Anaerobic infections

PART 3: Infection with Gram-negative obligate anaerobes (*Bacteroides* spp. and other abscess-forming bacteria)

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What are these lectures about?

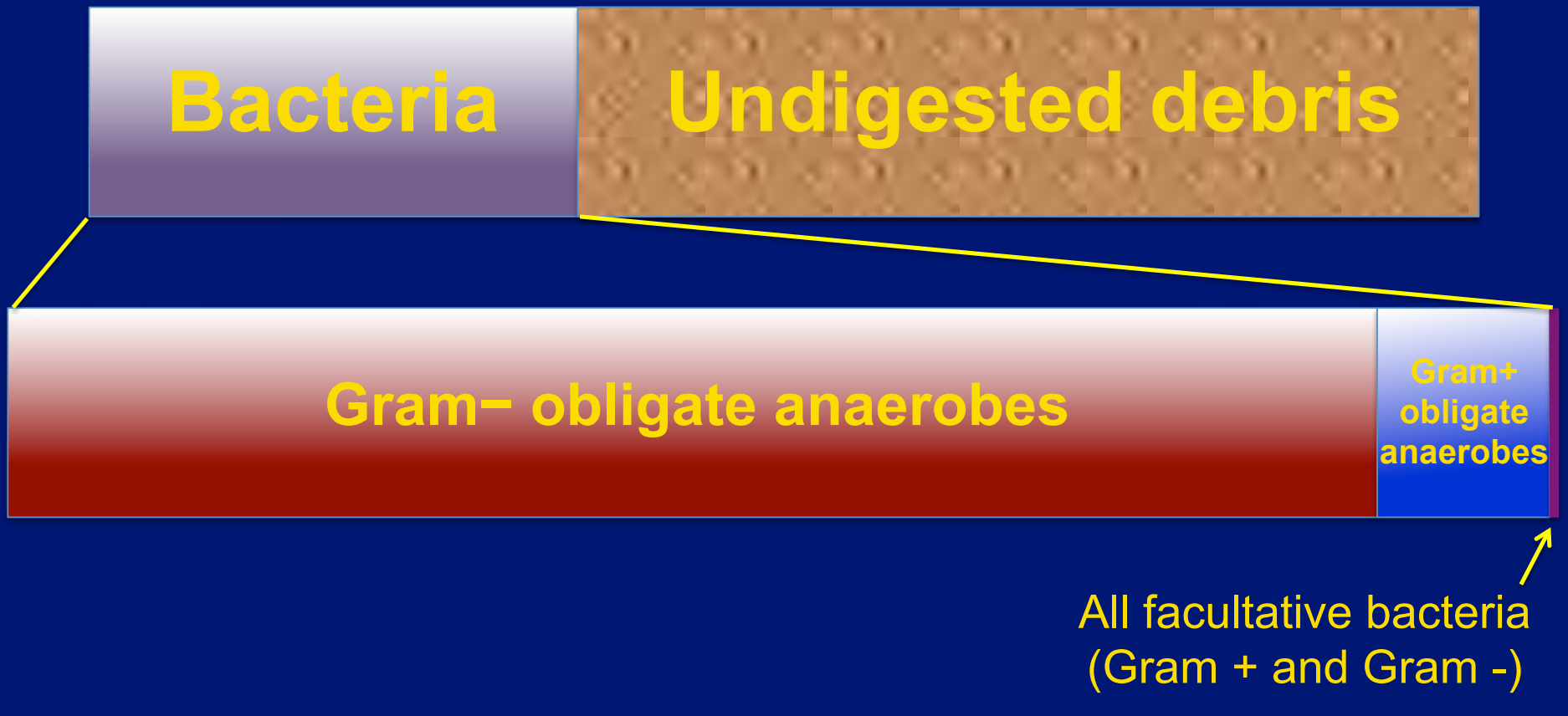
- *Clostridium* spp.
  - Gas gangrene/myonecrosis — *C. perfringens, C. septicum, C. histolyticum, C. novyi,* etc.
  - Tetanus — *C. tetani*
  - Botulism — *C. botulinum*
  - Antibiotic-associated colitis — *C. difficile*
- *Bacteroides* spp.
  - Abscesses — *B. fragilis, B. distasonis, B. thetaiotamicron*
- Other obligate anaerobes — *Fusobacterium, Prevotella, Porphyromonas* spp.

Bacterial species in the colon present in >90% of fecal specimens

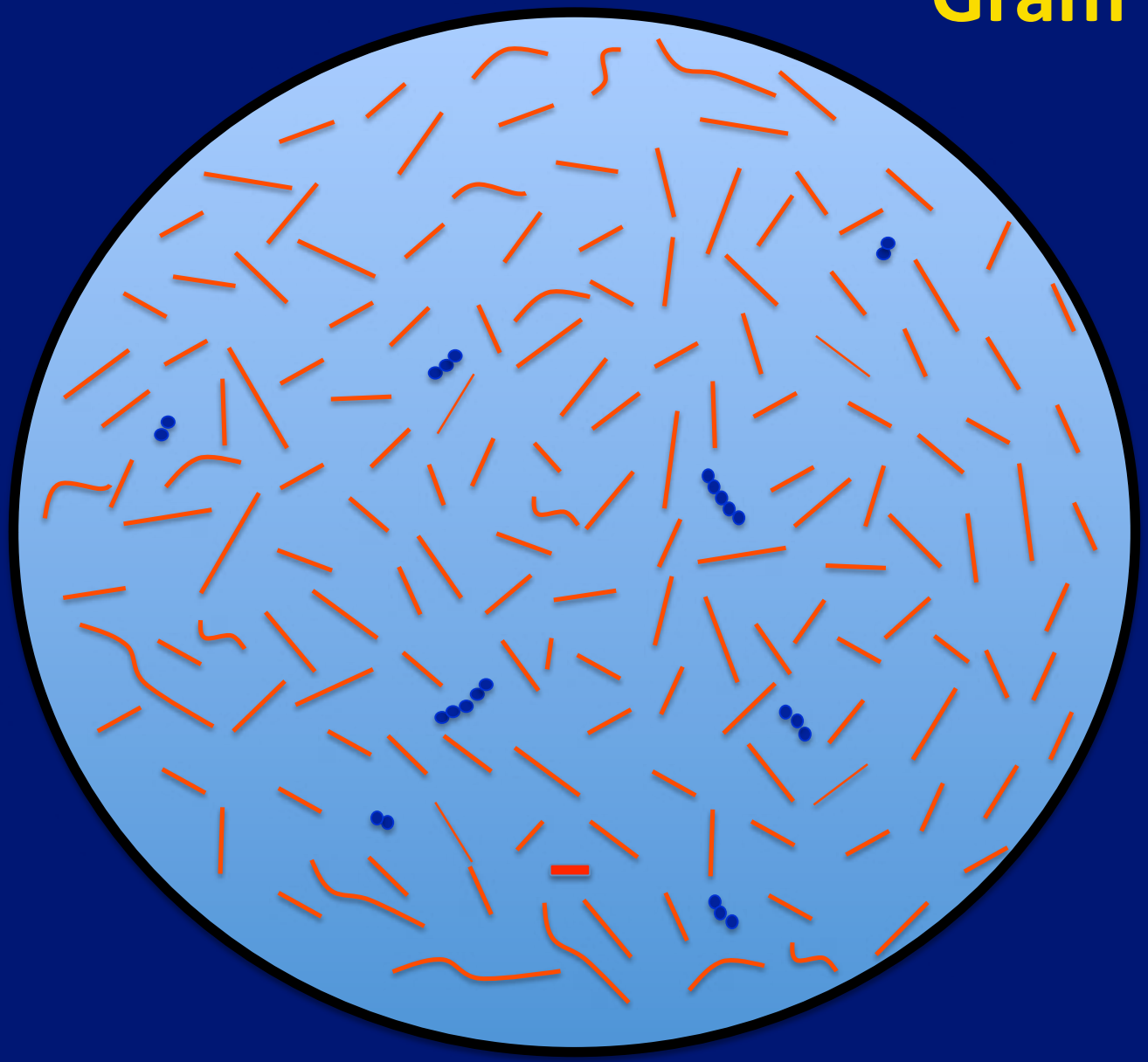
Bacterial Category	Log organisms/gm (dry weight)	Range of log organisms/ gm (dry weight)
Bacteroides	11.3	9.3 – 13.8
Eubacterium	10.8	5.1 – 13.6
Anaerobic cocci	10.7	4.0 – 13.6
Clostridium	9.9	4.0 – 13.2
Streptococcus	8.9	3.9 – 12.8
Gram-negative facultative	8.7	4.0 – 12.5
Other facultative organisms	6.8	1.0 – 12.5

