



Ten Cases of Fever – Ten Lessons Learned

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Case One:

A 32 year old woman presents in July with fever, severe headache, muscle aches, conjunctivitis and nausea. No one she knows has similar symptoms. Ten days before symptom onset, she did kayak drills in a road side pond.

Leptospirosis

- *Leptospira interrogans*
 - Spirochete with over 200 serovars
- Animal reservoirs
 - Persistent infection in renal tubules
 - Prolonged excretion in the urine
 - Water contamination
- Rats, but in the United States dogs and livestock (cattle, horses and pigs) cause more disease



Risk Factors for Leptospirosis

■ Occupational Groups

- Farmers & ranchers
- Abattoir workers
- Trappers
- Veterinarians
- Loggers
- Sewer workers
- Rice field workers
- Military personnel

■ Recreational Activities

- Freshwater swimming
- Canoeing & kayaking
- Trail biking
- Hunting

■ Household Environment

- Pet dogs
- Domestic livestock
- Rainwater catchment
- Rodent infestation

Clinical Disease in Humans

- Wide spectrum of manifestations: from subclinical to death
- Incubation period ranges from 2-20 days
- Two recognizable syndromes, each with 2 classic phases (biphasic febrile illness)
 - Icteric form (Weil Syndrome)
 - Influenza-like illness (90% of cases)

Treatment and Prevention

■ Treatment

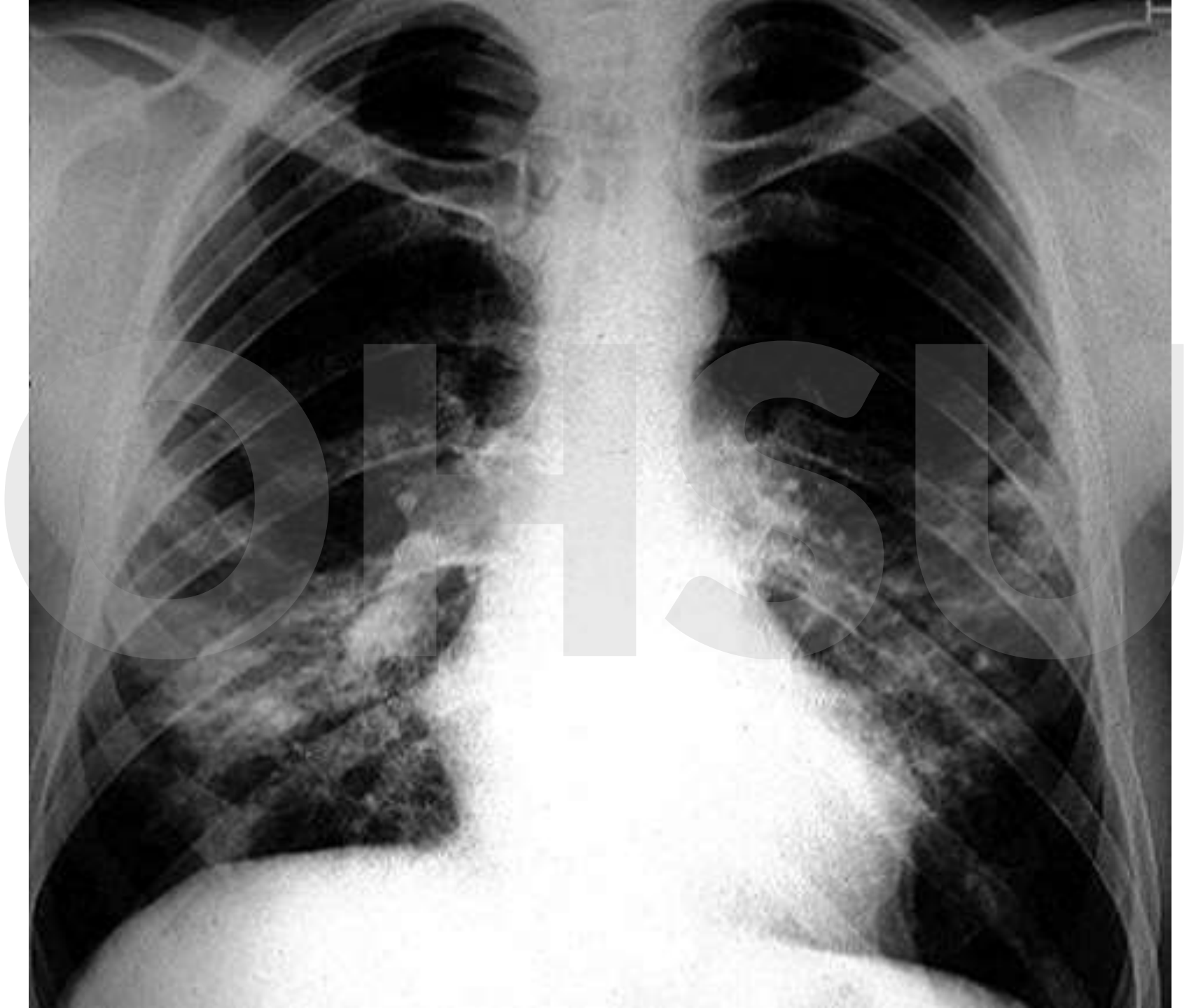
- Doxycycline 100 mg BID x 7 days
- Amoxicillin 500 mg po QID x 7 days

