



Photo quiz

Oct 2019
Handout

Vital Signs

- Vital Signs Given that **elevations in temperature** are often a **hallmark of infection**
- **Rectal temperatures more accurately reflect the core body temperature**
 - 0.4°C (0.7°F) and 0.8°C (1.4°F) higher than oral and axillary temperatures
 - **For every 1°C (1.8°F) increase in core temperature, the heart rate typically rises by 15–20 beats/ min.**

- **Relative bradycardia (Faget sign)**

- *Salmonella typhi*, *Brucella* spp., *Leptospira interrogans*, Tick-borne organisms *Rickettsia* spp., *Orientia tsutsugamushi* (scrub typhus), *C. burnetii* (Q Fever), Legionella
- Viruses/viral infections
 - Yellow fever virus, Dengue virus Viral hemorrhagic fever, Viral myocarditis

- Gram negative intracellular bacteria **except** leptospirosis
- Intracellular parasites
- Viruses responsible for hemorrhagic fever

Jean-Charles Faget

by Jarrad Hall and Dr Mike Cadogan, last update June 17, 2019



Description

- Faget Sign: Relative bradycardia in association with fever (Temperature-pulse dissociation).
- Originally described by [Jean-Charles Faget](#) in patients with yellow fever (1859). '*Discordance entre la courbe du pouls et celle de la température dans la fièvre jaune.*'. Subsequently observed in multiple febrile illnesses especially intracellular bacterial infection

Jean-Charles Faget (1818 – 1884) was a French physician.

Faget was famous for recognizing and recording the symptoms of Yellow Fever correctly (jaundice and vomit containing blood). He proposed Yellow Fever was a disease caused by a microorganism that was brought to New Orleans by shipping.

Faget reported an exception to the **Liebermeister rule** in his description of yellow fever [**Faget sign**] in 1858

Faget was an advocate of pain relief during childbirth and was the first doctor in Louisiana to administer chloroform during labour



Carl von Liebermeister (1833 – 1901)
was a German Physician

Liebermeister rule:

Defining the relationship between pulse frequency and body temperature in fever. In fever, when the body temperature increases by one degree centigrade, the pulse frequency increases by eight beats per minute

Proposed mechanisms of relative bradycardia

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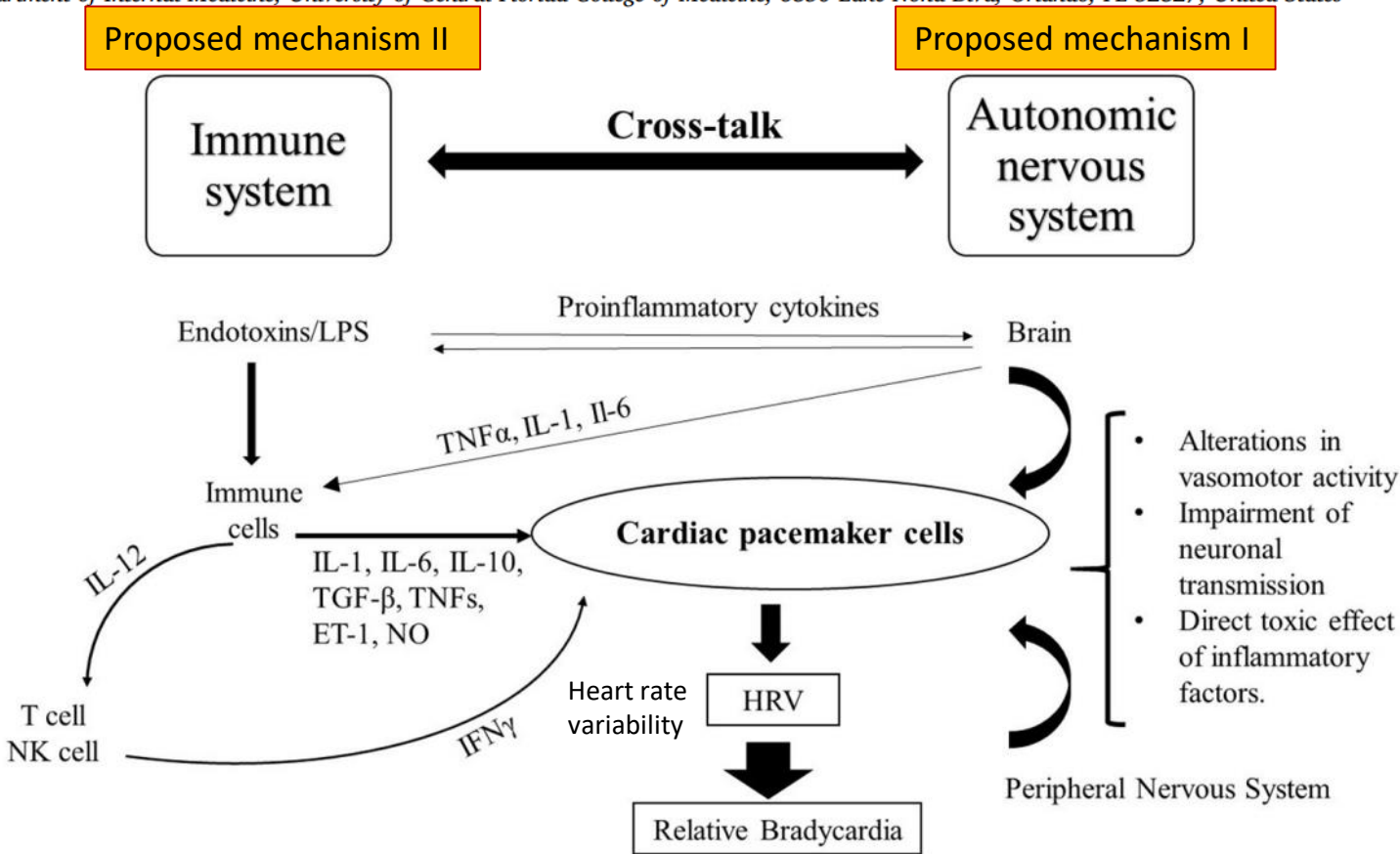
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Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy



- Hypothesis that major changes in HR are driven by **neurohumoral regulation**.
- The mechanisms that have been proposed for relative bradycardia include **an imbalance in sympathovagal activation and/or abnormal baroreflex function**;
- However, the mechanism by which systemic inflammation induces regularization of relative bradycardia is unclear.

Unclear

Cutis verticis gyrata

- **Cutis verticis gyrata (CVG)** is a rare congenital or acquired scalp condition characterized by **convoluted folds** and **deep furrows** that resemble the surface of the cerebral cortex
 - **Rare disorder**, with an estimated prevalence of 1 in 100,000 in males and 0.026 in 100,000 in females

CLASSIFICATION : CVG is classified as

Typically appears after puberty, with 90 percent of cases occurring before the age of 30 years

1. **Primary essential cutis verticis gyrata** occurs in isolation in otherwise normal individuals.
2. **The primary nonessential form** is associated with neuropsychiatric or ophthalmologic abnormalities.
3. **Secondary cutis verticis gyrata** results from neoplastic or inflammatory scalp conditions, systemic diseases, or genetic disorders.

Usually, the scalp folds and furrows show a disordered pattern and are **asymmetrically distributed** over the scalp

Associated conditions with secondary CVG

- **Benign scalp tumors and hamartomas**, including cerebriform intradermal nevus, neurofibromas, fibroma, cylindroma, collagenoma, nevus lipomatosus, and connective tissue nevi
- **Inflammatory dermatoses**, including eczema, psoriasis, acne, and pemphigus
- **Internal malignancies**
- **Endocrine diseases**, including **acromegaly**, myxedema, Graves disease, acanthosis nigricans, and insulin resistance syndrome
- **Amyloidosis**
- **Hyper-IgE syndrome**
- **Treatment** with vemurafenib and whole-brain radiotherapy (melanoma)
- **Human immunodeficiency virus (HIV)-related lipodystrophy**
- **Genetic syndromes**, including Turner syndrome, Klinefelter syndrome, Noonan syndrome, Darier disease, cutaneous leiomyomatosis, craniosynostosis syndromes (Apert syndrome, Beare-Stevenson syndrome)

Cutis Verticis Gyrata in Men Affected by HIV-Related Lipodystrophy



- **HIV-associated lipodystrophy (HIVLD)** is a condition characterized by an atypical distribution of body fat and metabolic abnormalities including insulin resistance and dyslipidemia.
 - It is estimated to **affect 13–62%**
- More commonly with regimens including **thymidine analog** nucleoside reverse transcriptase inhibitors (NRTIs) and selected protease inhibitors (PIs)
- **We report four patients with HIVLD** who developed cutis verticis gyrata (CVG).

Results and Discussion



FIGURE 1

- All four patients were male. At the time of presentation, their ages were 50, 52, 59, and 61, and they had been aware of their HIV-positive status for 16, 13, 30, and 16 years,
- Their most recent CD4 counts were 470, 531, 399, and 560 cells/mm³, and all patients had **undetectable viral loads**.
- NRTIs stavudine ($n=2$) and zidovudine ($n=3$)
- **Metabolic profile** ; Our patients did have impaired (5.6–7.0mmol/L; $n=3$) or diabetic range (>7.0 mg/dL; $n=1$) fasting glucose levels.

In summary

- Patients with CVG, who also have HIVLD (clinically diagnosed facial lipoatrophy and objective evidence of obesity and central fat accumulation), **appear to have higher fasting glucose, triglyceride, and insulin levels and a higher trunk fat: limb fat ratio than that of HIVLD patients** in the HIVLD case definition study


SUMMARY

- Primary cutis verticis gyrata is a benign condition and treatment is not needed.
 - However, patients with extensive or disfiguring lesions may require scalp reduction procedures for cosmetic reasons.
- Treatment of secondary cutis verticis gyrata is directed at the underlying condition.
- Aware for HIVLD in PLWH with CVG

Amebic VS. Pyogenic Liver abscess ?

Additional investigation ?

Epidemiological feature

Feature	Amebic liver abscess (%)	Pyogenic liver abscess (%)
Male/Female ratio	5-18	1-2.4
Duration (days)	< 14 days (75%)	5-26
Mortality (%)	10-25	0-5
Age (yr)	30-40	50-60
	Pyogenic liver abscess is disease of middle-aged persons	
Incidence (US) (case/million person/yr)	1 (10% of amebiasis)	11
	 incidence amebic liver abscess in tropical & developing country with poor sanitation	

Bennett, J. E., Dolin, R., & Blaser, M. J. (2019). *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-Book*. Elsevier Health Sciences.