Data Source: Mandell et al. Principles & Practice of infectious Diseases

Composition of Feces



Gram Stain of Feces



Gram-negative obligate anaerobes

Gram-positive obligate anaerobes

Gram-negative facultative bacteria

Gram-positive facultative bacteria

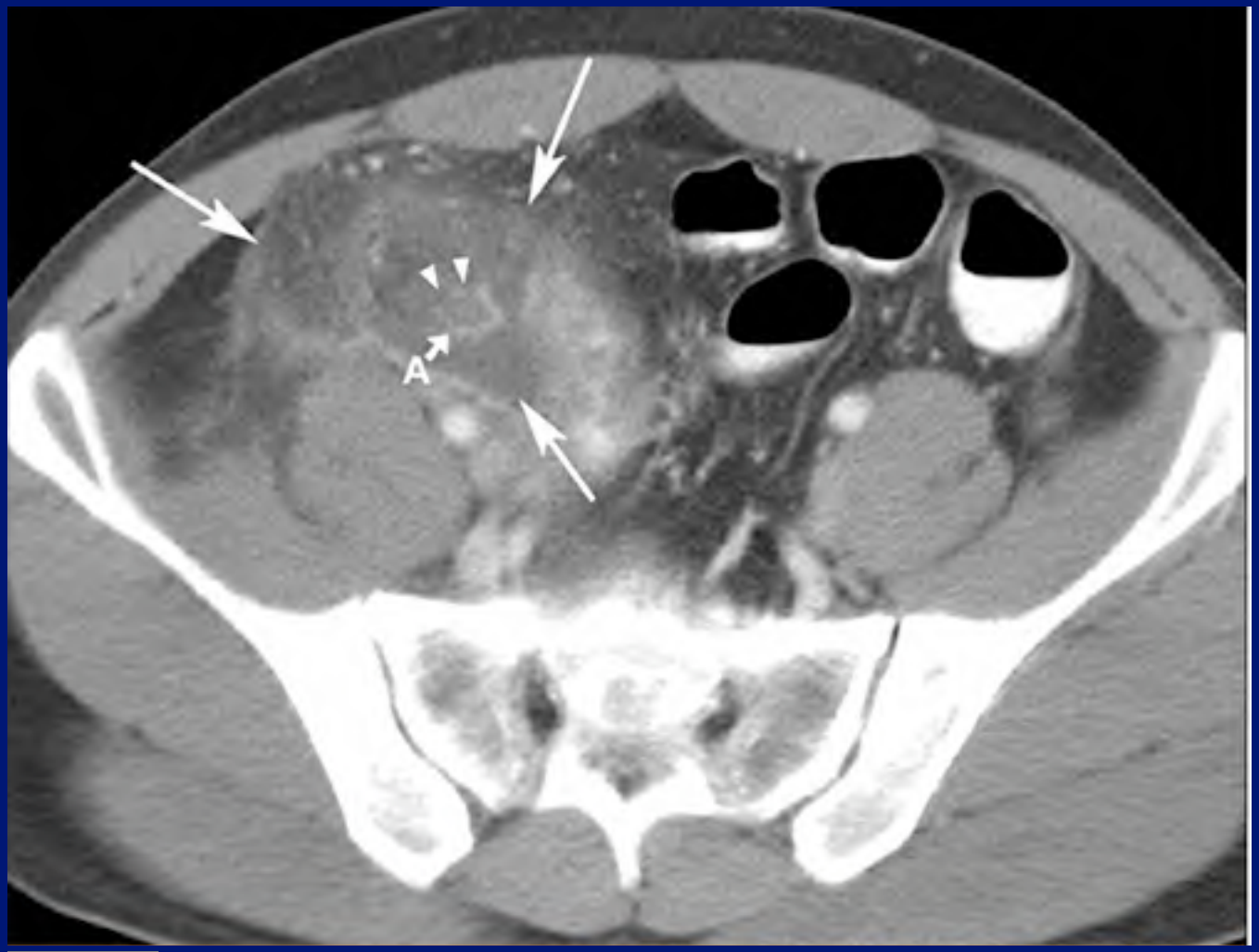
Case: appendicitis

- An 18-year-old college freshman comes to the hospital with diffuse abdominal pain, diarrhea, and nausea without vomiting. Pain is localized to the right side of the abdomen.
- P.E.: tenderness with rebound tenderness over the right lower quadrant.
- She is treated with a 1st generation cephalosporin
- She is taken to surgery where a perforated appendix is removed. The surrounding peritoneum is irrigated.
- Cultures of the peritoneum grow a mixture of bacteria, typical of those found in stool.

Case (continued)

- On post-op day #2, her temp spikes to 38.6°C.
- Blood cultures obtained preoperatively grow *E. coli.*
- She completes a 7-day course of cefazolin and improves. Since she has no further symptoms and follow-up blood cultures are negative, the antibiotic is stopped.
- 36 hours later, her temperature is 38.8°C and she feels diffuse pain over the site of the appendectomy.
- A CT scan of her abdomen reveals a retroperitoneal abscess.

