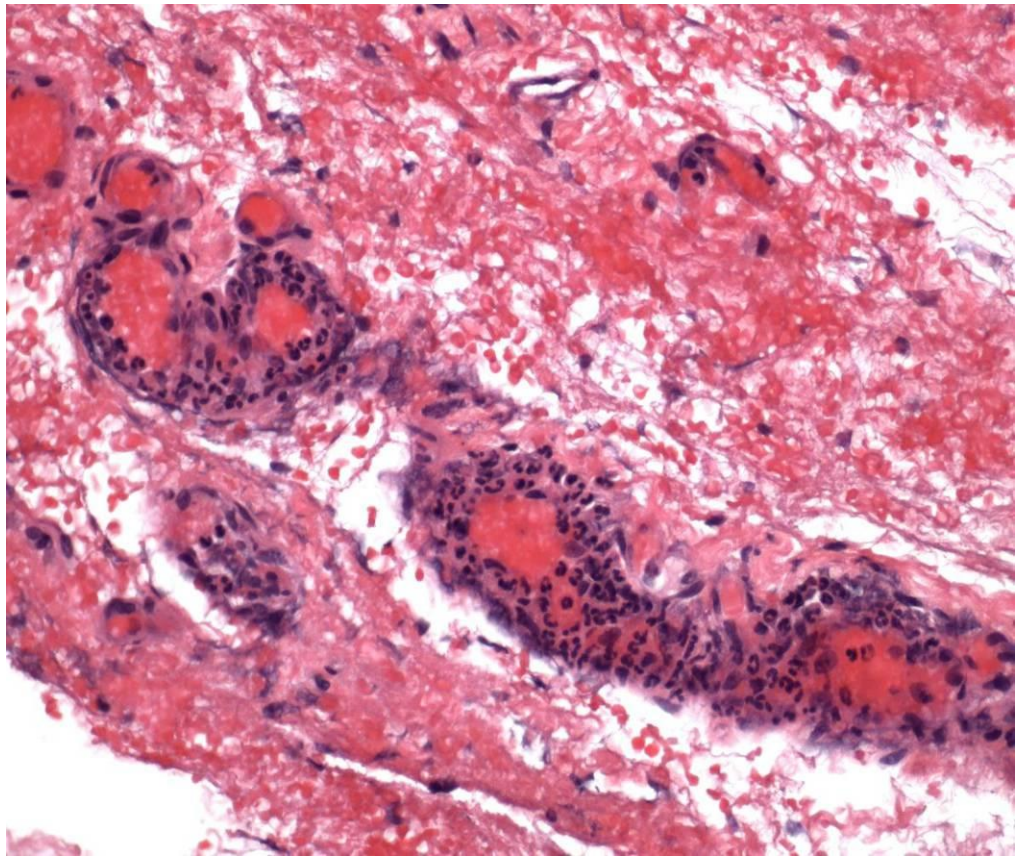
Letters in the bioterrorism attack of 2001