Akgun Y, Tacyildiz IH, Celik Y: Amebic liver abscess: Changing trends over 20 years. *World J Surg* 23102-106, 1999.

Summary of notifiable diseases, United States. *MMWR Morb Mortal Wkly Rep.* 1994;43:800.

Johannsen EC, Sifri CD, Madoff LC. Pyogenic liver abscesses. *Infect Dis Clin North Am.* 2000;14:547-563, vii.

Hansen PS, Schonheyder HC. Pyogenic hepatic abscess: a 10-year population-based retrospective study. *APMIS.* 1998;106:396-402.

In Asia, the incidence of pyogenic liver abscess may be **5- to 10-fold higher** and is associated with the emergence of community acquired *Klebsiella pneumoniae* infection.

Epidemiological feature

Factors associated with amebic liver abscess:

- Oral-anal sexual practices
 - MSM
- Heavy alcohol consumption (>150g/day)
 - impairing Kupffer cell function or
 - impairing both cellular and humoral immunologic responses

Seeto RK, Rockey DC Amebic liver abscess: Epidemiology, clinical features, and outcome. West J Med 1999;170:104-409.

Hughes MA, Petri WA Jr. Amebic liver abscess. Infect Dis Clin North Am 2000;14(3):565-82, viii.

Bennett, J. E., Dolin, R., & Blaser, M. J. (2019). *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-Book*. Elsevier Health Sciences.

Clinical manifestation

Symptoms & signs	Amebic liver abscess (%)	Pyogenic liver abscess (%)
Fever	80	80
Weight loss	40	30
Abdominal pain	80	55
Diarrhea	15-35	10-20
Cough	10	5-10
Jaundice	10-15	10-25
RUQ tenderness	75	25-55
Leukocytosis	80	75
Elevated alkaline phosphatase	80	65
Solitary lesion	70	70

Lab. test

Clinical manifestations

- Possibly suggestive of pyogenic liver abscess

Septic Shock

Organ dysfunction or failure

Gas-forming liver abscess (Anaerobic bacteria)

Complication from cholangitis: underlying biliary tract obstruction

Direct extension from contiguous of infection: Cholecystitis, intraabdominal abscess (e.g., Subphrenic abscess, perinephric abscess)

Complication from systemic bacteremia via hepatic artery: e.g., endocarditis, CRBSI

Extension of infection via portal vein (pylephlebitis): diverticulitis, pancreatitis, IBD, postoperative infection, omphalitis, untreated appendicitis

Predisposing host factors associated with cryptogenic abscess (primary bacteremia): DM, malignancy, cirrhosis, hemochromatosis, Chronic granulomatous disease (CGD), Job's syndrome (hyper IgE syndrome)

Radiographic imaging

Magnetic resonance imaging (MRI) studies are seldom required, but they may be better at distinguishing abscesses from noninfectious liver lesions such as neoplasia.

Ultrasonography

Study of choice: avoid IV contrast & radiation exposure

Sensitivity 70-90%
Operator dependence

CT scan with IV contrast

Superior to guiding complex percutaneous aspiration drainage procedure

Improved Sensitivity ~ 95%
2/3 need IV contrast for optimal imaging

Amebic liver abscess

Classically present with a single large abscess in the right lobe of the liver, but the abscess can be anywhere and multiple lesions are not infrequent.

Serum for anti-*Entamoeba histolytica* Antibody IgG

- Amebic serology test are a cornerstone of the diagnosis of amebic liver abscess, **but lack of an accurately defined “gold standard”**

Indirect hemagglutinin assay
(IHA)

Enzyme-linked
immunosorbent assays (ELISA)

- Sensitivity & specificity ~ 95-99%
- Standard cut-off value depend on individual's test
- IHA $\geq 1:256$

False-negative results

May be obtained early (<2weeks) in the course of disease: recommend repeat serology

False-positive results

Past & current infection any form of infection

lower sensitivity was attributed to the high (5%) background titer of *E. histolytica* infection (High incidence & endemic area)
specificity was limited by high 5-10% baseline seropositivity of populations from endemic countries

Petri WA, Haque R. Entamoeba species, including amebic colitis and liver abscess. In: Benett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Canada: Saunders, an imprint of Elsevier Inc.; 2015. p. 3047-58.

Sifri CD, Madoff LC. Infections of the liver and biliary system (liver abscess, cholangitis, choecystitis). In: Benett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Canada: Saunders, an imprint of Elsevier Inc.; 2015. p. 960-8.