CT scan: Ruptured Appendix

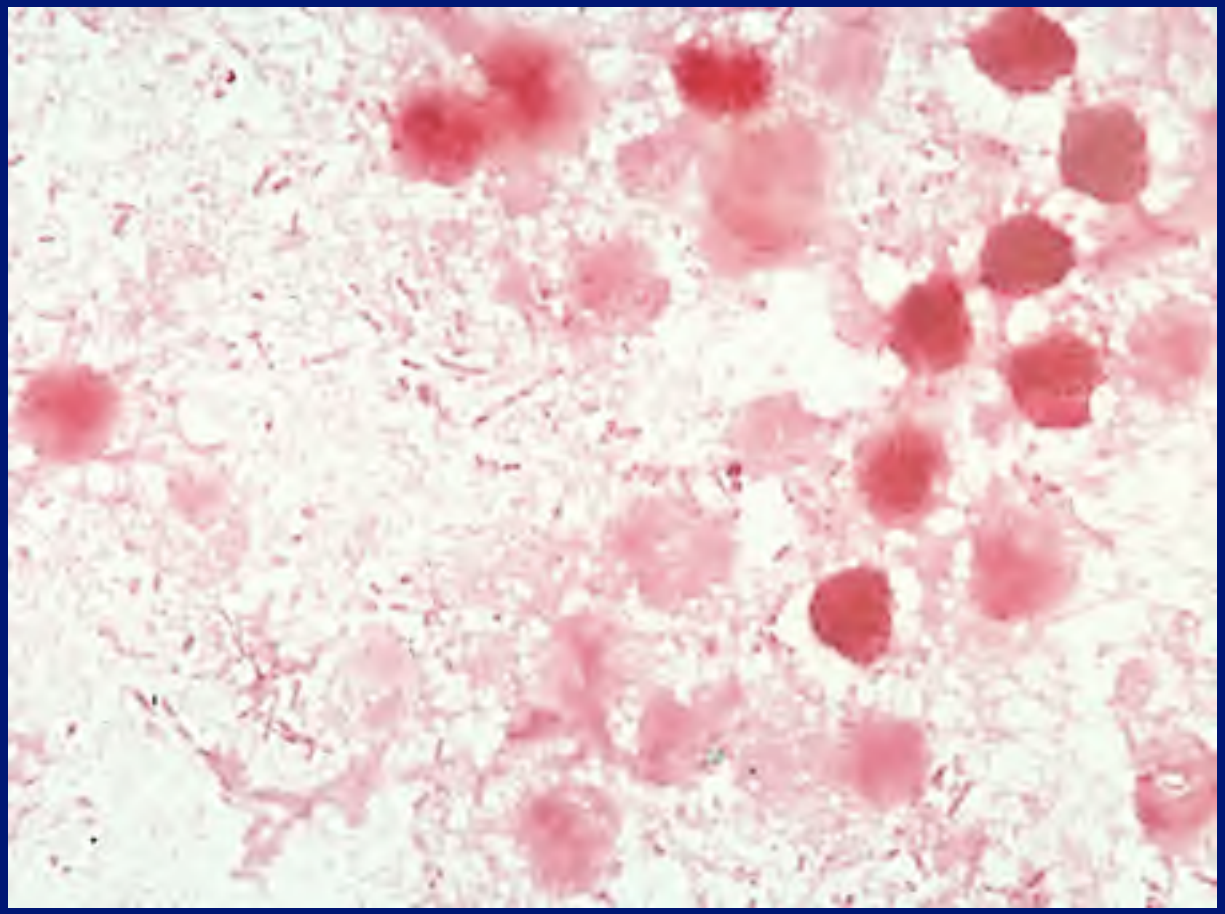


 Yu J et al. Am J Roentgenol. 2005;184(4):1136-1142.

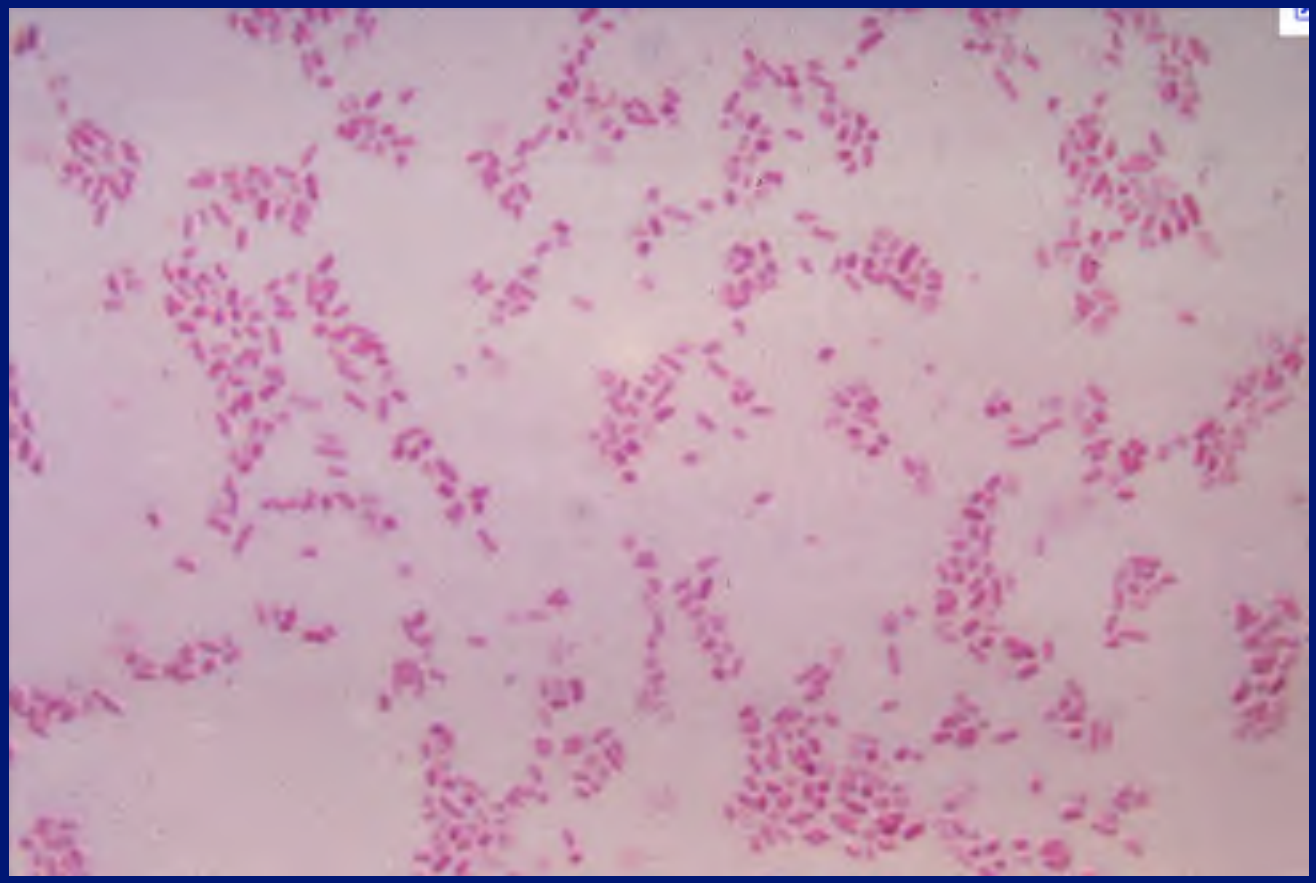
Case (continued)

- The abscess is drained, and cultures of pus from the drainage grow *Bacteroides fragilis*.
- She is treated with ampicillin-sulbactam for 14 more days. Her drain is pulled after 7 days, and she has an uneventful recovery.