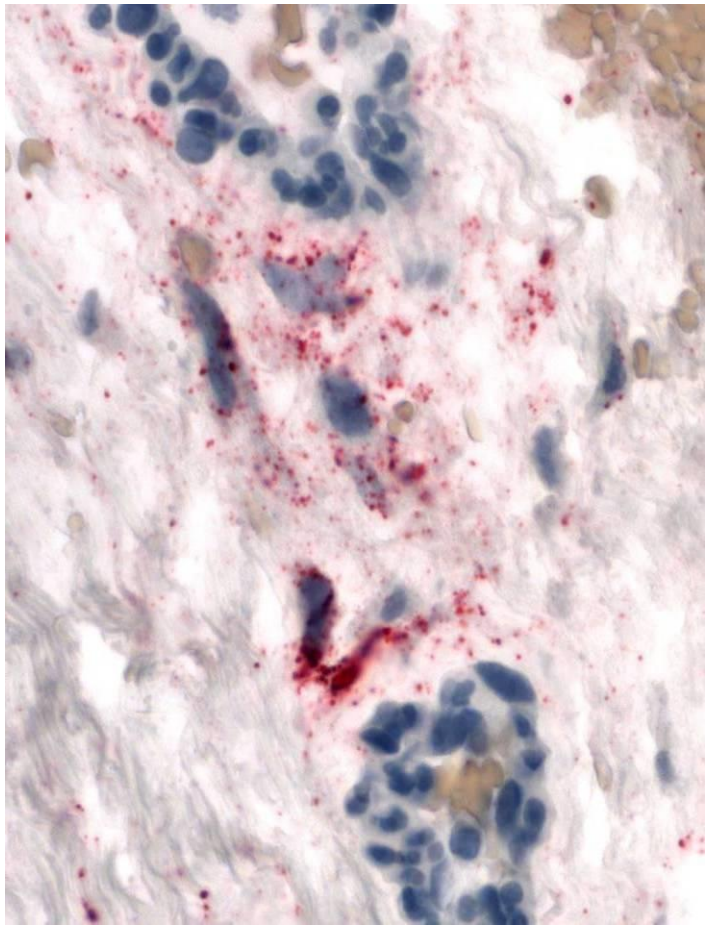




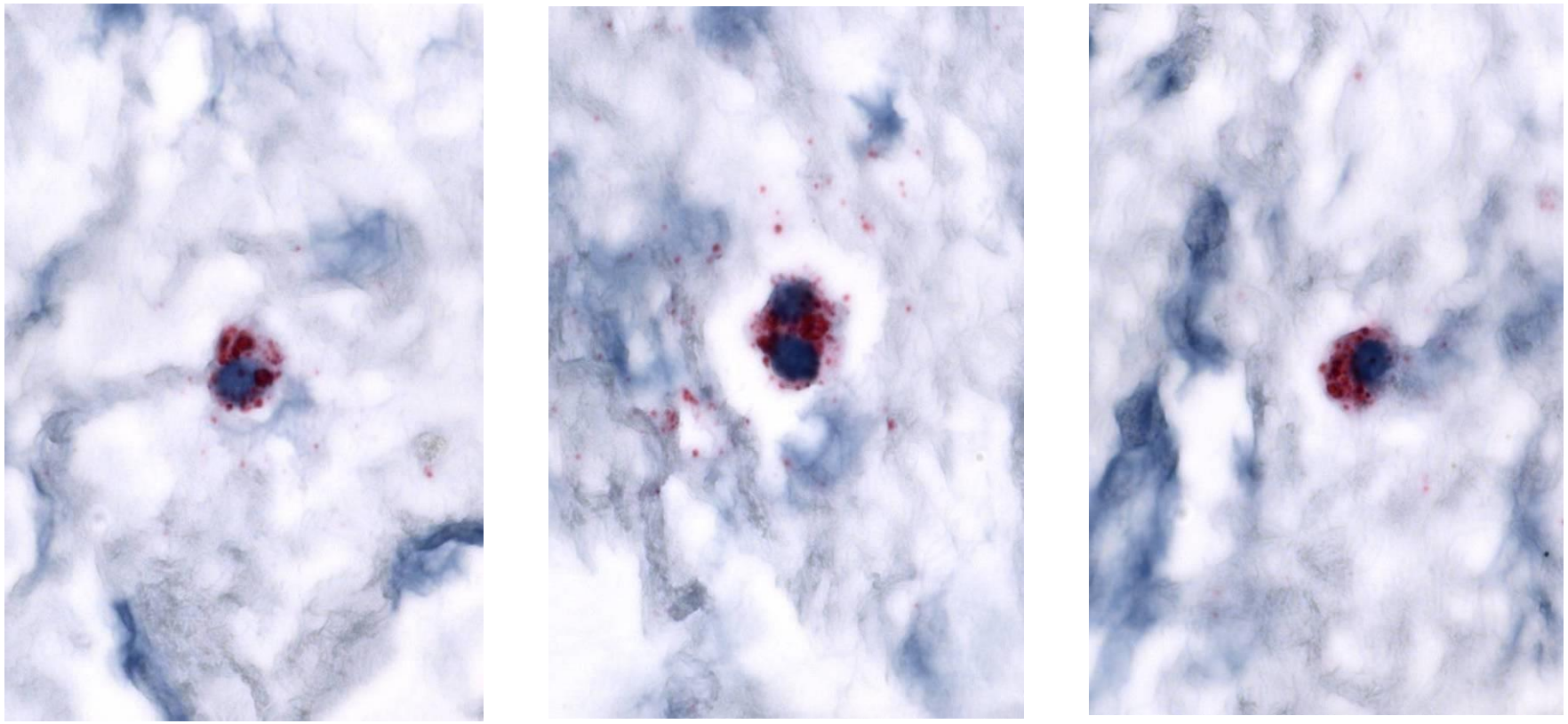
Case continues

- Change in antibiotic regimen to moxifloxacin, clindamycin, and ampicillin.
- Pleural effusions kept up happening even 10 days after initiation of treatment.
- Patient was discharged from the hospital 35 days after admission.

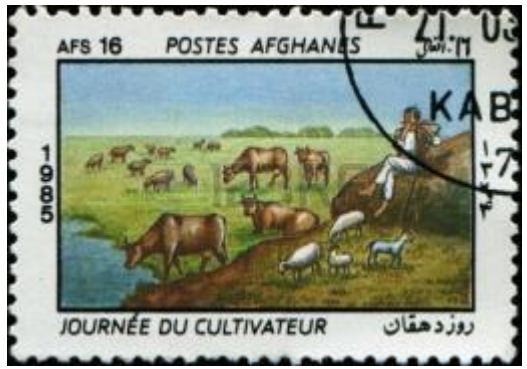




Presence of anthrax antigens in pleural effusions 10 days after antibiotic treatment had been started



Walsh JJ, et al. A case of naturally acquired inhalation anthrax: clinical care and analyses of anti-protective antigen immunoglobulin G and lethal factor. Clin Infect Dis. 2007;44:968-71.