■ Prevention

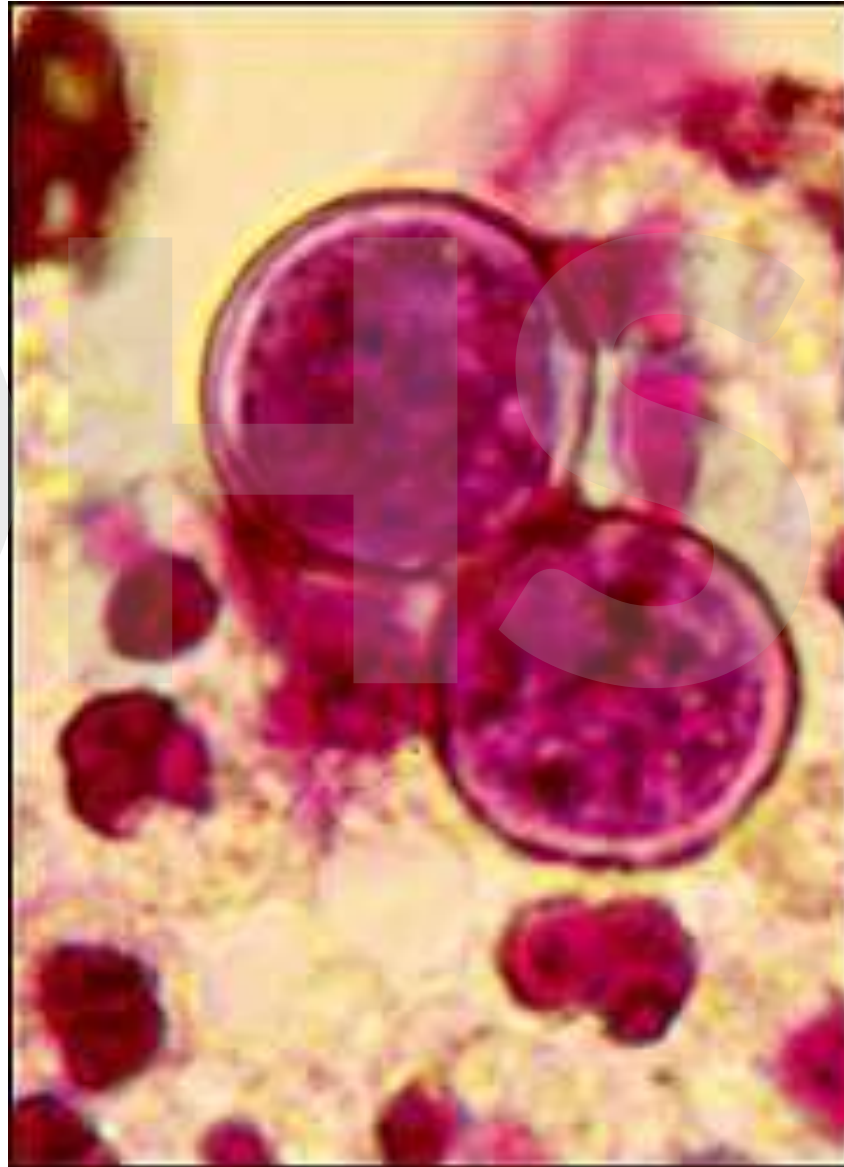
- Vaccination of domestic livestock & pet dogs
 - Animals may still excrete live organisms in urine
- Oral doxycycline 200 mg weekly
- Protective clothing for occupations at risk
- Rodent control measures
- Avoid swimming in freshwater bodies of water

Case Two:

A 44 year old man presents with both fever and shortness of breath. He has had a dry cough for two months. He has lost 15 pounds and feels weak. He is an avid sportsman and likes to camp in Northern Wisconsin. His dog died a few weeks ago. His CXR shows:



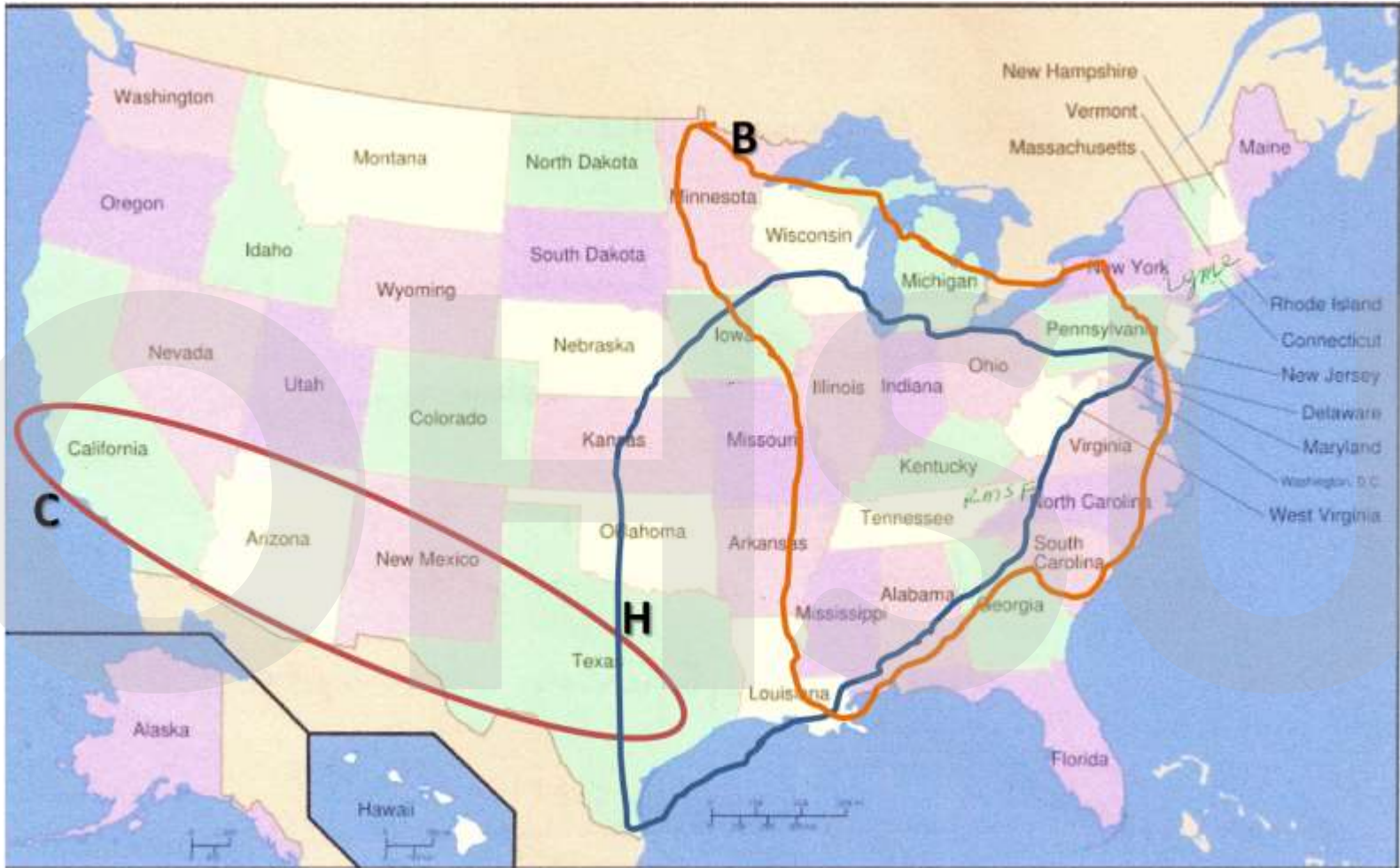
Blastomyces dermatitidis



Blastomycosis

- Presentation can mimic TB and cancer
- Organism readily isolated
 - 86% of sputum; 100% of bronchial washings
- Urinary antigen assay
 - Shows cross-reactivity with other fungi, particularly *Histoplasma capsulatum*
 - Role in diagnosis has not been established

[Clinical Infect Diseases 2008; 46: 1801-1812.]