Gram stain of drainage



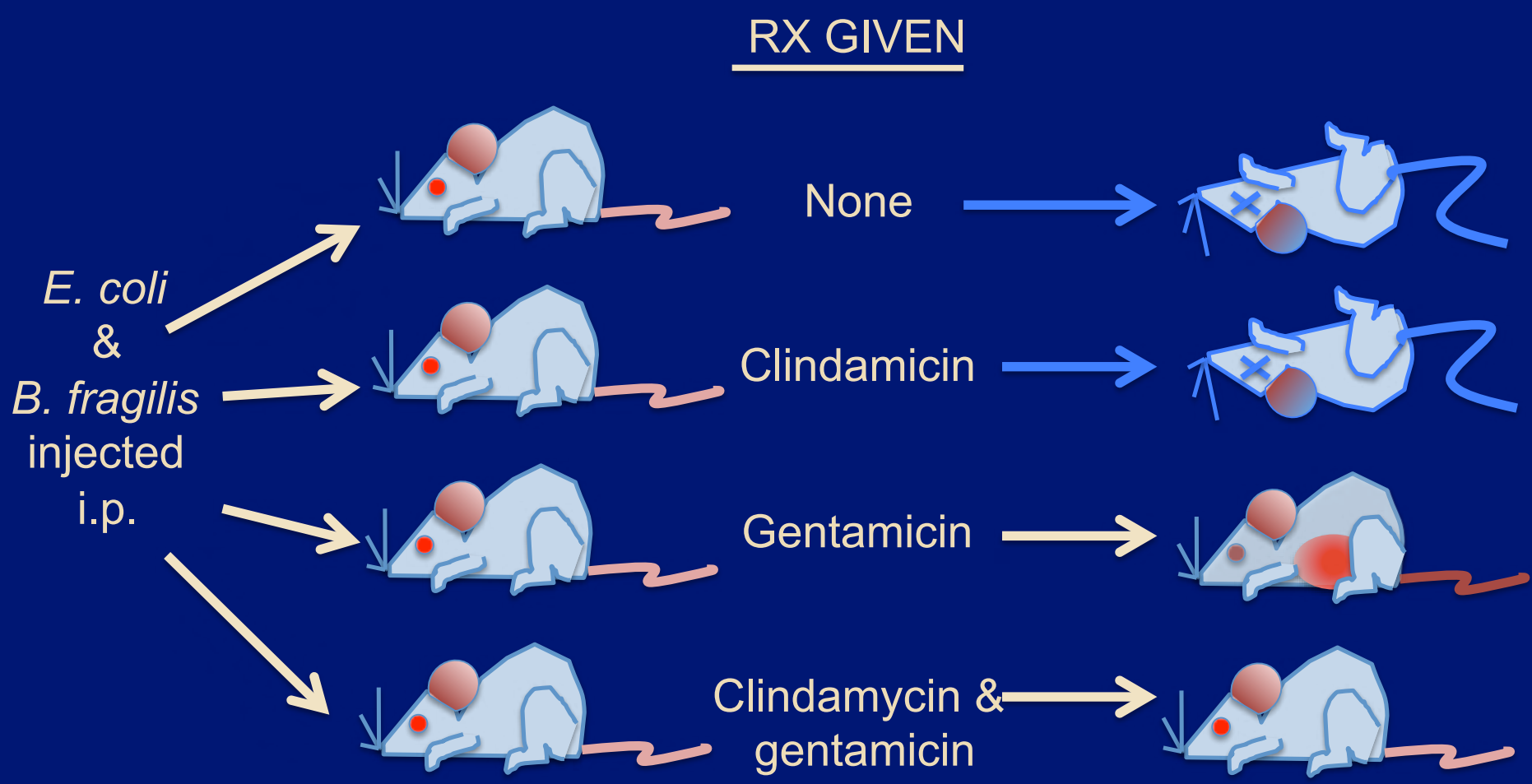
B. fragilis in pure culture



Questions to consider

- How did the two episodes of her disease differ with regard to pathogenesis and to the kind of bacteria involved?
- Why did *B. fragilis* survive the first course of antibiotic treatment?
- Was she treated properly? What could have been done to lessen the likelihood of abscess formation?
- How does *B. fragilis* facilitate intra-abdominal abscess formation?

Gorbach's experiment



Bacteroides spp.

- Obligate anaerobes
- 25% of all colonic bacteria
- Usually involved in infections resulting from perforation of an abdominal viscus
  - ruptured appendix
  - diverticulitis
  - post-op after bowel surgery and/or dehiscence of a surgical anastamosis
- Any *Bacteroides* spp. may be involved in a polymicrobial infection, but most abscesses contain *B. fragilis*

Survival features of *Bacteroides*

- Bacterial enzymes digest complex polysaccharides
  - Nutritional advantage
  - May improve human nutrition by digesting complex plant polysaccharides in food (symbiosis with the host)
  - Can digest and consume human glycans, (e.g., mucin, hyaluronate, chondroitin SO_4)
  - Neuraminidase: exposes sialylated polysaccharides to enzyme digestion (required for abscess formation)
- *Bacteroides* spp. are relatively aerotolerant
  - Human peritoneum and tissues are less anaerobic than the colon

What's special about *B. fragilis* ?

1. More aerotolerant than other species and more resistant to reactive oxygen species
   - Possesses a superoxide dismutase (SOD)
   - Possesses catalase (CAT)

$$O_2^{\cdot} + 2H_2O \xrightarrow{SOD} 2H_2O_2$$

$$2H_2O_2 \xrightarrow{CAT} 2H_2O + O_2$$

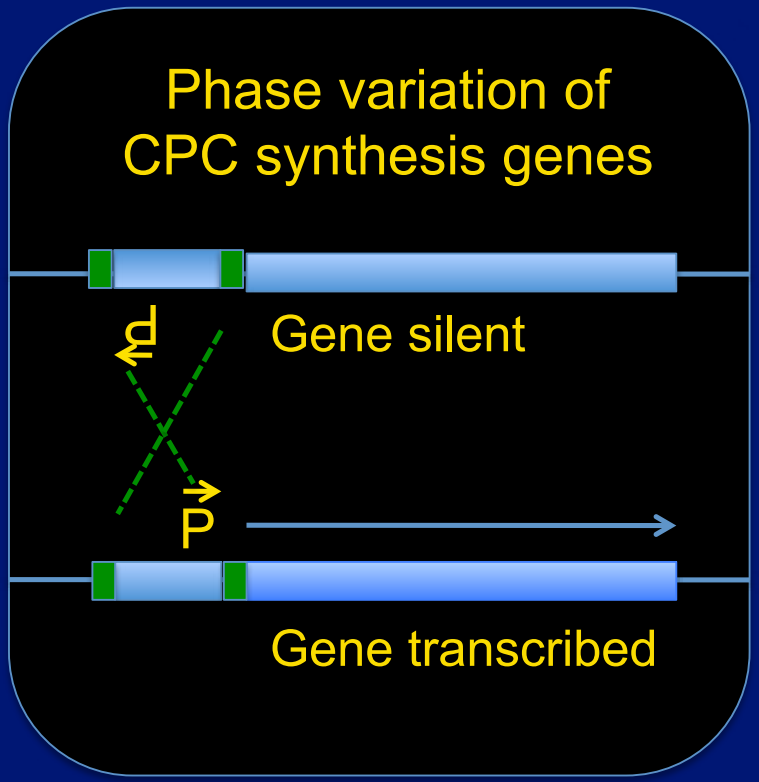
What's special about *B. fragilis* ?

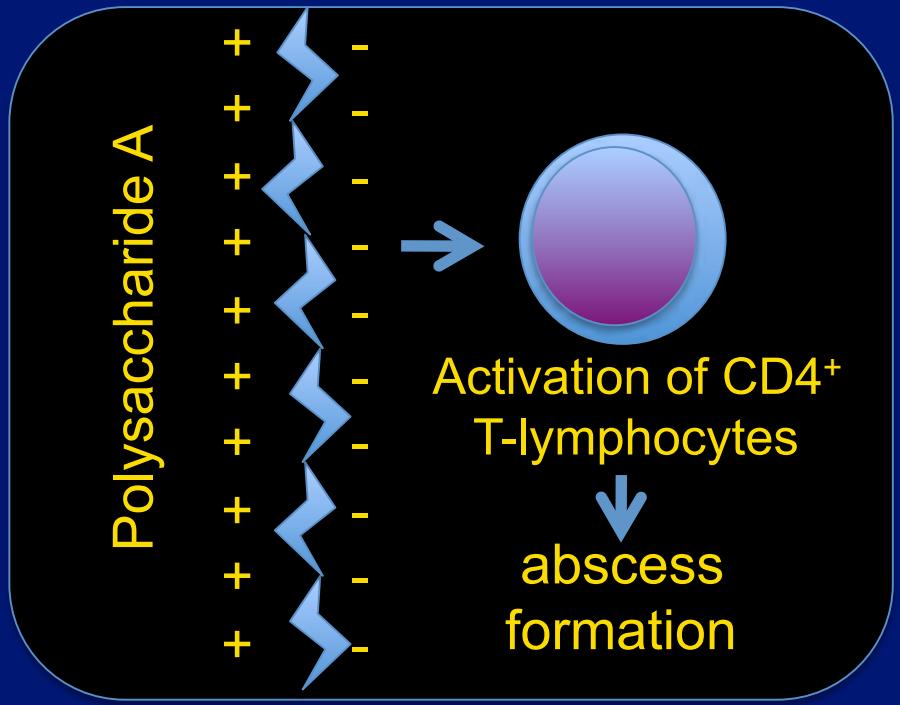
2. The outer membrane LPS (lipid A) is modified to be less toxic than that of *E. coli*
   - Allows for host tolerance of large numbers of organisms without toxicity

What's special about *B. fragilis* ?