Case 3

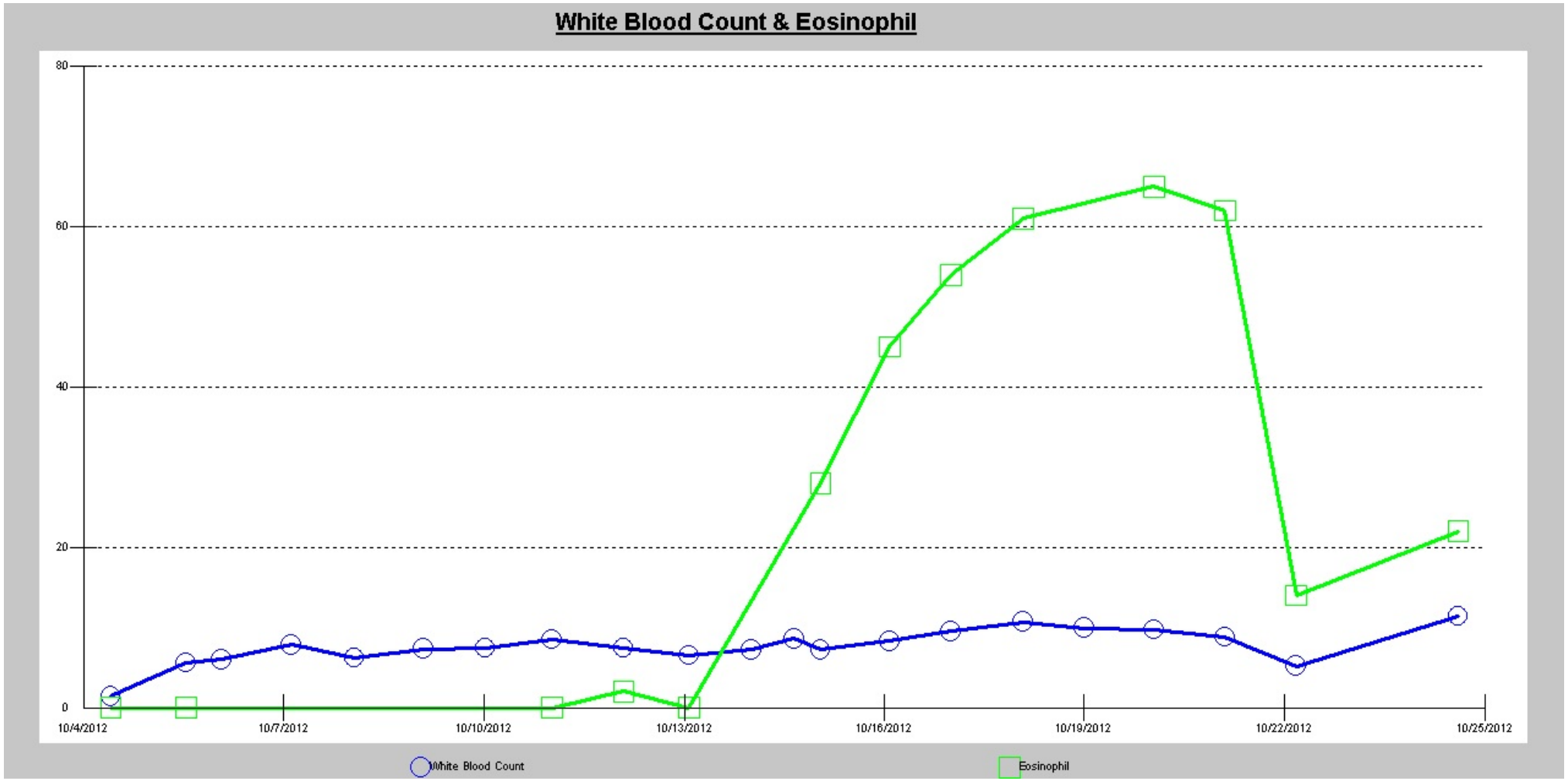
- 39 year old male presents with fever, abdominal pain, and diffuse bone pain
- He had CML diagnosed 7 years ago but developed blast crisis four months prior to presentation
- Blast crisis, treated with dasatinib and H-CVAD
- Blood cultures grew *Escherichia coli* and coagulase negative Staph treated with vancomycin and meropenem
- He is found to have pulmonary nodules empirically treated with voriconazole
- Fevers persist

Case continues

- Family: no contributory history
- Social: from El Salvador but has been in Atlanta for 20 years.
  - Last travel to El Salvador three years ago
- Worked as a painter until illness

- Physical exam: Temp 38.3˚C
- Abdomen: diffuse, mild tenderness

Laboratory Examination



Causes of eosinophilia in a patient such as this, include:

- Drug associated
- Allergic
- Parasites
- Fungi
- Viruses

QUESTION: What parasites are observed in one O&P stool specimen stained with trichrome?

1. *Entamoeba* sp.
2. *Strongyloides stercoralis*
3. Cyclospora

QUESTION: If you are thinking this could be *Strongyloides*, what test would have the highest yield?

1. Multiplex PCR in stool
2. Serology for *Strongyloides*
3. Microscopy of duodenal aspirate

Zhang H, et al. Multiplex polymerase chain reaction tests for detection of pathogens associated with gastroenteritis. *Clin Lab Med*. 2015;35(2):461