<http://countdown2ck.blogspot.com/2012/05/histo-blasto-coccidiomycosis.html>

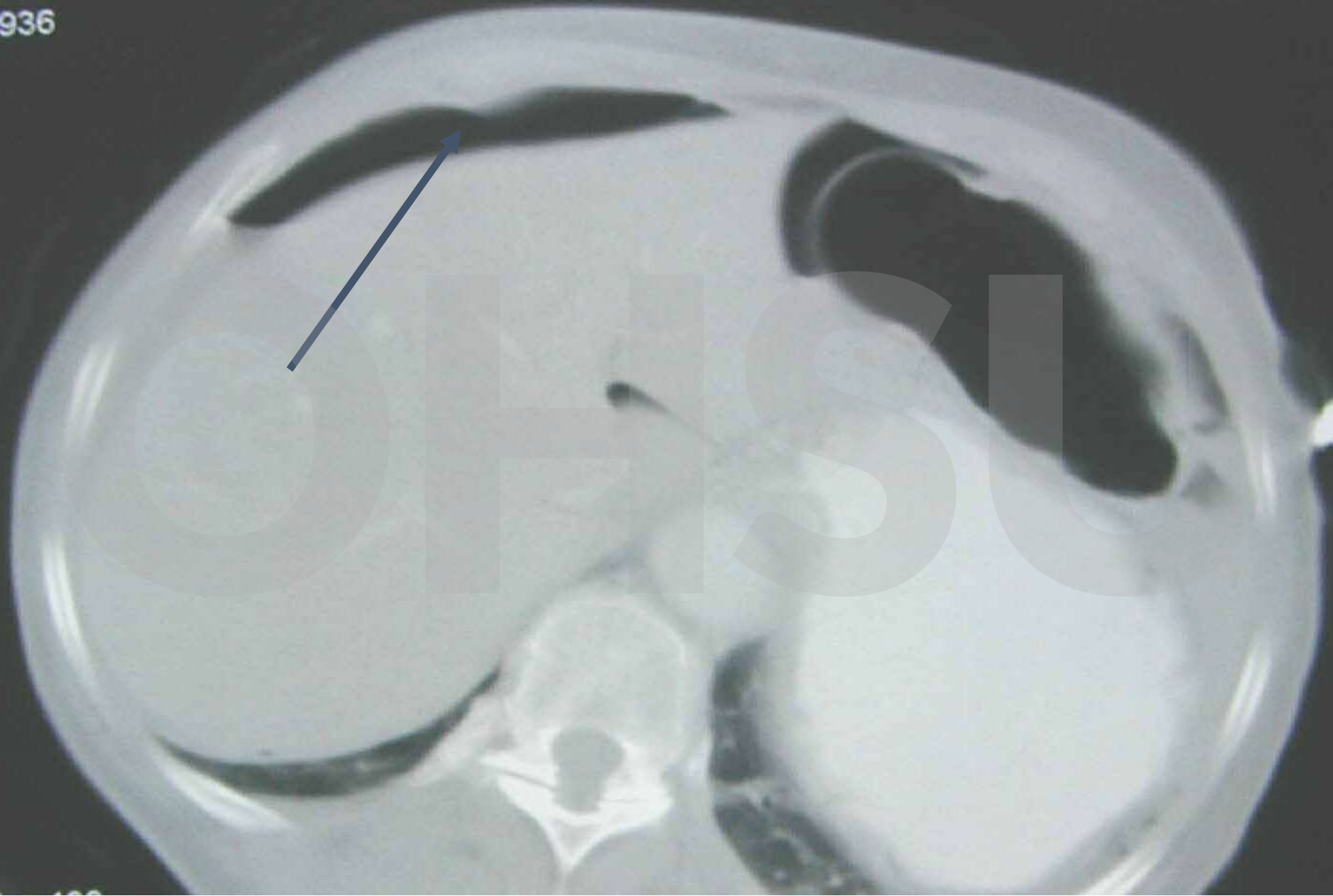
Case Three:

A 53 year old man presents to the emergency department with a 5 day history of sharp left lower quadrant pain and constipation. One day prior to presentation, he developed fevers and chills. CT imaging reveals a large bowel obstruction and diverticulitis. He is admitted for bowel rest and started on IV antibiotics (ciprofloxacin and metronidazole).

Clinical Course

- Overnight, the abdominal pain acutely worsens and he develops peritoneal signs
- Repeat CT scan → free air in the abdomen with signs of a bowel perforation
- Taken to the operating room for emergent exploratory laparotomy
 - Cecal and sigmoid diverticuli with perforations
 - Right hemicolectomy, sigmoidectomy, end ileostomy with a Hartmann's pouch

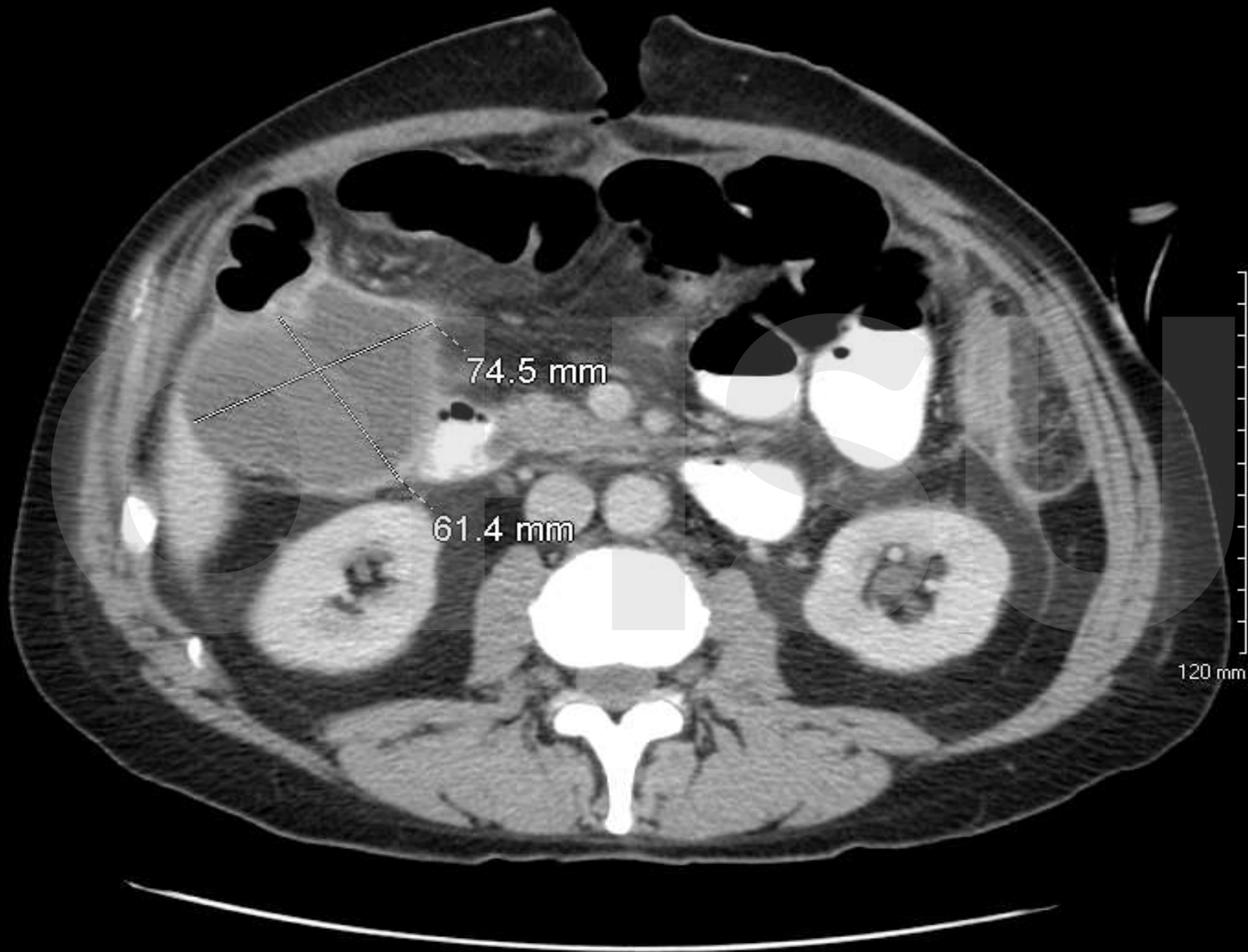
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Case Three Continues...