Stool examination

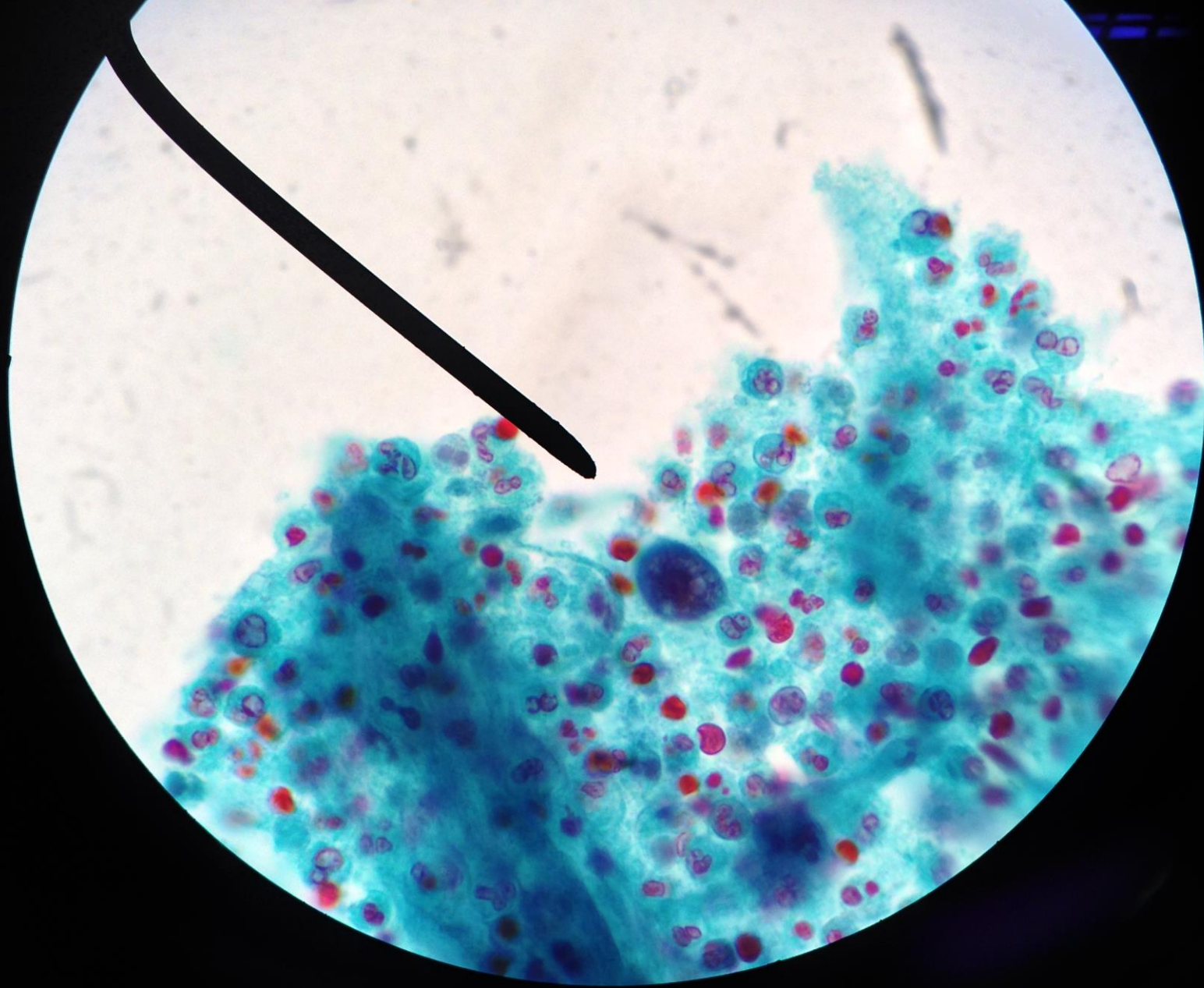
- Direct saline (wet) mount **is a very insensitive method (<10%)**
- **Presence of Entameba in stool:** is not sufficient to establish the cause of liver abscess
- **Only cyst form is found:** could not be concluded that is asymptomatic infection
- **Three morphologically identical amebae *E. histolytica*, *E. dispar*, and *E. moshkovskii*:**
 - Quadrinucleated cyst clade, 10 to 20 μm in diameter
 - *E. histolytica* trophozoites are 12-60 μm in diameter
- **Presence of ingested erythrocytes was the sole morphologic characteristic**
 - 68% *E. histolytica*
 - 16% *E. dispar* (No apparent propensity for invasive disease)

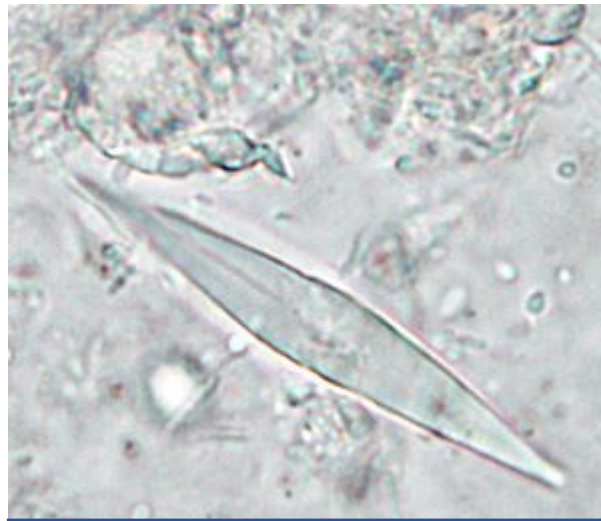
Stool culture

- **Sensitivity:**
 - Antigen detection or PCR test > stool culture > wet mount
- **Available in **only a few research laboratories****
- **Antigen detection or PCR test must be used on only cultured material**