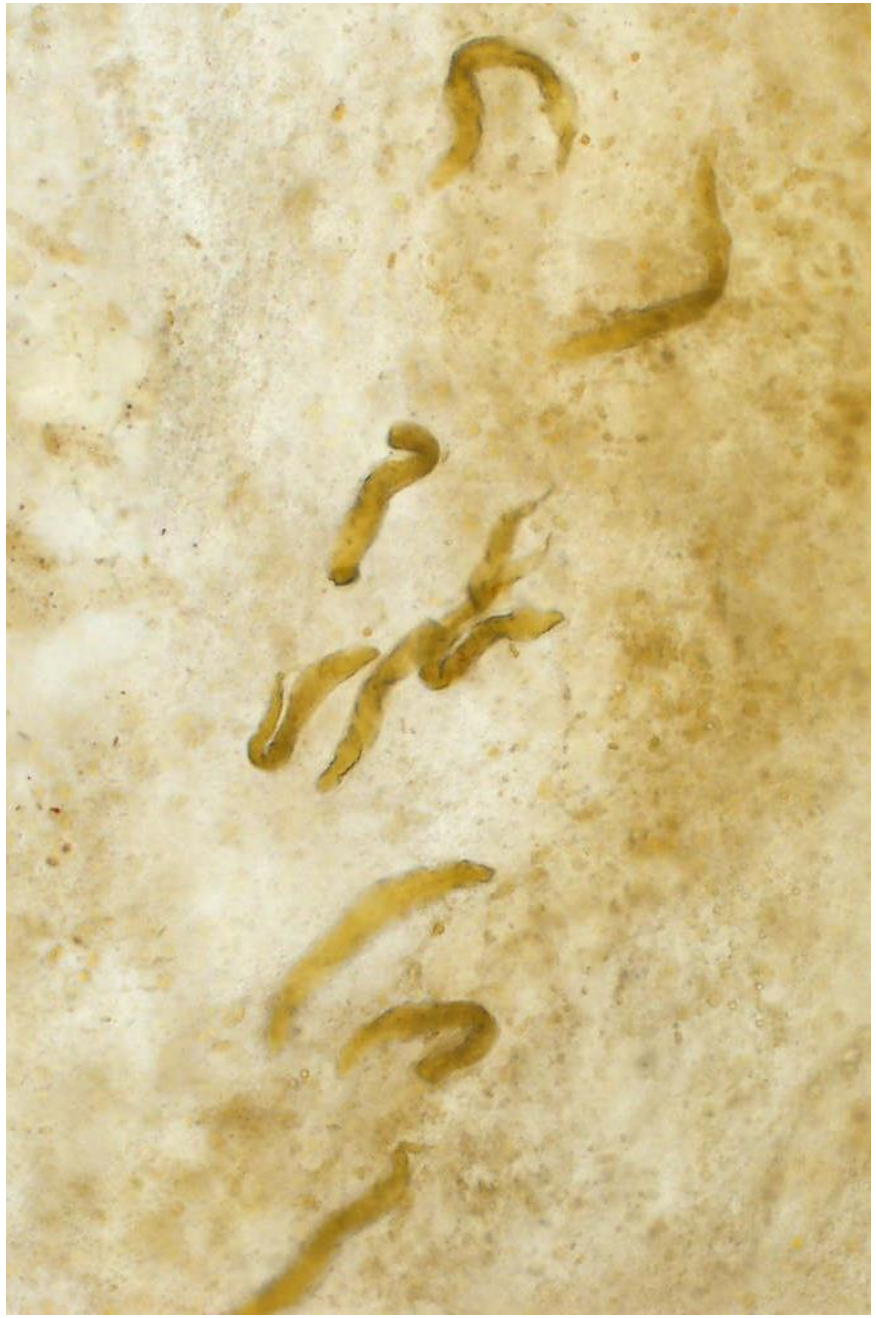
Manufacture/Assay	*Aeromonas*	*Campylobacter*	*Clostridium difficile*	*Clostridium perfringens*	Enteroaggregative *E. coli* (EAEC)	Enteropathogenic *E. coli* (EPEC)	Enterotoxigenic *E. coli* (ETEC) *lt/st*	Shiga toxin *E. coli* (STEC) *stx1/stx2*	*E. coli* O157	Listeria monocytogenes	*Plesiomonas shigelloides*	*Salmonella*	*Shigella*	*Vibrio*	*Vibrio cholerae*	*Yersinia enterocolitica*	Adenovirus F40/41	Astrovirus	Enterovirus	Norovirus GI/GII	Rotavirus A	Sapovirus	*Cryptosporidium*	*Blastocystis hominis*	Dientamoba fragilis	*Cyclospora cayetanensis*	*Entamoeba histolytica*	*Giardia lamblia*
Luminex - xTAG GPP		✓	✓				✓	✓	✓			✓	✓		✓	✓*	✓			✓	✓		✓				✓	✓
BioFire – FilmArray GI	✓*	✓	✓		✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓			✓	✓	✓
BD MAX - Enteric bacterial (B), Virus* (V), Parasite* (P)		✓ B						✓ B				✓ B	✓ B							✓ V	✓ V		✓ P				✓ P	✓ P
Nanosphere - Verigene Enteric Pathogen		✓						✓				✓	✓	✓		✓				✓	✓							
Hologic (Gen-Probe) - ProGastro SSCS		✓						✓				✓	✓															
PathoFinder - Gastrofinder Smart 17 Fast	✓	✓	✓				✓	✓	✓			✓	✓			✓	✓	✓		✓	✓		✓		✓		✓	✓
r-Biopharm - Rida Gene - Hospital stool (HS), Bacterial Stool (BS) Viral Stool (VS), Parasitic Stool (PS)		✓ B	✓ HS									✓ B				✓ B	✓ V2	✓ V2		✓ V2	✓ V2		✓ P		✓ P		✓ P	✓ P
Seegene - SeeplexDiarrhea ACE - Viral (V), Bacterial 1 (Ba) and 2 (Bb)	✓ Bb	✓ Ba	✓ Ba	✓ Bb				✓ Bb	✓ Bb			✓ Ba	✓ Ba	✓ Ba		✓ Ba	✓ V	✓ V		✓ V	✓ V							
Serosep - EntericBio Gastro Panel 1 (P1) and 2 (P2)		✓						✓				✓	✓										✓					✓
Fast-Track Diagnostics - FTD Stool Parasites (P), EPA, Bacterial (B), Viral (V)		✓ B2	✓ B2					✓ B2				✓ B2	✓ B2			✓ B2	✓ V3	✓ V3		✓ V3	✓ V3	✓ V3	✓ P				✓ P	✓ P
Diagenode- G-DiaBact (B), G-DiaNota (V), G-Diapara (P)		✓ B										✓B											✓ P				✓ P	✓ P
Genetic Signatures - EasyScreen Enteric Bacteria (B), Viral (V), Protozoan (P)	✓ P3	✓ P3	✓ P3					✓ P3		✓ P3		✓ P3	✓ P3	✓ P3		✓ P3	✓ V3	✓ V3	✓ V3	✓ V3	✓ V3		✓ P2	✓ P2	✓ P2		✓ P2	✓ P2
AusDiagnostics - Faecal Bacteria (B), GI Parasites (P)		✓ B	✓ B									✓ B	✓ B										✓ P		✓ P		✓ P	✓ P
Genomica – CLART EnteroBac	✓	✓	✓		← undifferentiated →							✓	✓			✓												