- Antibiotic treatment continued in the post-operative period with both ciprofloxacin and metronidazole
- Despite source control, the patient remained febrile with WBC ~16K for four days
- No localizing symptoms
- Surgical wound clean and abdominal examination is benign



Suspected Treatment Failure

- Persistent or recurrent clinical evidence of intra-abdominal infection after 4-7 days of therapy → re-image the abdomen & pelvis
- For patients who do not respond and the focus of infection remains
 - Need repeat cultures (aerobic and anaerobic)
 - Inoculation of anaerobic blood culture bottle may improve yield

[Clinical Infectious Diseases 2010; 50:133–64]

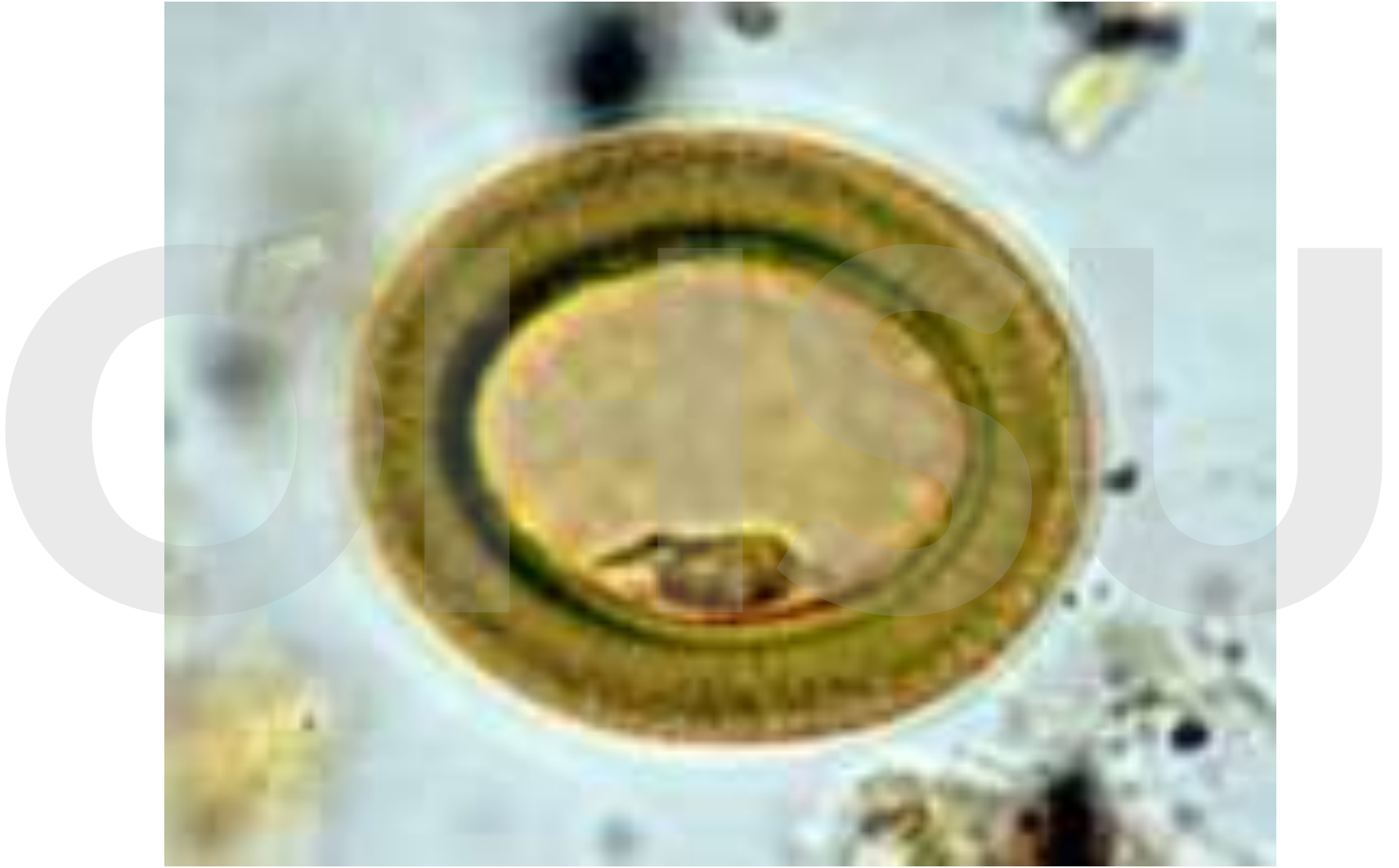
Case Four:

A 41 year old immigrant from Peru presents with new onset of tonic-clonic seizures. She denies any other medical problems and was on no medications prior to presentation. She denies headache, motor weakness, weight loss, GI symptoms or HIV risk factors. She has had subjective fevers. A head CT reveals:



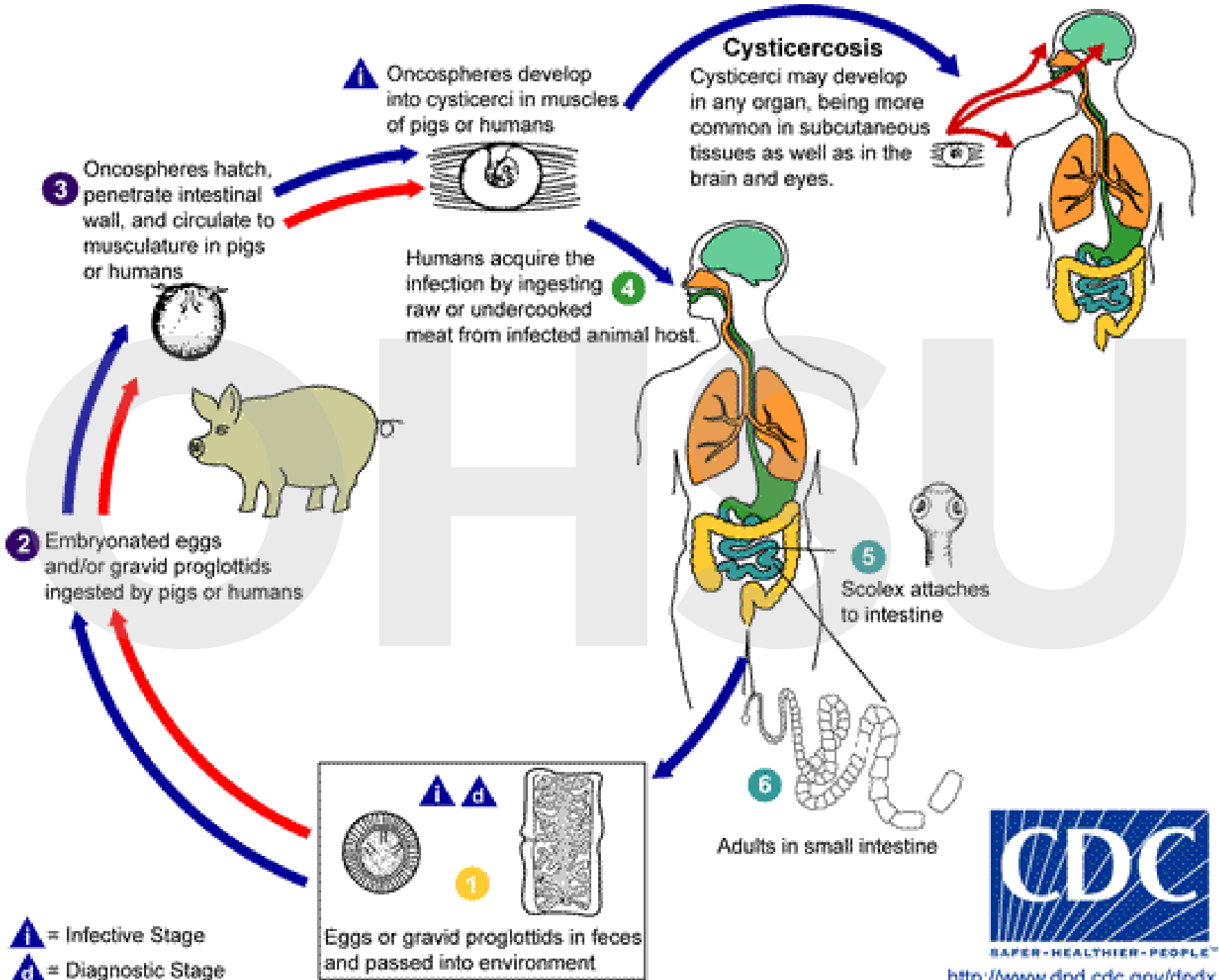
OHSU

This is an axial MRI scan of the brain. The image shows a cross-section of the brain with various anatomical structures visible. A large, semi-transparent watermark reading 'OHSU' is overlaid across the center of the image. The watermark is in a bold, sans-serif font and is centered horizontally and vertically. The background of the image is a grayscale MRI scan, showing the brain's internal structure and the surrounding skull. The watermark is a large, semi-transparent, light gray 'OHSU' centered over the brain scan.



Cysticercosis

- Caused by the larval form of the pork tapeworm: *Teania soleum*
- Adult worm found in human GI tract and passes thousands of eggs daily
- Pigs or humans eat food contaminated with human waste and ingest the eggs
- Larva from eggs make their way via the bloodstream to distant sites & form cysts
- Humans eat undercooked pork and ingest encysted larva (which mature into adults)



Case Five:

A 54 year old homeless man develops severe fatigue over a three month period. He then develops shortness of breath and painful spots on her hands and feet. He seeks medical attention in your urgent care. The exam reveals a loud murmur and an echo reveals vegetations on the mitral valve. Off antibiotics, all blood cultures are negative.



Changing Microbiology of IE

- *Staphylococcus aureus* now the most common cause worldwide, 31% of patients
- Other Gram positive organisms important
 - Viridans streptococcus, coagulase-negative staphylococcus and *Enterococcus* species
- 10% → culture negative endocarditis
- Fastidious organisms
 - HACEK 2% (0.3% in North America)
 - *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella* and *Kingella* species
 - Fungi and yeast 2%

[Arch Intern Medicine 2009;169]

Most Common Identified Causes of Culture Negative Endocarditis

- *Coxiella burnetii* 3-48%
- *Bartonella* species 10-28%
- *Staphylococcus* species 2-11%
- *Streptococcus* species 1-6%
- HACEK 0.5-3%
- Fungi 1-6%
 - *Candida*, *Aspergillus*, *Cryptococcus*, endemic fungi, others
- *Tropheryma whipplei* 0.3-3%
- Others: *Legionella*, *Chlamydia* and *Brucella*

[Clinical Infect Diseases 2010;96]

Bartonella species

- Endocarditis linked to *B. henselae* as well as *B. quintana*
- Both species globally endemic
- *B. henselae* transmission via cats
 - Etiology of cat scratch disease
- *B. quintana* causes trench fever
 - Vector is the human body louse

Bartonella Endocarditis

- *B. quintana* associated with alcohol dependence and homelessness
- Significant proportion are afebrile but have advanced valvular disease as well as embolic phenomenon
- Diagnosed with culture; serologic assay IgG > 1:800; PCR testing; or histology and immunohistochemistry of valve

Five Lessons Learned So Far

Case	Lesson
Leptospirosis	People do strange things
Blastomycosis	History really does matter
Intra-abdominal Abscess	If they're not getting better, keep looking for an answer
Neurocysticercosis	Think about infections even when they are not likely
Bartonella Endocarditis	Unusual bugs may cause common/typical diseases

Case Six:

A 27 year old public health nurse was referred to the outpatient infectious disease clinic because of a four week history of malaise, fatigue and daily fevers. Except for a broken ankle, her past medical history was unremarkable. She denied having any other symptoms.

Case Six (continued):

The workup included a normal CBC, RF, ANA, electrolytes, creatinine and UA. The ALT was 85 and AST was 91. The ESR was 48 and CRP was 3. An HIV ELISA, monospot test, and the serologic assays negative for Hepatitis A, Hepatitis B and Hepatitis C Viruses.

Case Six (continued):

A CT scan of the chest, abdomen, and pelvis showed only a simple cyst in the liver. A TTE showed no vegetations. A urine culture and three blood cultures were negative. When she came to the ID clinic, the patient appeared tired and had normal vital signs and normal exam.