3. It has a complex capsular polysaccharide that is essential for abscess formation
   - Composed of at least 8 polysaccharides
   - Each is capable of transcriptional phase variation (synthesis genes preceded by an invertable region containing a promotor)
   - Polysaccharide A is essential for abscesses in animal models and is zwitterionic

Special features of *B. fragilis* CPC





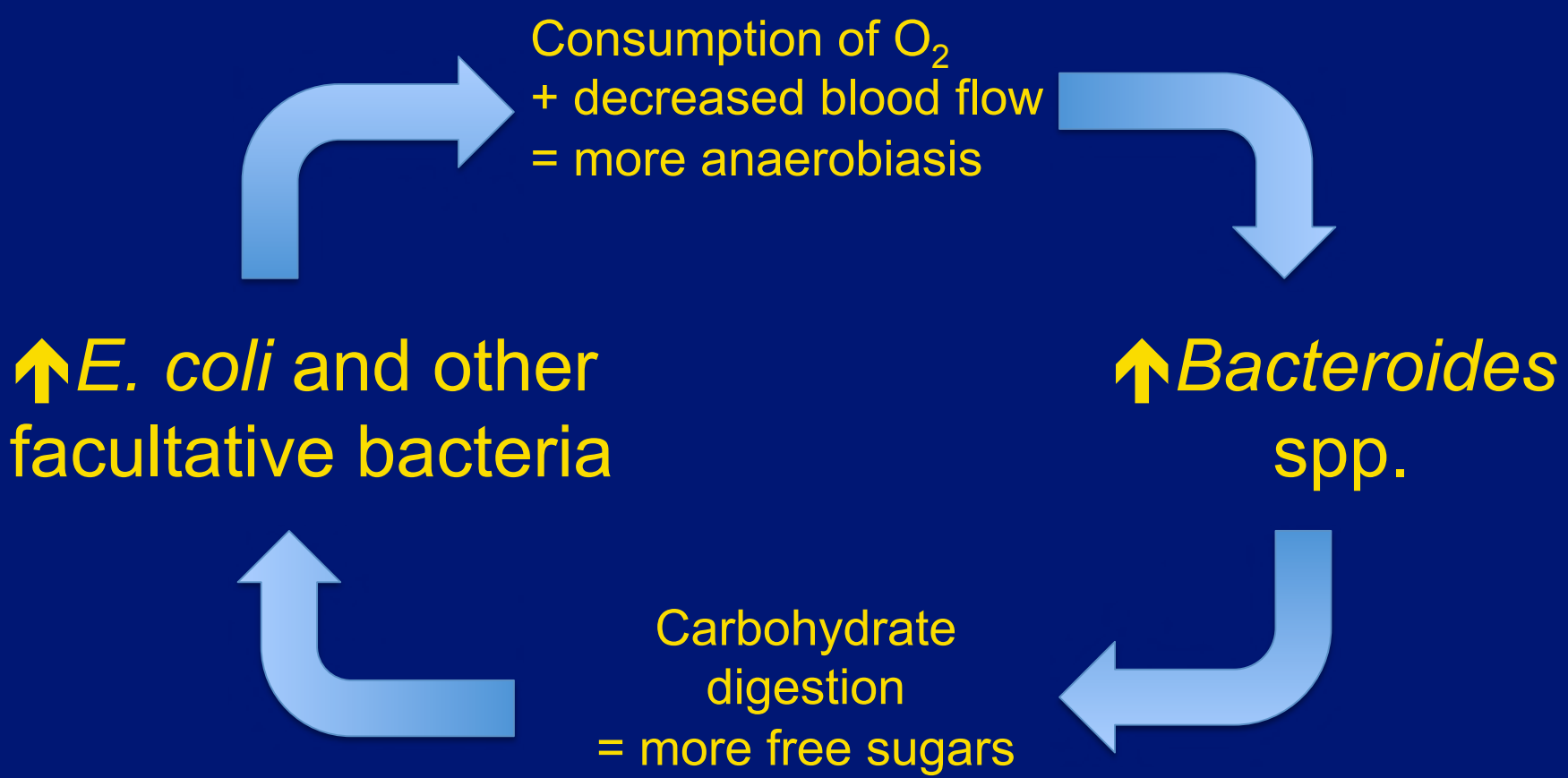
Antibiotic resistance in *Bacteroides*

- Most carry a beta-lactamase gene (resistant to penicillin, ampicillin, 1st gen. ceph.)
- Harbors conjugative transposons
  - Can exchange genes with other *Bacteroides* and with other species
  - ex. clindamycin resistance (only ~60% sensitive now)

Abscess formation

- Infectious inoculum is high
- Spillage of intestinal contents into the peritoneum → most are killed by the immediate inflammatory response
- Containment by the omentum
- Facultative bacteria establish first
- Aerotolerant anaerobes survive
- Microbial synergy is usually required

Microbial synergy in abscess formation



Response to bacteria in the peritoneum

- Role of the omentum
- Inflammatory mediators increase vascular permeability → plasma and fibrin influx
  - fibrous collagenous capsule forms around site
  - central area features acidic pH, live and dead PMNs, and mixed bacterial flora
  - may include other *Bacteroides*, *Clostridia*, or *Peptostreptococcus* spp.)

Treatment of peritonitis and peritoneal abscesses

- Abscesses must be drained surgically or by percutaneous catheters (+ repair any leak)
- Antibiotic therapy effective against colonic flora, including facultative and obligate anaerobic organisms
  - β-lactams or cephalosporins + metronidazole
  - β-lactam-β-lactamase inhibitor combinations
  - Carbepenems
  - Clindamycin is becoming less useful

Questions to consider

- How did the two episodes of her disease differ with regard to pathogenesis and to the kind of bacteria involved?
- Why did *B. fragilis* survive the first course of antibiotic treatment?
- Was she treated properly? What could have been done to lessen the likelihood of abscess formation?
- How does *B. fragilis* facilitate intra-abdominal abscess formation?

Other *Bacteroides*-associated diseases and other obligate anaerobes of interest

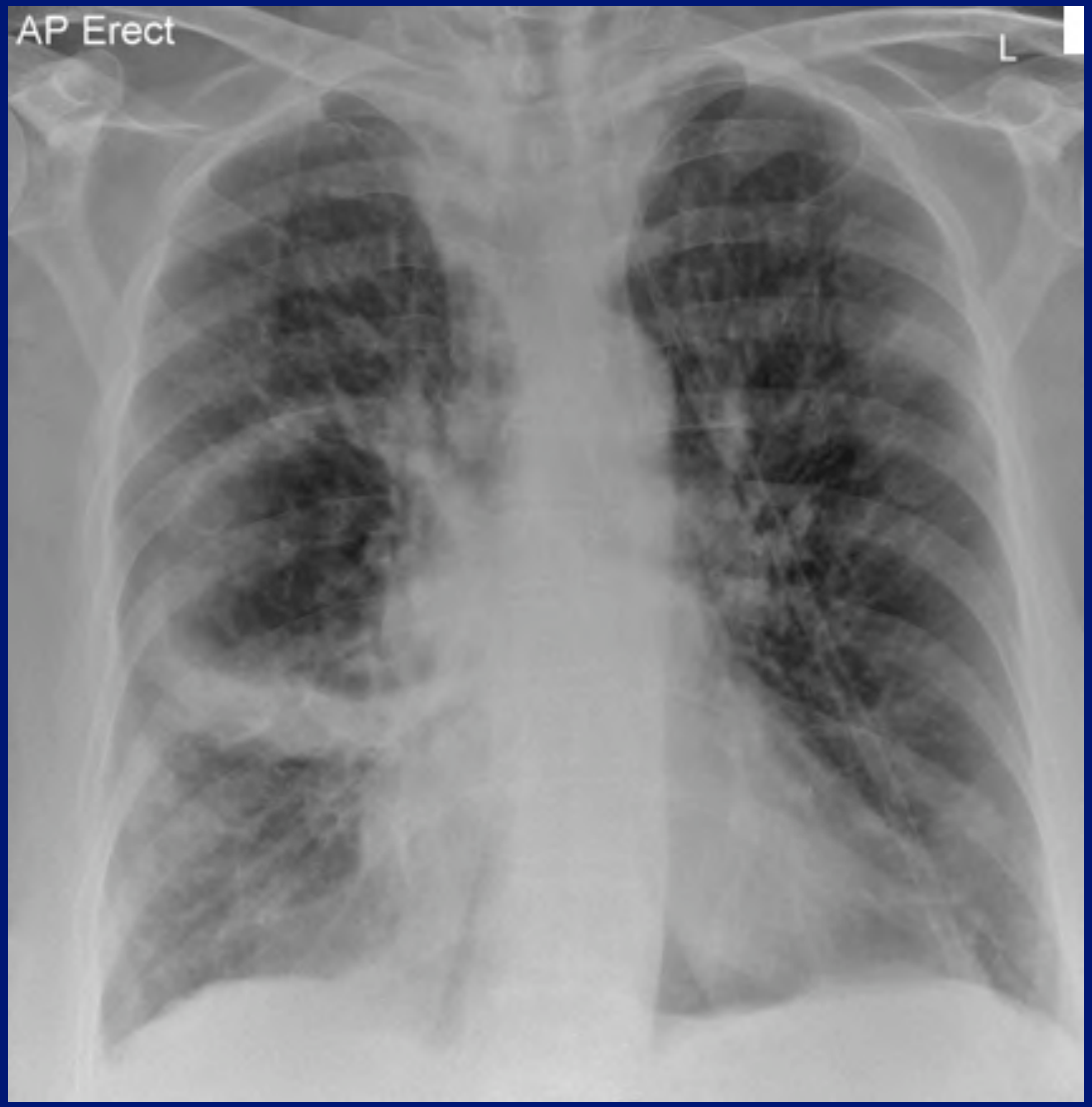
Case: Fever, cough, chest pain, and *really* bad breath