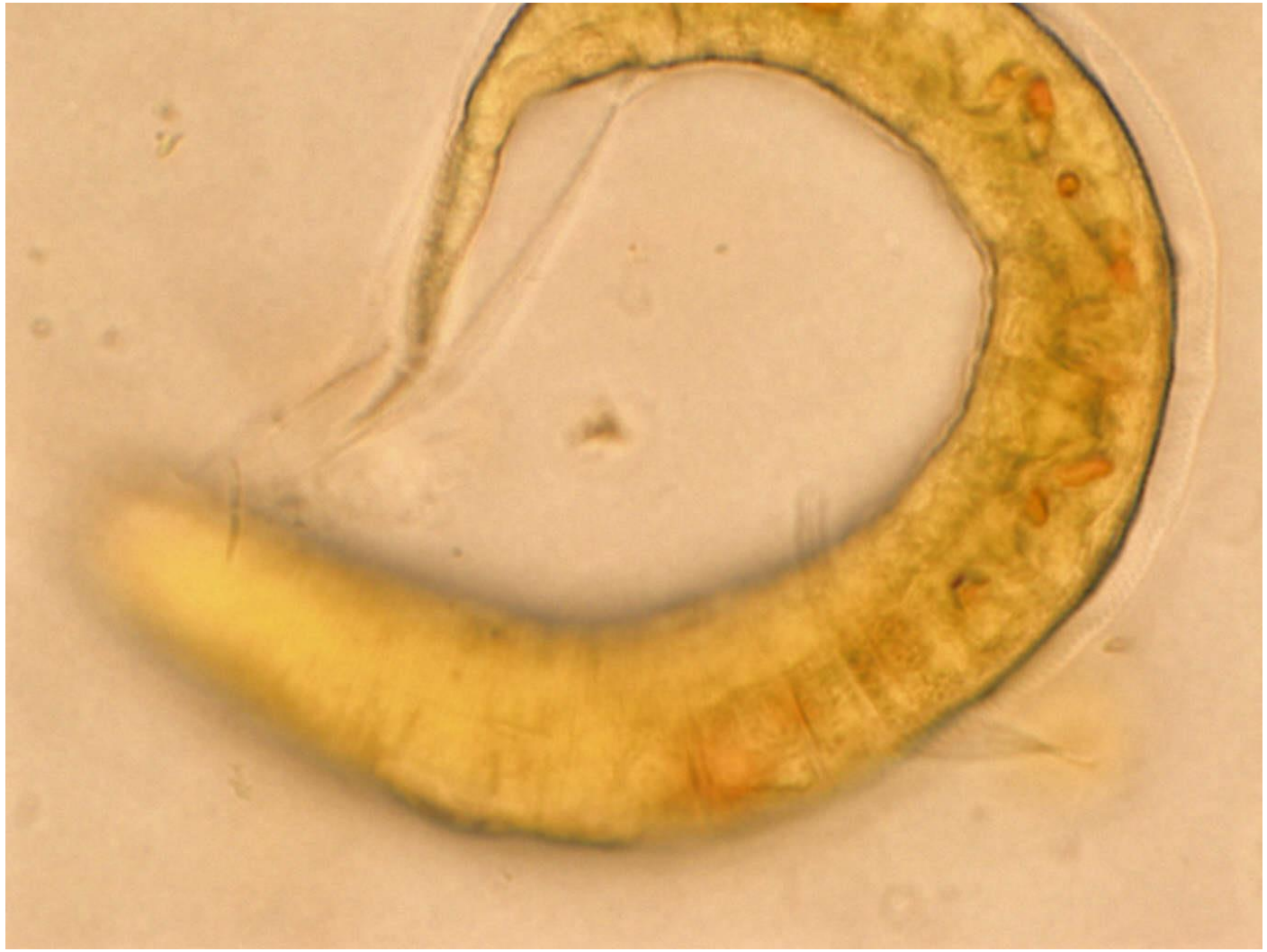
Private Information

QUESTION: Which lab should the specimen go to?