Fever of Unknown Origin

- Temperature over 101° F on several occasions
- Duration is longer than 3 weeks
- Extensive work up unrevealing (one week hospital stay no longer needed)

Fever of Unknown Origin

- Infections (30-40%)
- Neoplasms (20-30%)
- Collagen vascular diseases (10-20%)
- Miscellaneous conditions
e.g., drug fever (15-20%)
- Unknown (5-15%)

EBV Serologic Profiles

Heterophile Antibodies	VCA IgG	VCA IgM	EBNA	Interpretation
+/-	+	+	-	Acute infection
-	+	-	+	Past infection
-	-	-	-	No infection
+/-	+	-	-	Indeterminate
-	+	+	+	Indeterminate
-	-	+	-	Indeterminate

[Journal of Clinical Microbiology 2004; 42(8): 3381-3387]

Case Seven:

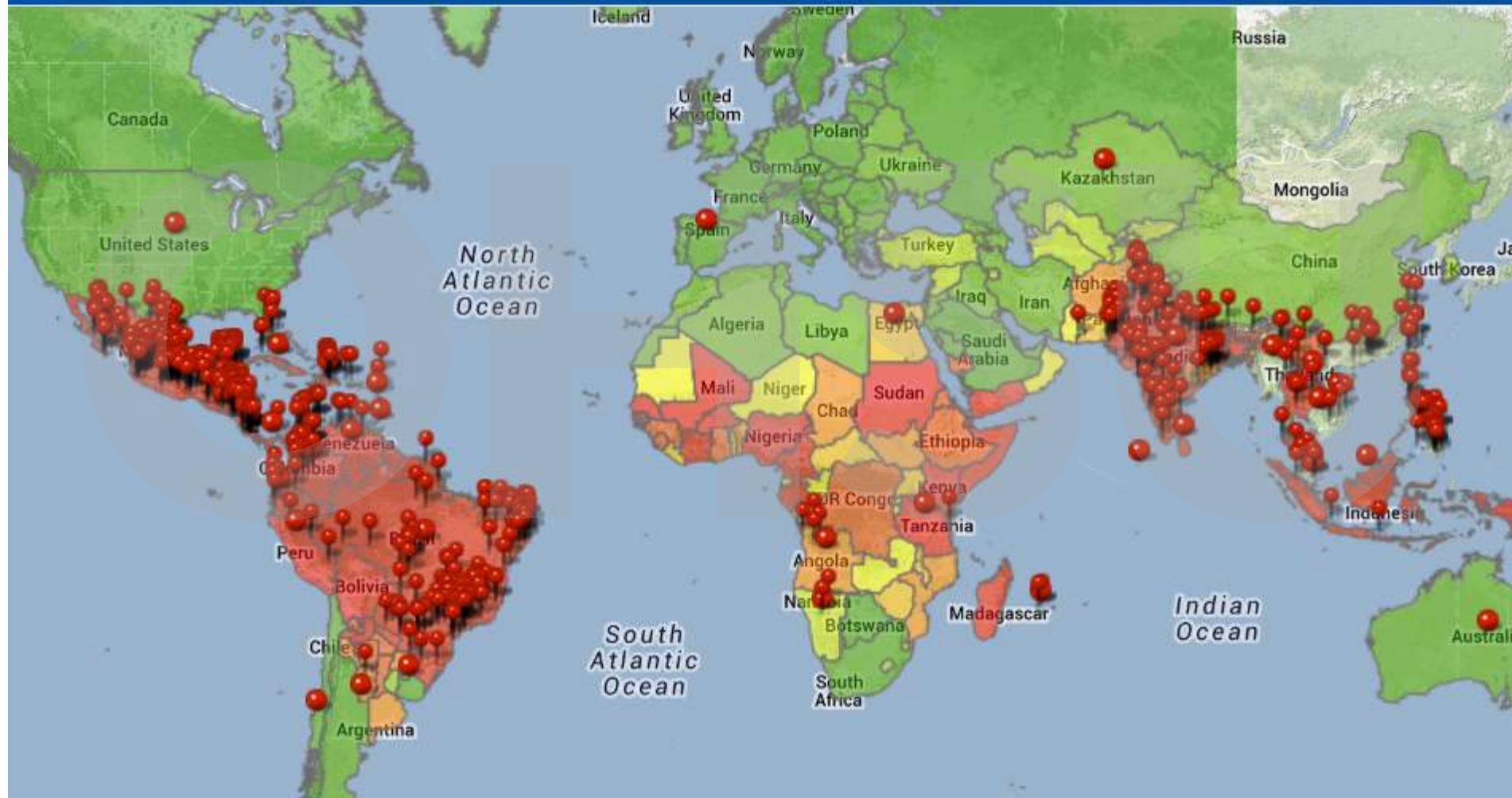
A 43 year old woman returns from Costa Rica to see the birds in the rain forest. She took malaria prophylaxis but did not use insect repellent because she doesn't like "chemicals" on her body. She reports pain behind her eyes, headache, myalgia, fevers and chills since returning home 3 days ago.

Dengue Distribution

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www.healthmap.org/dengue/index.php

Average annual number of DF/DHF cases reported to WHO & average annual number of countries reporting dengue