- A 53 year old man comes to the ED for fever and chest pain. He is coughing spasmodically with minimal sputum production.
- The patient is a heavy alcohol user and has had “blackouts” and seizures
- P.E. T=38.4. carious teeth noted, many fractured. Crackles over the left lung noted.

Case (continued)

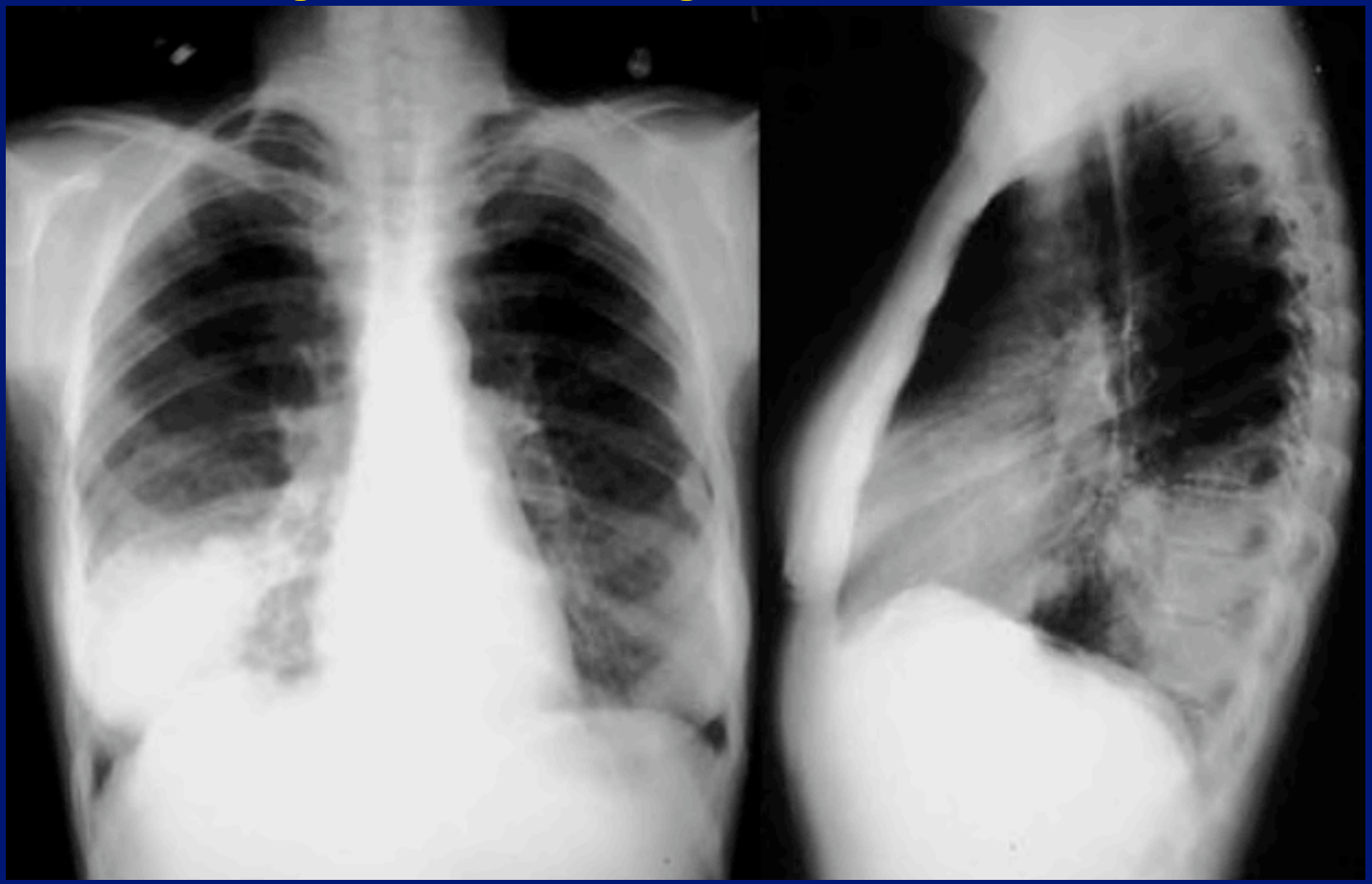
- He is admitted and started on ceftriaxone for probably pneumonia
- Later the same night, the patient starts coughing copious amounts of grayish, putrid sputum that can be detected on the next ward.
- A chest xray is taken, and treatment with metronidazole is added.