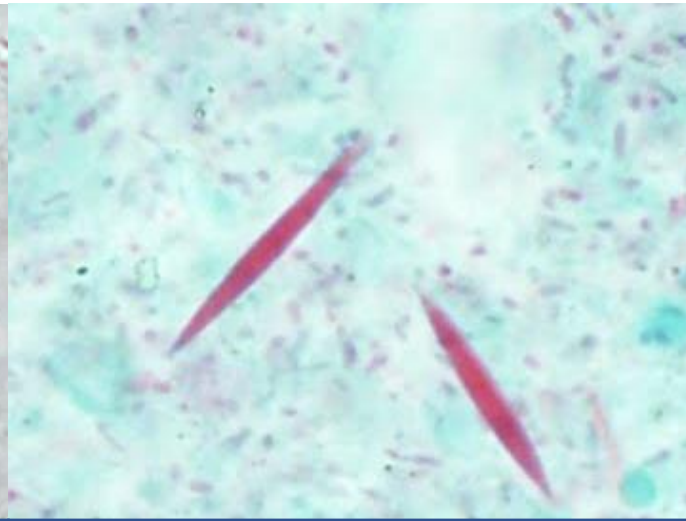


FIGURE 274-9 Endoscopic and pathologic features of intestinal amebiasis. **A**, Colonoscopic appearance of intestinal amebiasis. **B**, Colonic ulcers averaging 1 to 2 mm in diameter, on gross pathologic examination. **C**, Cross section of a flask-shaped colonic ulcer (hematoxylin and eosin stain; magnification, $\times 20$). **D**, Inflammatory response to intestinal invasion by *Entamoeba histolytica* (hematoxylin and eosin stain; magnification, $\times 100$). **Arrows** indicate *E. histolytica* trophozoites. **E** and **F**, *E. histolytica* cysts in a saline preparation (magnification, $\times 1000$). **G**, Iodine-stained cyst from stool (magnification, $\times 1000$). **H**, *E. histolytica* trophozoite with an ingested erythrocyte, in a saline preparation from stool (magnification, $\times 1000$). **I**, Trophozoite from stool stained with trichrome (magnification, $\times 1000$). (**B**, **C**, and **D** courtesy the late Dr. Harrison Juniper. From Haque R, Huston CD, Hughes M, et al. Current concepts: amebiasis. N Engl J Med. 2003;348:1565-1573.)





Fresh smear

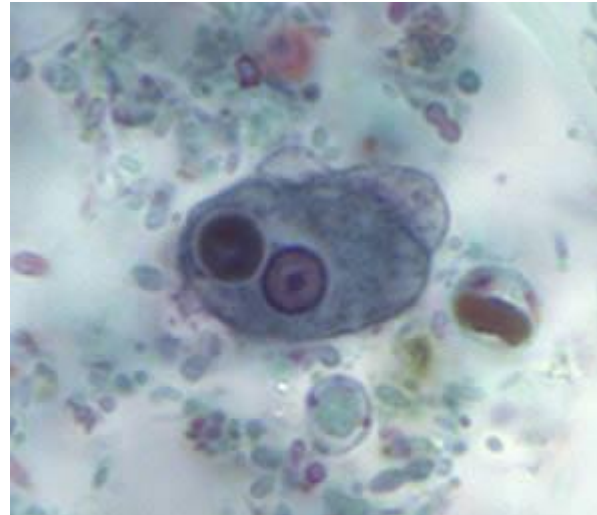


Trichrome stain

Charcot-Leyden crystals



Entamoeba histolytica trophozoite



Trichrome stain

Entamoeba histolytica trophozoite

Trophozoites มีรูปร่างที่ไม่แน่นอน มีขนาดที่แตกต่างกันมาก คือตั้งแต่ 12-50 ไมโครเมตร มีนิวเคลียสหนึ่งอันมีลักษณะเป็นแบบล้อเกวียน (cart-wheel type) โดยมี karyozome ขนาดเล็ก อยู่ตรงกลาง และมีก้อนโครมาตินขนาดเล็กเรียงตัวกันอย่างมีระเบียบที่ขอบในของเยื่อ

PCR for *E. histolytica*

- **Real-time PCR, DNA microarrays, multiplex PCR**
 - Serve as a rapid tool to diagnose amoebic liver abscess
 - A potential diagnostic tool for aspirated pus or other body fluids from patients with amoebic liver abscess, but its use is currently limited to research laboratories.
- **Fecal sample is the most complex specimens for direct PCR testing**
 - Because of the presence of PCR inhibitors (such as heme, bilirubins, bile salts, and complex carbohydrates)
 - Often coextracted along with pathogen DNA

In areas of low incidence

- Suspected amebic liver abscess should be aspirated to exclude pyogenic liver abscess
 - if there is no response to initial empirical therapy