1. Cytology
2. Microbiology

Duodenal aspiration





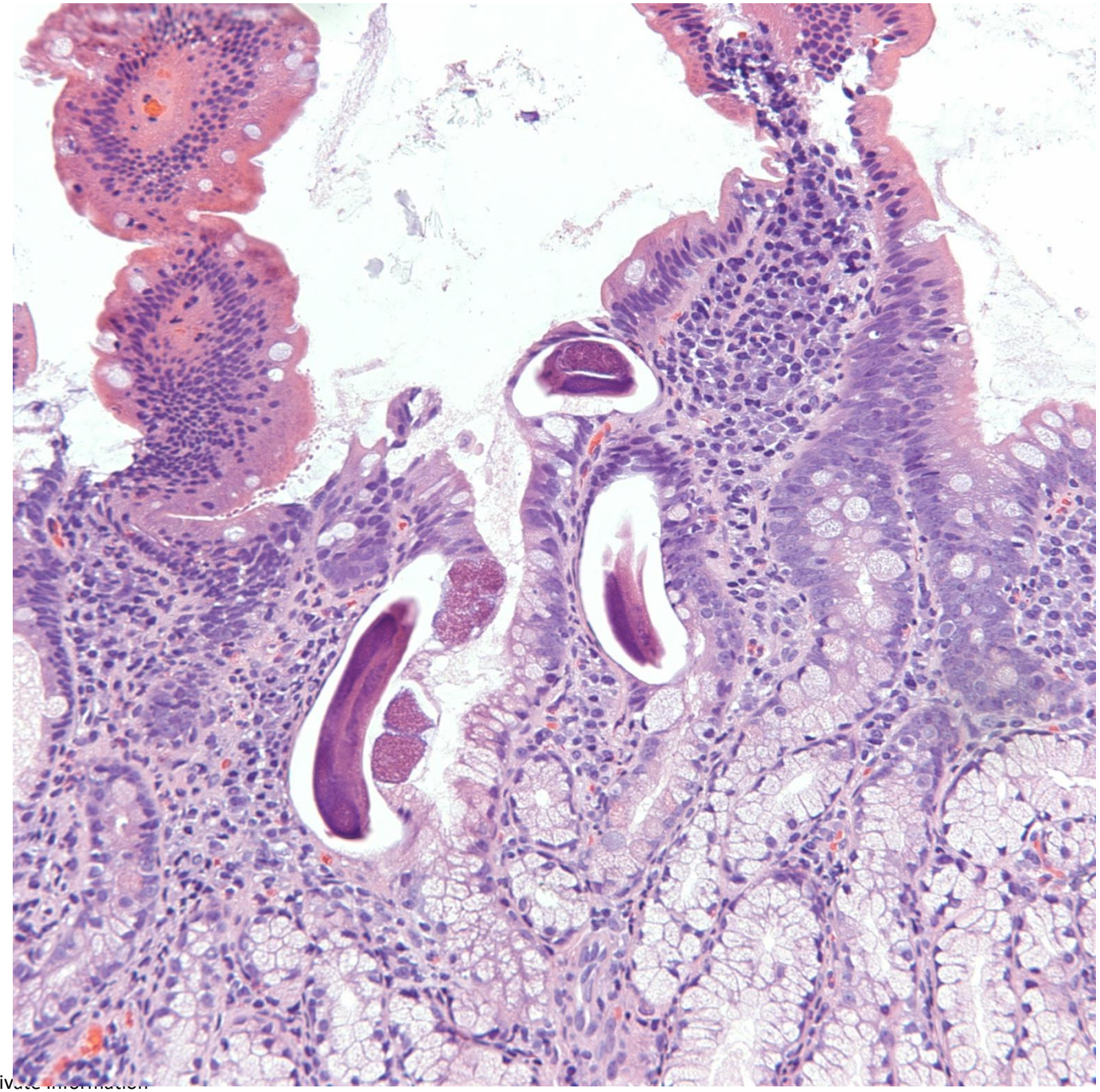
My experience working at INCan

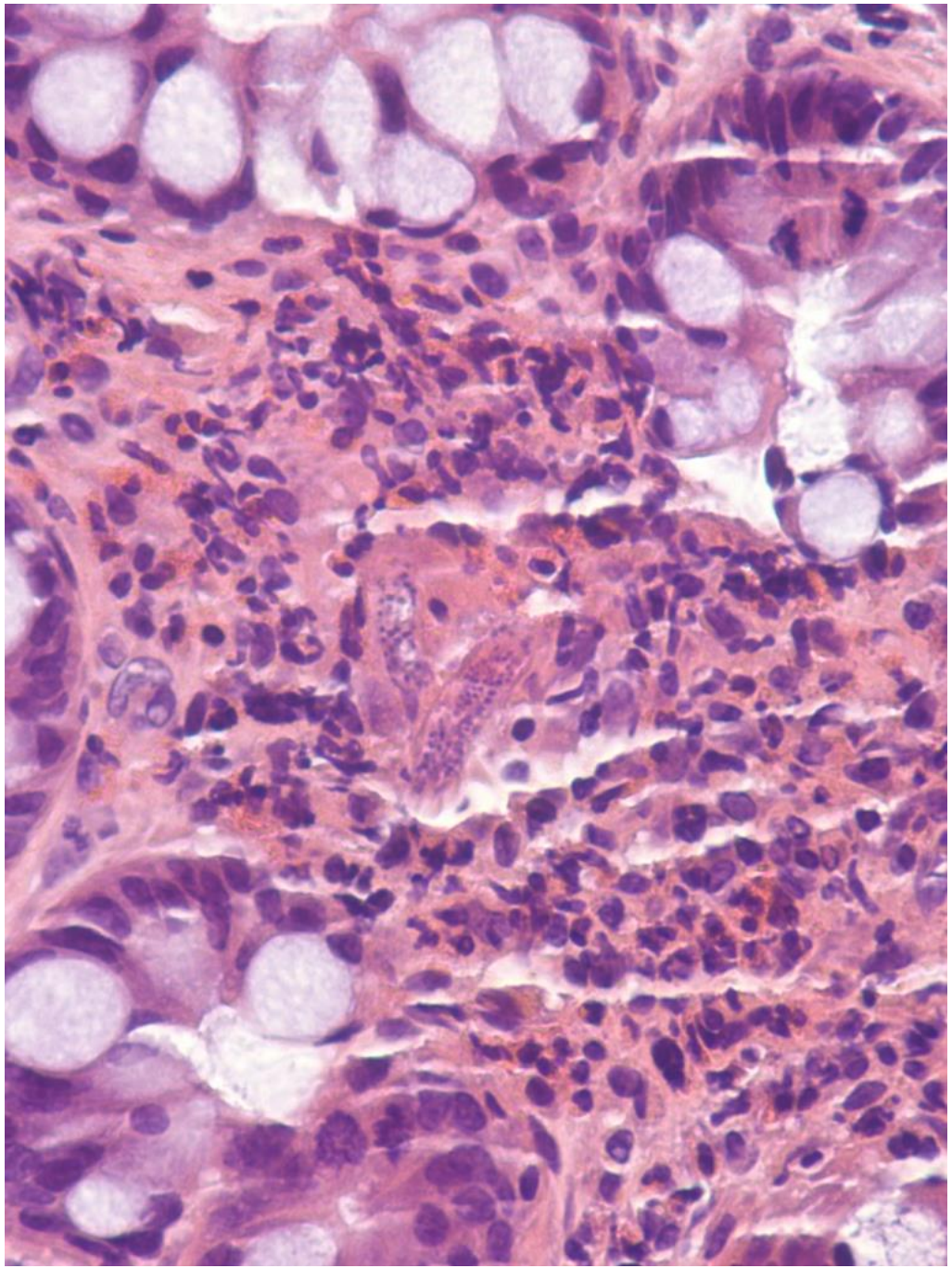
- Approximately 28% of the Mexican population has intestinal parasites.
- Oncologic patients receiving chemotherapy have 3 (serial) coproparasitoscopic studies to avoid disseminated parasitic infections.
- All patients were asked to give us 3 stool samples.