Lung abscess

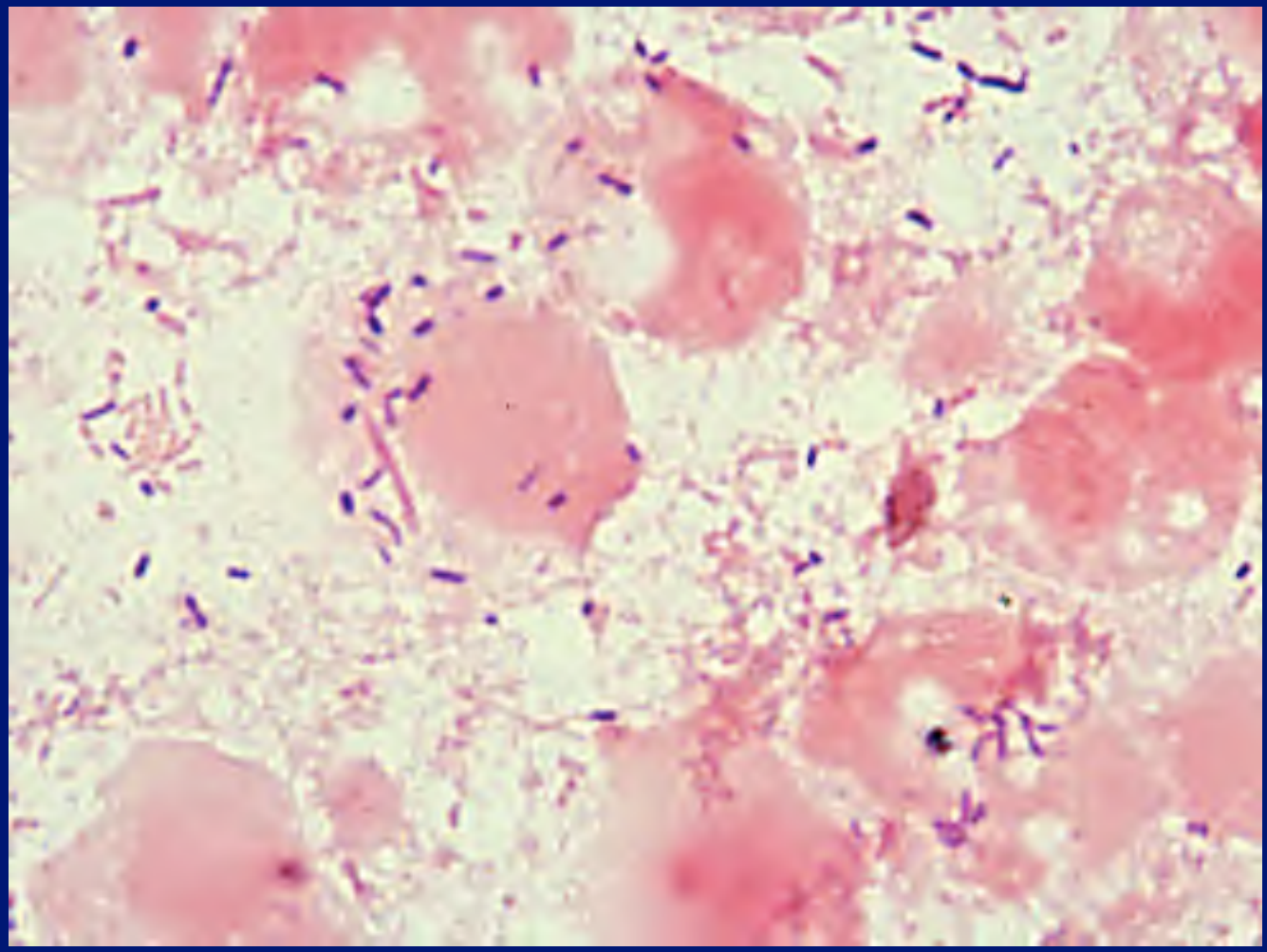


 Abhijit Datir, radiopaedia.org

Aspiration pneumonia



Gram stain of mixed oral flora



Oral, Gram-negative anaerobes

- Common pathogens in dental infections, chronic sinusitis, aspiration pneumonia, lung abscesses
  - *Porphyromonas asaccharolytica, gingivalis, forsythus*
  - *Prevotella melaninogenicus* (named for brown pigment production)
- These species are usually (not always) sensitive to clindamycin. PCN+metronidazole usually works well.
- Infections are polymicrobial and usually include oral (viridans) streptococci, anaerobic strep, and other oral bacteria.

Case: pelvic inflammatory disease

- A 24 year old woman presents with pelvic pain and vaginal discharge.
- She has been treated for gonorrhea in the past and has had two prior episodes of the current illness in the past year.
- P.E. Temp=38C. There is lower abdominal tenderness in the RLQ and exquisite tenderness of the cervix and enlargement of the right Fallopian tube on pelvic exam

Case (continued)

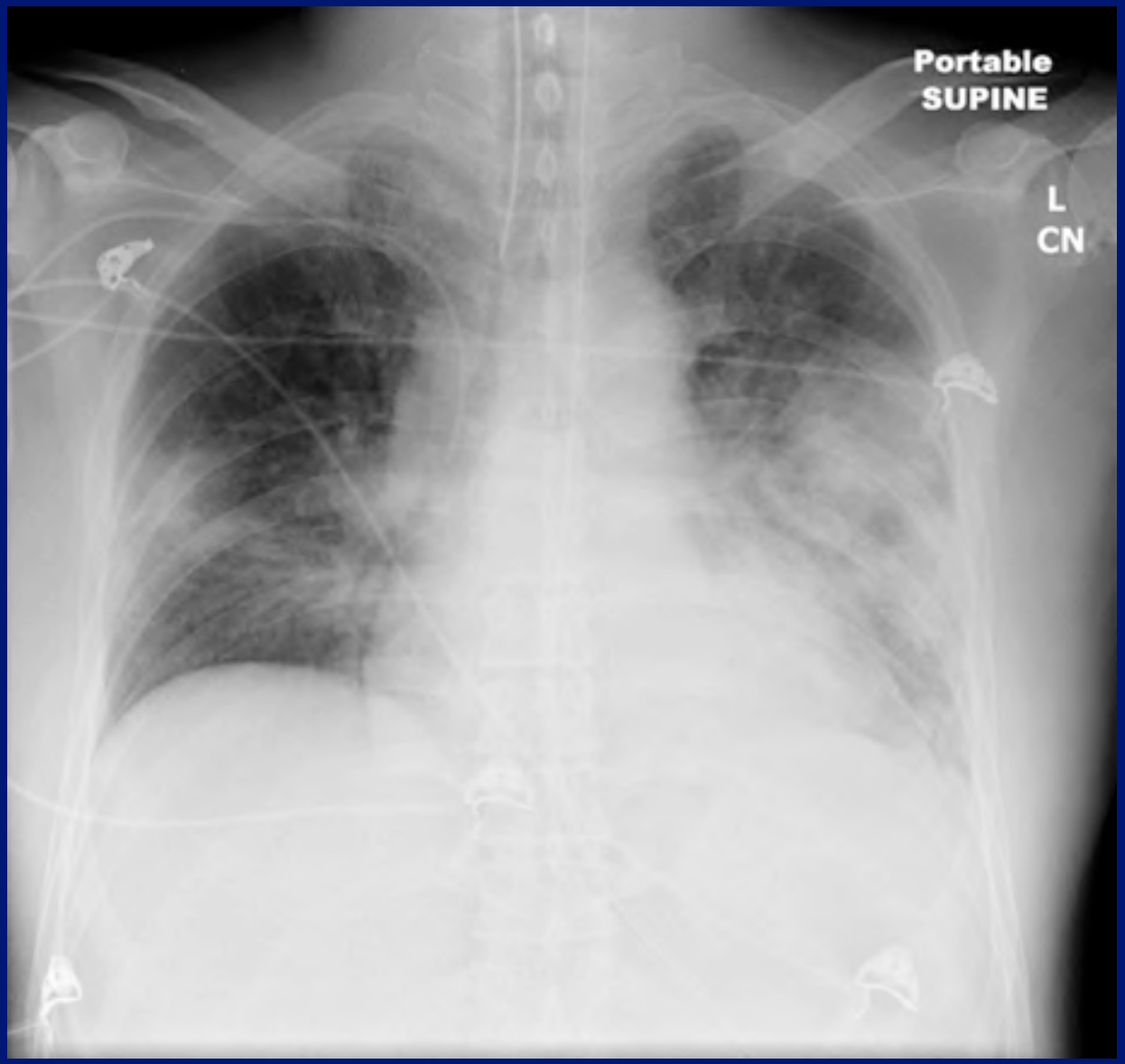
- A pregnancy test is negative
- Because she has been unable to eat without vomiting, she is admitted and treated with IV ceftriaxone, oral doxycycline, and oral metronidazole
- No cultures are obtained; an HIV test is negative
- Why is metronidazole used?