Some investigators have argued

ข้อที่ 4

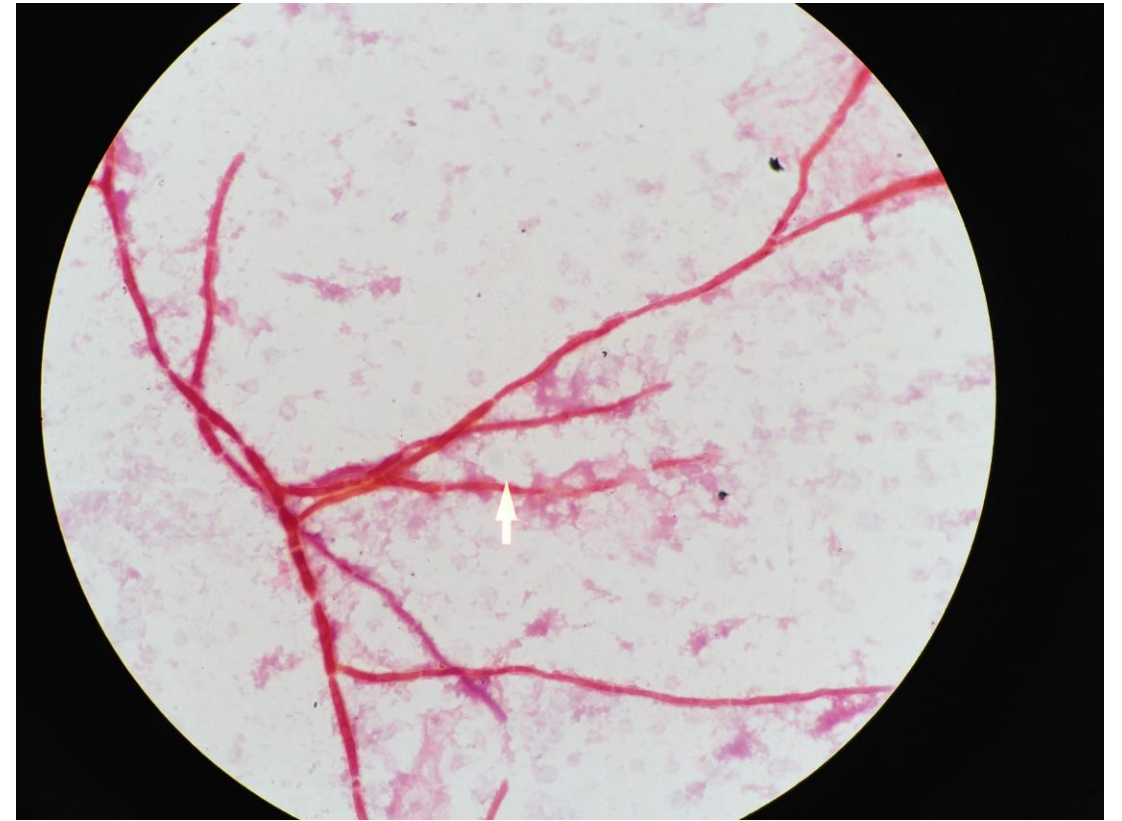
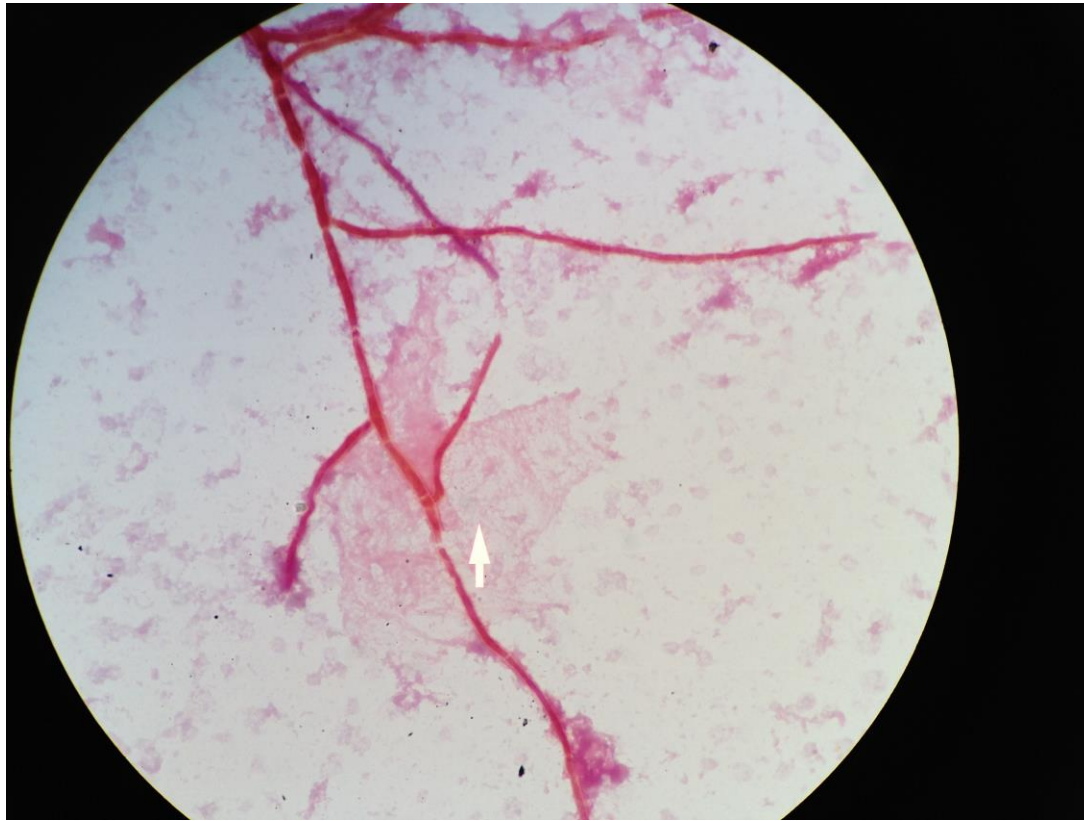
Case ผู้ป่วยชายไทยอายุ 22 ปี โรคประจำตัว Refractory T-cell Acute Lymphoblastic Leukemia หลังได้รับ 2nd line เคมีบำบัด cycle ที่ 2 นาน 5 วัน มี ANC = 0 cell/mcL