Study at INCan

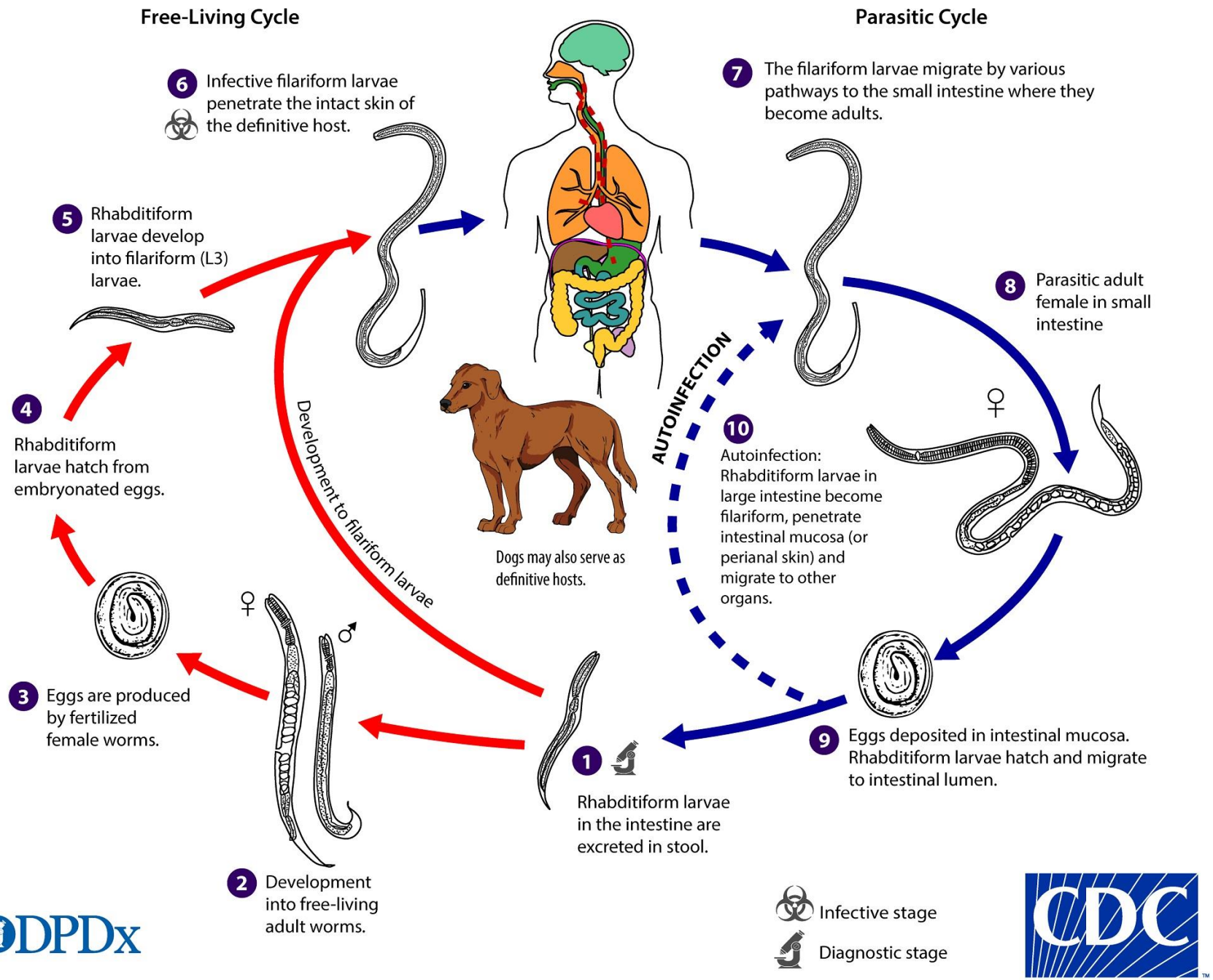
- Evaluated in 100 diarrheic (DS) and 100 formed stools (FS) from distinct adult patients recently diagnosed with cancer.
- 26% patients with DS and 15% with FS had one or more parasites: *Entamoeba histolytica* was found in 12 DS and in 2 FS (p = 0.01), *Giardia lamblia* in 3 DS and 6 FS and *Hymenolepis nana* in 8 DS and 10 FS. Other pathogenic parasites were found only in DS: *Cryptosporidium* sp. in 5, *Ascaris lumbricoides* in 2 *Strongyloides stercoralis* in 2 and *Isospora* sp. in one.
- *Cryptosporidium* and *Isospora* were only identified by wet mounts stained with Kinyoun.