PID microbiology

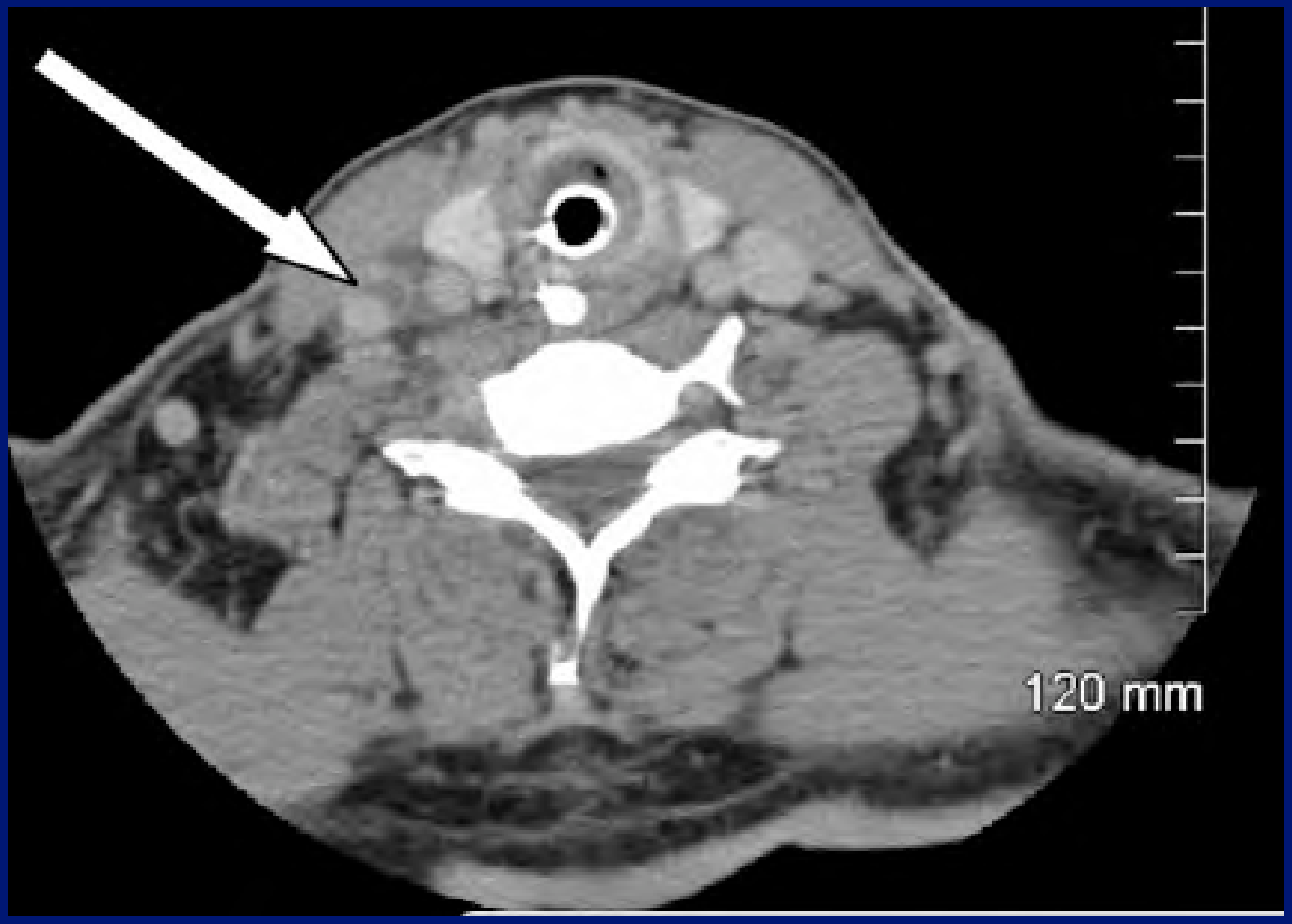
- Primary pathogens: gonococcus, chlamydia
- Secondary pathogens:
  - Facultative enteric organisms (e.g., *E. coli*)
  - GI and vaginal anaerobes
    - *Prevotella bivius* and *Prevotella disiens*
    - *Peptostreptococcus* spp.
  - *Haemophilus*

Case: neck and chest pain

- A 22 year old male who recently had an prolonged episode of pharyngitis now presents with high fever, and exquisite pain, tenderness and swelling of his left neck for 2 days.
- This morning, he developed sharp pain in the left lower chest with deep breathing
- A blood culture is positive for an anaerobe

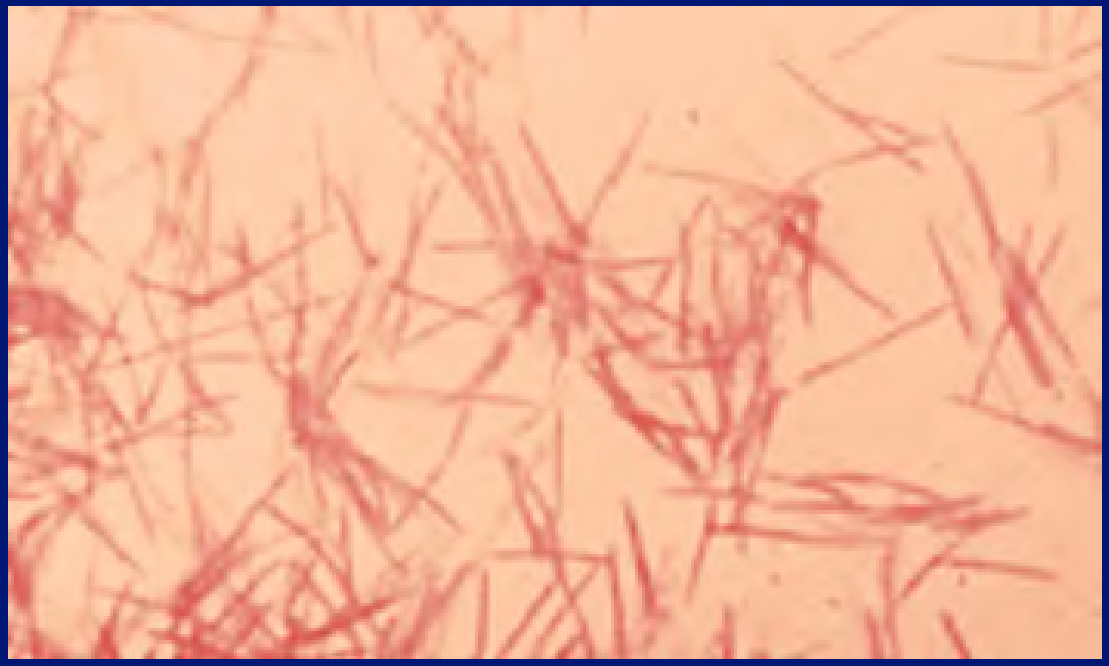


 Lin D, Suwanantarat Nm Young RS. Hawaii Med J 2010; 69(7):161-3



 Lin D, Suwanantarat Nm Young RS. Hawaii Med J 2010; 69(7):161-3

Fusobacterium



Lemierre's syndrome

- Or "post-anginal sepsis" (very rare)
- Occurs after prolonged or severe pharyngitis
- Septic thrombophlebitis with *Fusobacterium necrophorum* (probably from the mouth) associated with septic pulmonary emboli to the lungs

What have you learned about Gram-negative, obligate anaerobes

- *Bacteroides* participate in intra-abdominal abscesses when intestinal contents spill into the peritoneum
- Formation of abscesses is a synergistic process involving anaerobes & facultative bacteria
- *B. fragilis* has special capacity to tolerate oxygen and to induce abscess formation via its CPC
- Other *Bacteroides*-like anaerobes are involved in polymicrobial dental, lung, or pelvic infections

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Slide 10: Yu J, Fulcher AS, Turner MA, Halvorsen RA. Helical CT Evaluation of Acute Right Lower Quadrant Pain: Part I, Common Mimics of Appendicitis Am J Roentgenol. 2005;184(4):1136-1142. Resource: medscape.com

Slide 12: Source undetermined

Slide 13: CDC: Public Health Image Library/Dr. V.R. Dowell, Jr.,1972, http://phil.cdc.gov/phil_images/20030203/6/PHIL_3084_lores.jpg

Slide 31: Abhijit Datir, Lung Abscess, Radiopaeidia.org, http://radiopaedia.org/articles/lung_abscess

Slide 32: Source undetermined

Slide 33: Source undetermined

Slide 39 & 40: Lin D, Suwantarat N, Young RS. Lemierre's Syndrome mimicking leptospirosis. Hawaii Med J. 2010; 69(7):161-63. http://www.hawaiimedicaljournal.org/69.07.161.htm

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