หลังได้เคมีบำบัดนาน 10 วัน สังเกต มีแผลง่ามนิวเท้า แดงกดเจ็บ (ภาพที่ 1) ไม่มีไข้ หลังได้รับยาปฏิชีวนะทางหลอดเลือด ผู้ป่วยมีไข้สูง และเท้าปวดบวมแดงร้อนมากขึ้น (ภาพที่ 2) และผื่นขึ้นตามตัวเป็น subcutaneous nodule 0.5-1.5 cm (ภาพที่ 3)

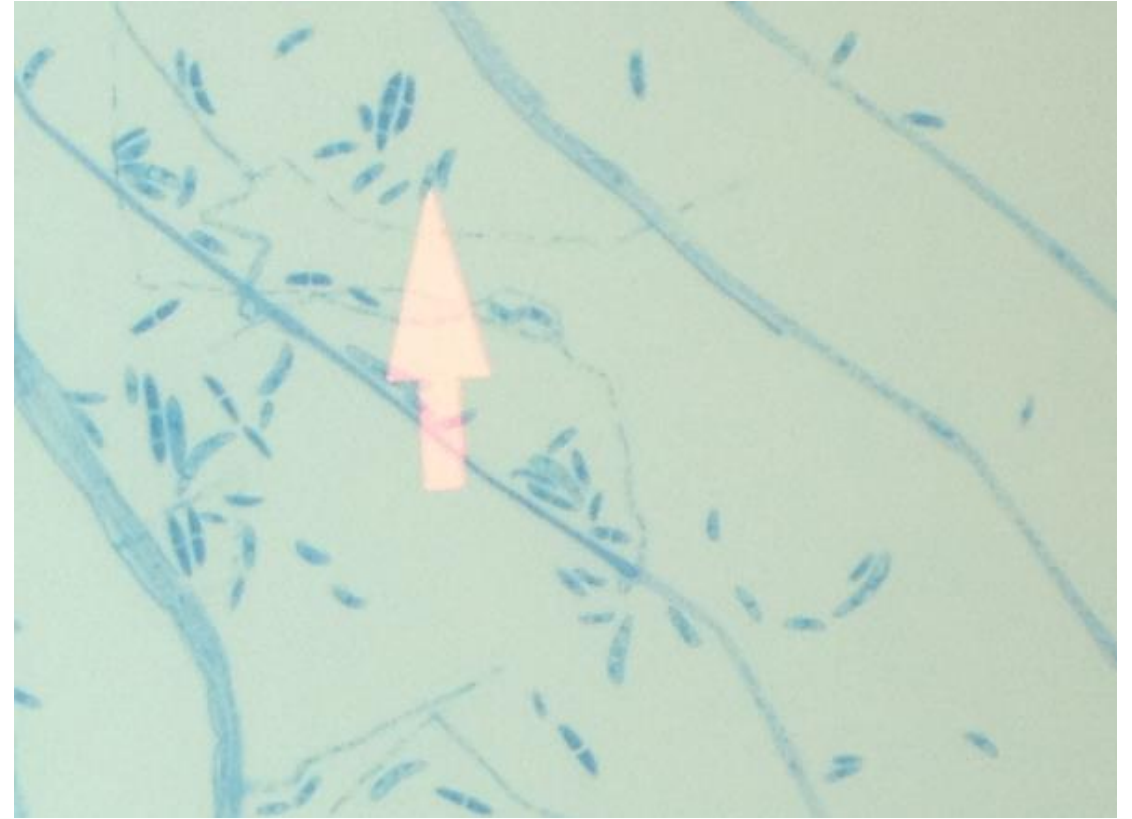
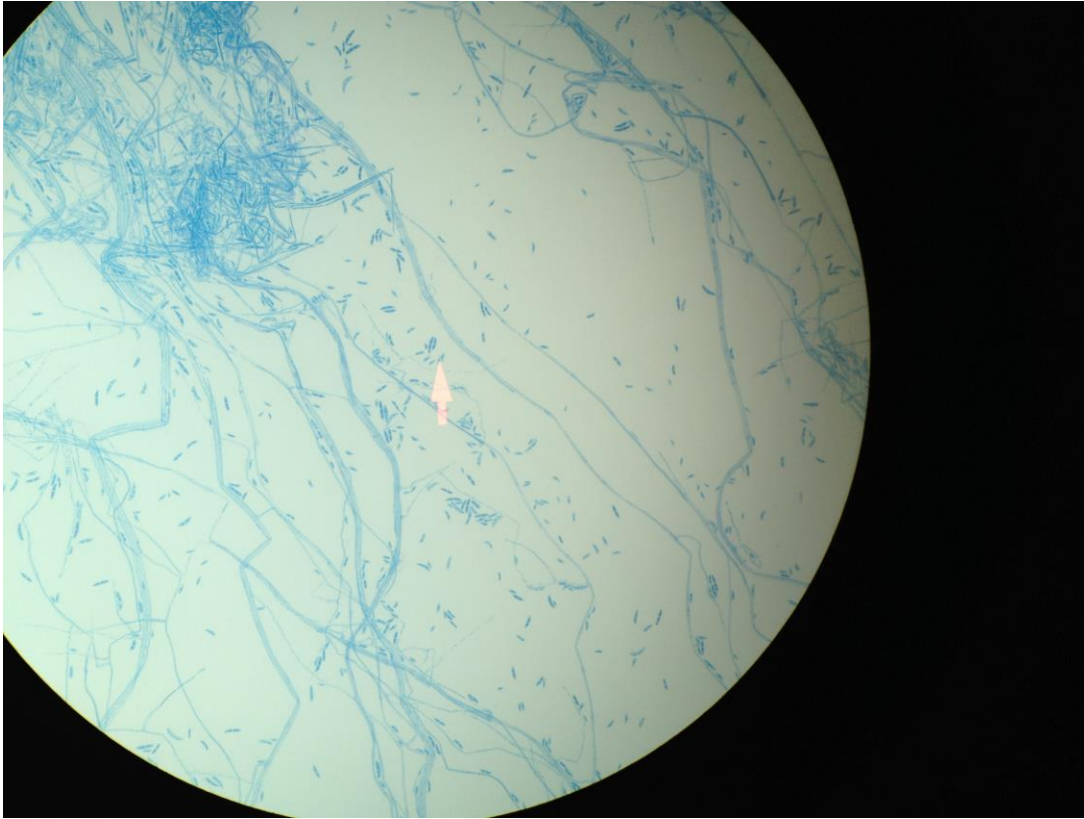
คำถาม ผลเพาะเชื้อจากเลือด (hemoculture) รายงานว่าพบจุลชีพ