Guarner J, et al. Frequency of intestinal parasites in adult cancer patients in Mexico. Arch Med Res. 1997;28:219-22.





Strongyloides stercoralis



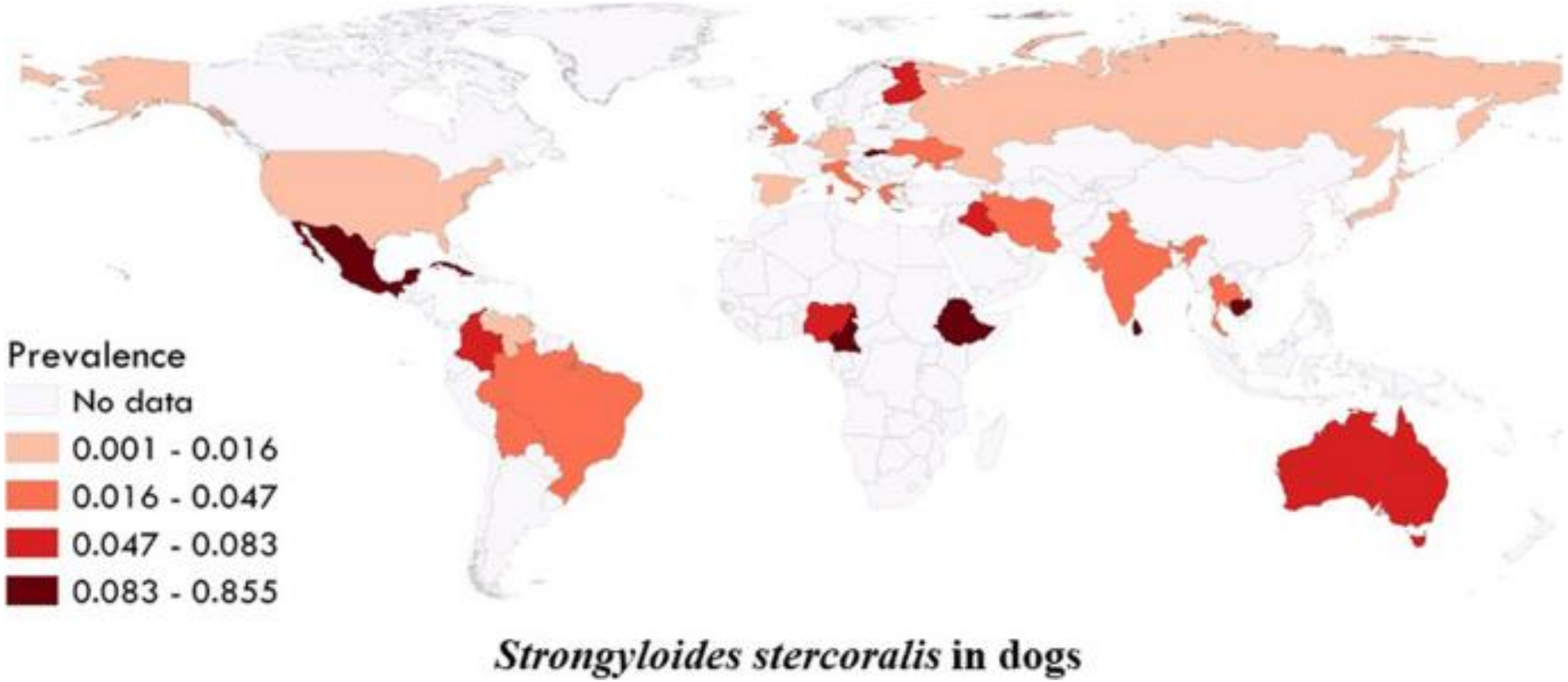
DPDx

CDC

Private Information

Hyperinfection syndrome and disseminated strongyloidiasis

- Seen in patients receiving high-dose corticosteroids that have subclinical infection.
- Impaired host immunity leads to accelerated autoinfection and an overwhelming number of migrating larvae.
- In chronic strongyloidiasis and hyperinfection syndrome, the larvae are limited to the GI tract and the lungs, whereas in disseminated strongyloidiasis the larvae invade numerous organs.
- If untreated, the mortality rates can approach 90%.



***Strongyloides stercoralis* in dogs**

Eslahi, AV, *et al.* Global prevalence and epidemiology of *Strongyloides stercoralis* in dogs: a systematic review and meta-analysis. *Parasites Vectors* **15,** 21 (2022).

Since the end of December, 2019 to today:

Three Emerging Coronaviruses in Two Decades

The Story of SARS, MERS, and Now COVID-19

Jeannette Guarner, MD

Am J Clin Pathol 2020;153:420-421
DOI: 10.1093/ajcp/aqaa029

Monkeypox in 2022

A New Outbreak of an Old Disease

Jeannette Guarner, MD

From the Department of Pathology and Laboratory Medicine, Emory University, Atlanta, GA, USA.

AJCP | EDITORIAL

KEY WORDS

Monkeypox; Testing; Pathology

Am J Clin Pathol August
2022;158:160-161
HTTPS://DOI.ORG/10.1093/AJCP/AQAC091

Final thoughts

- People travel or have lived in another location and can bring with them a microorganism
- Organisms can travel in animals (live or dead), fomites and other.
- Knowing what is prevalent in different parts of the world informs diagnostic tests and samples to be used.