Chart Title

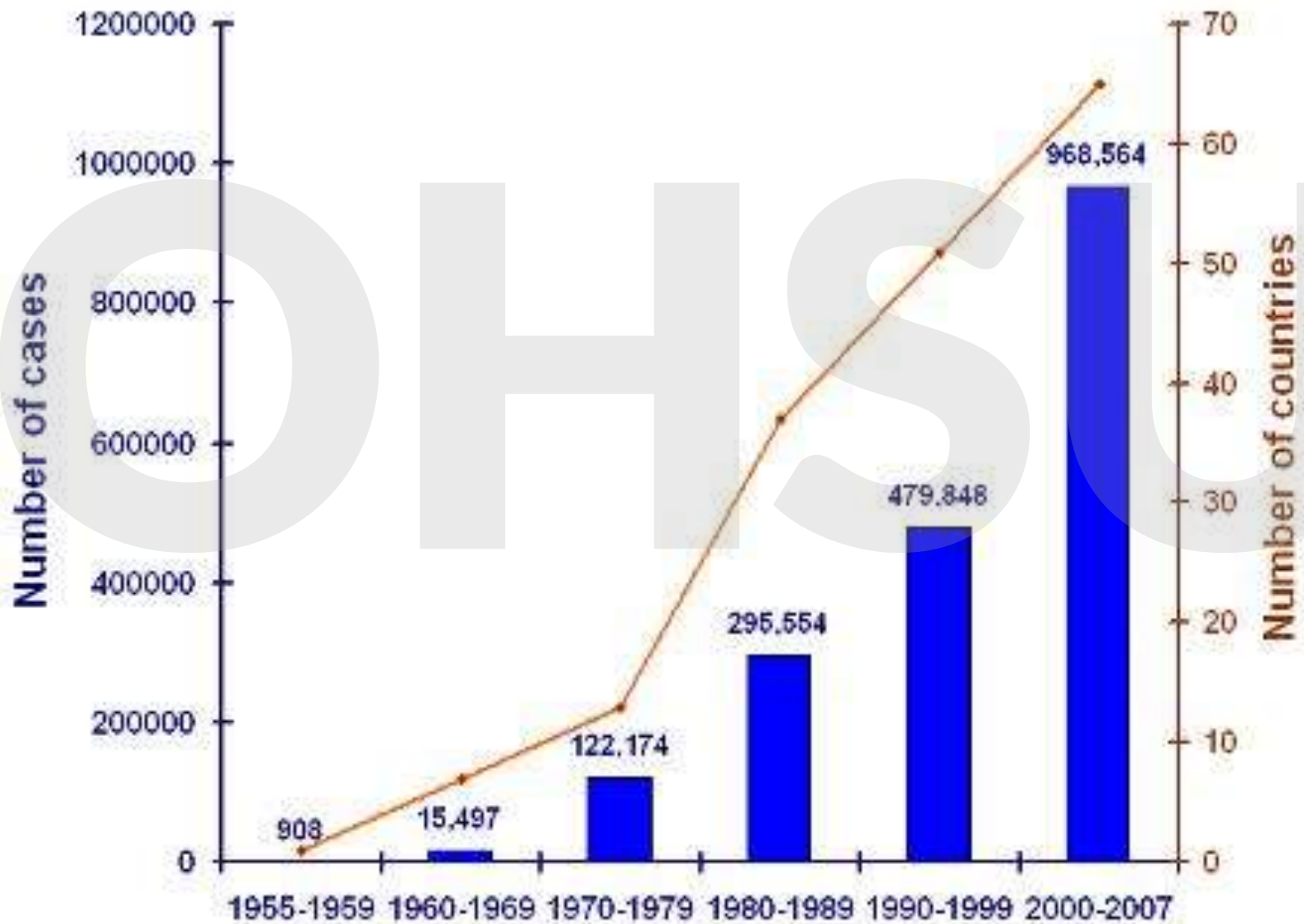


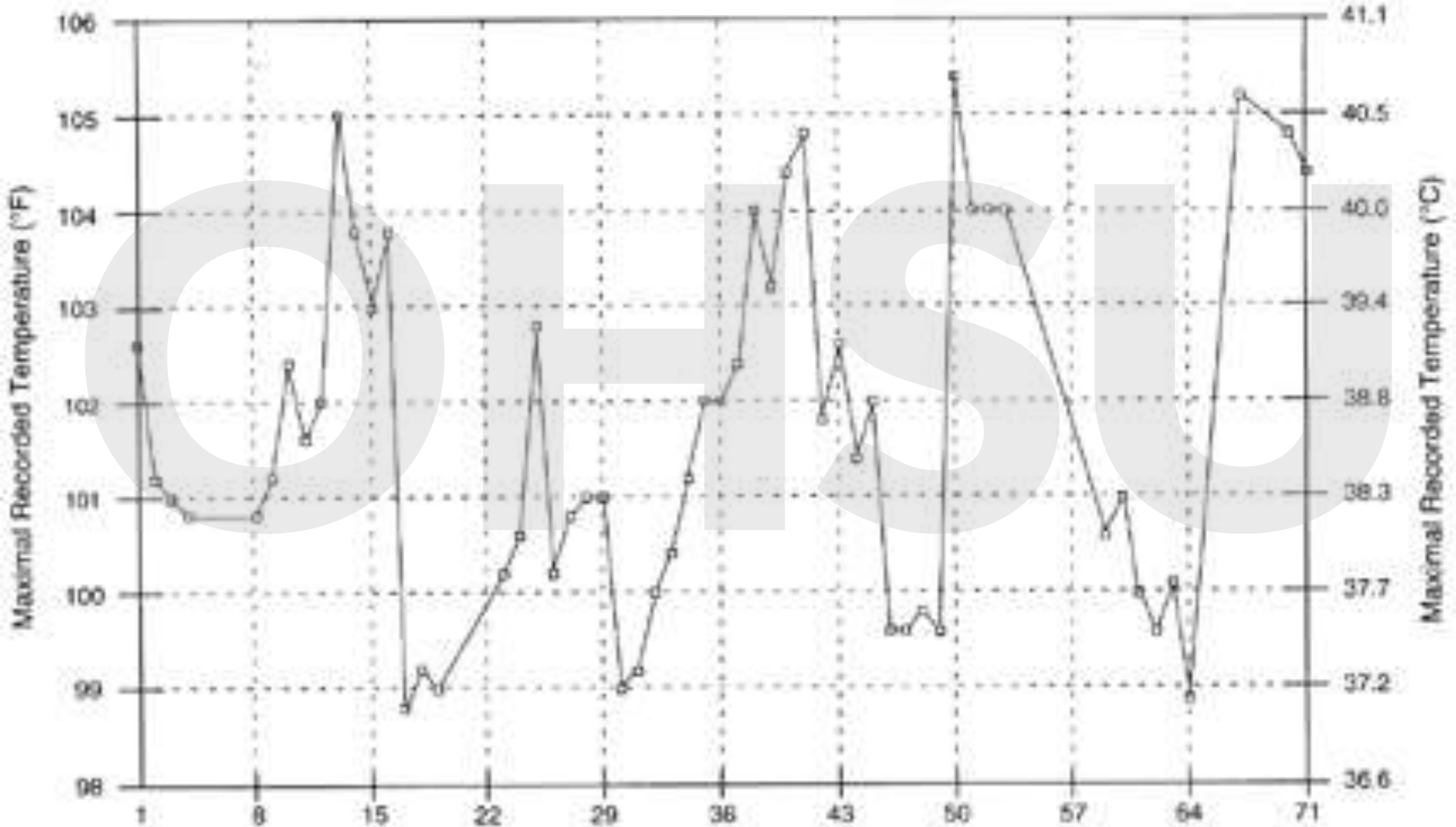
Table 5-02. Common causes of fever, by geographic area

GEOGRAPHIC AREA	COMMON TROPICAL DISEASE CAUSING FEVER	OTHER INFECTIONS CAUSING OUTBREAKS OR CLUSTERS IN TRAVELERS
Caribbean	Dengue, malaria (Haiti)	Acute histoplasmosis, leptospirosis
Central America	Dengue, malaria (primarily <i>Plasmodium vivax</i>)	Leptospirosis, histoplasmosis, coccidioidomycosis
South America	Dengue, malaria (primarily <i>P. vivax</i>)	Bartonellosis, leptospirosis, histoplasmosis
South-central Asia	Dengue, enteric fever, malaria (primarily non-falciparum)	Chikungunya virus infection
Southeast Asia	Dengue, malaria (primarily non-falciparum)	Chikungunya virus infection, leptospirosis
Sub-Saharan Africa	Malaria (primarily <i>P. falciparum</i>), tickborne rickettsiae, acute schistosomiasis, filariasis	African trypanosomiasis