1. จงบรรยายลักษณะจุลชีพ ที่พบจากการย้อมน้ำเลี้ยงเชื้อด้วย Gram stain
2. จงบอกชื่อสายพันธุ์ของเชื้อก่อโรค (species) ที่พบ

Hemoculture gram stain



Lactophenol cotton blue



ឆេត

1. Acute angle branching, septate hyphae with fusiform and septate macroconidia

2. Fusarium spp.

FUSARIUM SPP

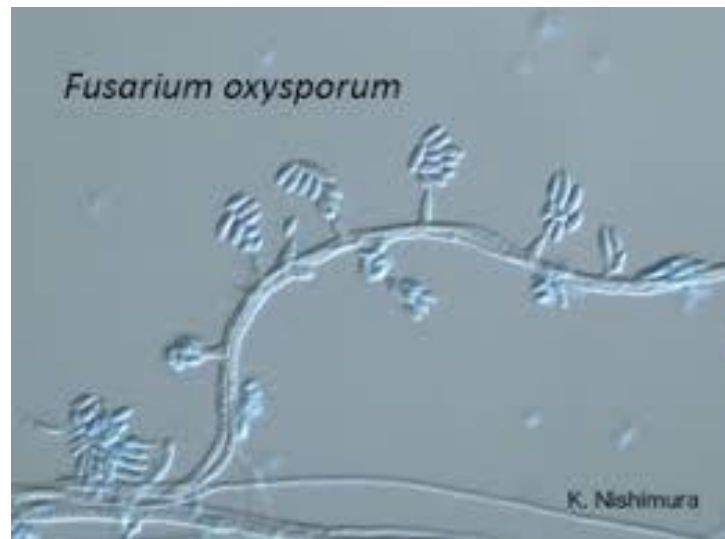
- Can cause **disseminated infection in immunocompromised patients**
- Common cause of **keratitis and other eye infections** in contact lens wearers and following trauma
- Skin and soft tissue infection after trauma, onychomycosis; can cause mycetoma
- **Epidemiology**
 - Common plant pathogens; found in soil and organic debris
 - Has been recovered in hospital water supplies
- **Microbiology**
 - *F. solani* is the most common pathogen, although other species may also cause infection.
 - **Fusarium produces banana- (or crescent)- shaped multicellular macroconidia in culture.**
- **Diagnosis**
 - Recovery of the fungus from culture of an otherwise sterile site
 - **One of the few molds that are commonly recovered from blood culture**
- **Therapy**
 - Optimum therapy is not known.
 - Recovery from neutropenia is essential in response to therapy of disseminated infection.
 - Amphotericin B or voriconazole is suggested.



FIG. 268.9 Cutaneous lesions of disseminated infection caused by *Fusarium moniliforme*. (From Beneke ES, Rogers AL. Medical Mycology and Human Mycoses. Belmont, CA: Star Publishing Company; 1996.)



FIG. 268.10 Multiple necrotic skin lesions in a neutropenic patient with hematogenously disseminated fusariosis.



Classic sickle or canoe shaped macroconidia of *Fusarium*. Photo credit: <http://quizlet.com/5109839/mycology-photos-flash-cards/>