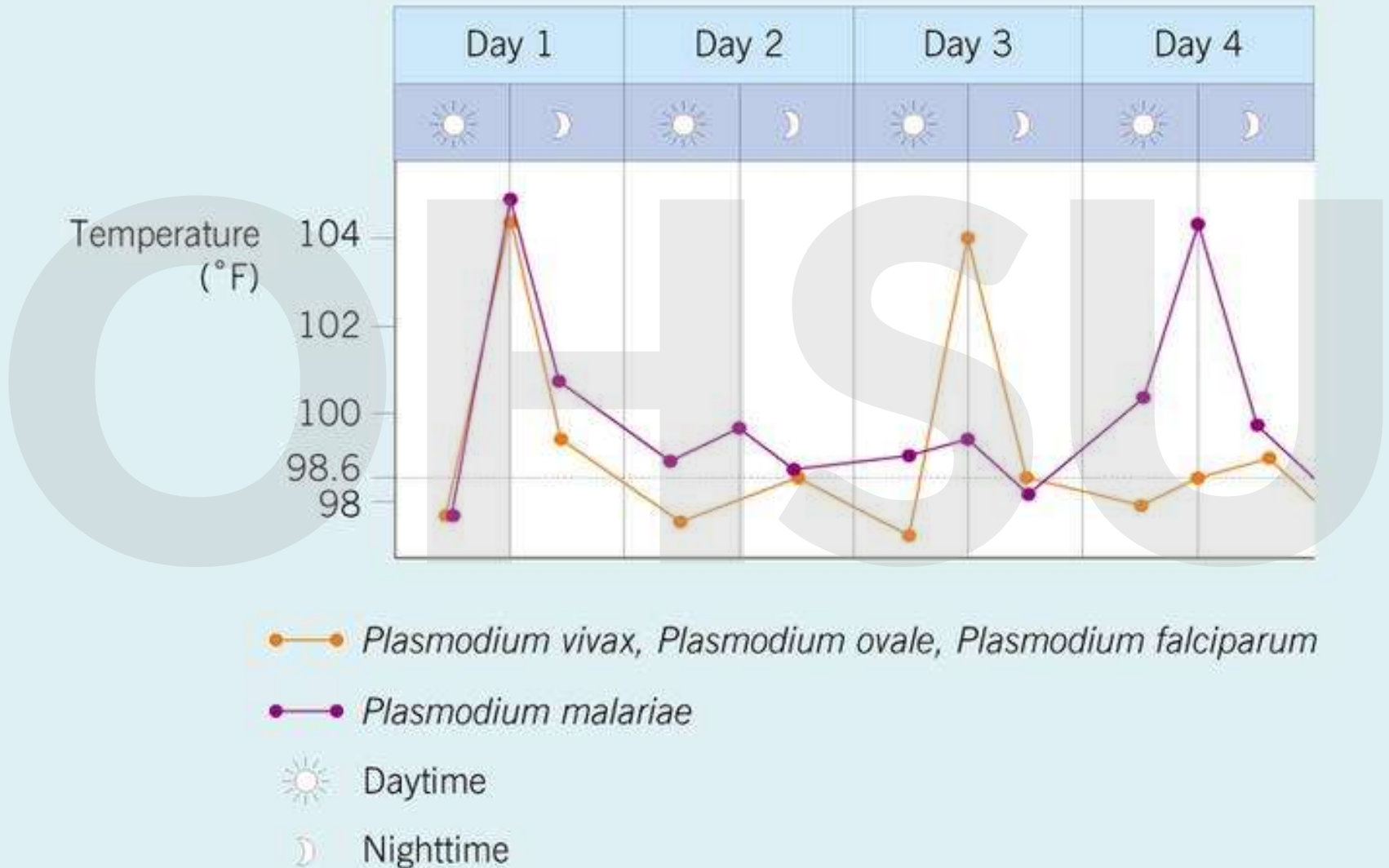
Case Eight:

A 34 year old truck driver seeks medical attention because of an intermittent fever. He has lost his appetite and has lost 10 pounds. He also has fatigue. He denies cough, dyspnea, muscle aches, vomiting, diarrhea, abdominal pain or rash. The fevers wax and wane every 1-2 weeks.

Pel Ebstein Fever



TERTIAN AND QUARTAN MALARIAL FEVER PATTERNS



Case Nine:

A 34 year old male presents with a one week history of cough, fever and mild confusion. Exam is normal except for temperature of 104, pulse = 108, RR = 24 and rales in both bases. Room air pO_2 is 66 mm Hg, HCT = 32, WBC = 6.4 (15% L), LFT's normal. Chest CT shows:



Case Nine (continued):

The patient is found to be seropositive for HIV with a CD₄ count = 6 cells. The TBO stain is positive for *P. jiroveci* but the patient does not improve after adding trimethoprim-sulfamethoxazole and prednisone.

Case Nine (continued):

After intubation, a BAL is done which reveals a CMV DNA capture of 480. The patient slowly improves after ganciclovir is added to the regimen. The patient fails highly active antiretroviral therapy but does well with long term secondary prophylaxis against *P. jiroveci* and CMV.

***Pneumocystis jiroveci* Infections in Transplant Recipients Who Did Not Receive Prophylaxis**

Incidence	5-10% for most types but > 25% for lung transplant recipients
Clinical Presentation	Prodrome < 5 days; pO ₂ often < 60 mm Hg
Survival Rates	90% in renal transplant recipients
Preventive Measures	Allo BMT recipients during months 2-6, longer if there is chronic GVHD; consider in auto BMT recipients with intense conditioning; solid organ transplant recipients for 6-12 months; lung transplant recipients for > 12 months

[Clinical Infect Diseases 2002; 34:1098-107]

Importance of a Specific Diagnosis

- Patients may have more than one diagnosis
- Optimal treatment of each agent is unique
- Clinical presentation of diseases due to noninfectious causes as well as infectious causes may be identical
- Early treatment of some infections improves outcome (example: *Aspergillus* species)

Case Ten:

A patient presents with fever, abdominal pain, nausea and vomiting. She has a long history of alcohol dependence. An amylase and lipase are obtained and the results confirm pancreatitis.

Non-Infectious Causes of Fever

- Malignancy
 - Lymphoma and renal cell carcinoma
- Collagen Vascular Disease
 - Lupus, RA, temporal arteritis, etc.
- Granulomatous diseases
 - Sarcoid, granulomatous hepatitis, etc.
- Drug (e.g., phenytoin)
- Factitious

Five More Lessons Learned

Case	Lesson
Mononucleosis & FUO	Common things are common
Dengue Fever	Fever in a traveler → think first of Dengue and malaria
Hodgkin's Lymphoma	Pay attention to the pattern
CMV and Pneumocystis	Decreased immunity should make you throw out the Razor
Pancreatitis	Not all fevers signify infection

Thank you!!!