

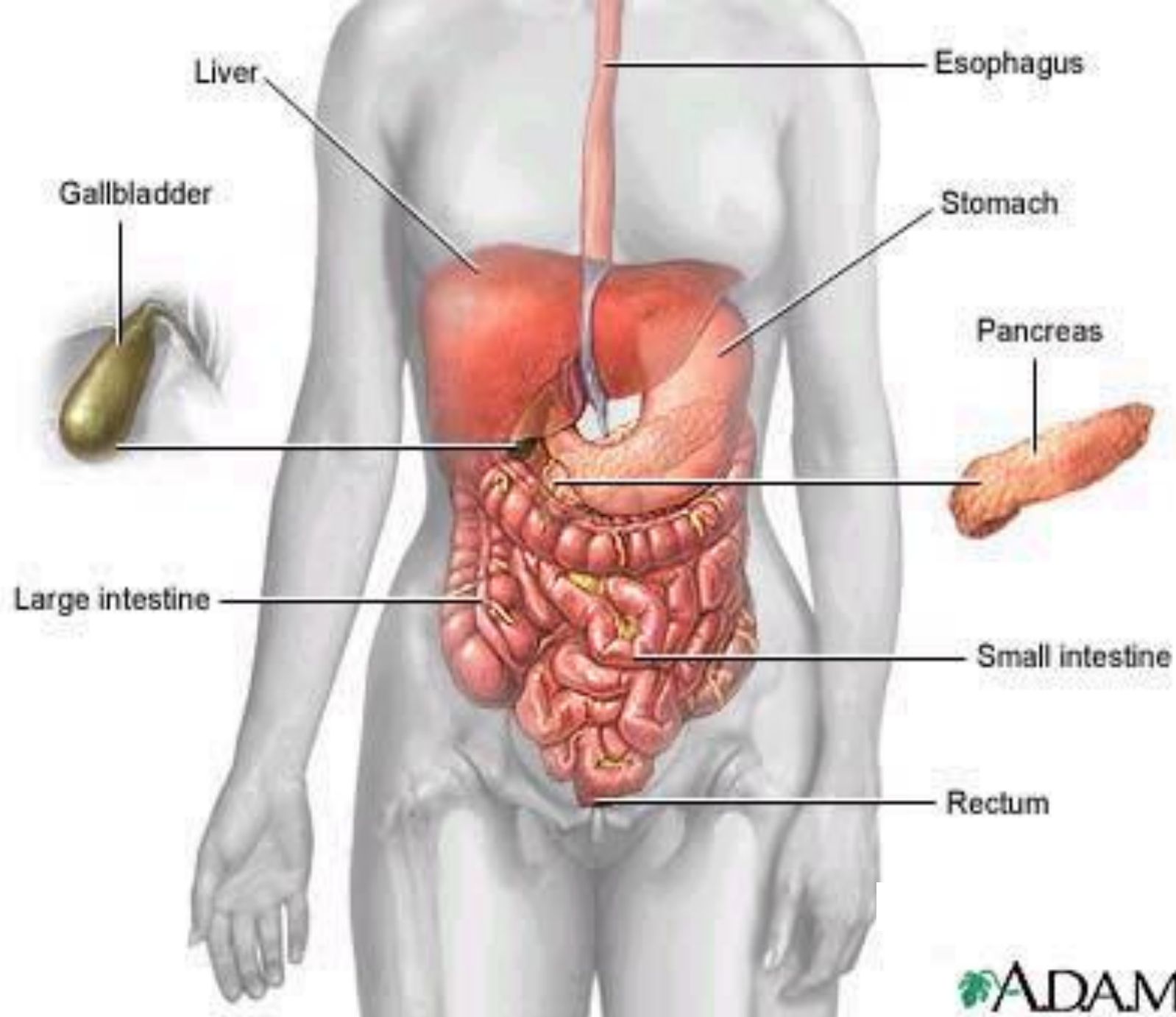
# Intra-abdominal Infection

## 腹腔內感染

楊雅頌

# 學習內容

- 認識腹腔內構造
- 認識腹腔內感染(IAI)之特性
- 認識腹腔內感染治療



# IAI

## (intra-abdominal Infection)

- 常發生於正常腸胃壁遭受破壞(如發炎、穿孔、手術)時，導致腹腔器官受細菌感染：
  - 闌尾或大腸憩室(diverticulum)破裂或胃潰瘍
  - 腸壁因缺氧、腫瘤、發炎
  - 鄰近區域有發炎反應，如：
    - 胰臟炎→使消化酵素釋放入腹腔
    - 骨盆發炎→使細菌跑入腹腔

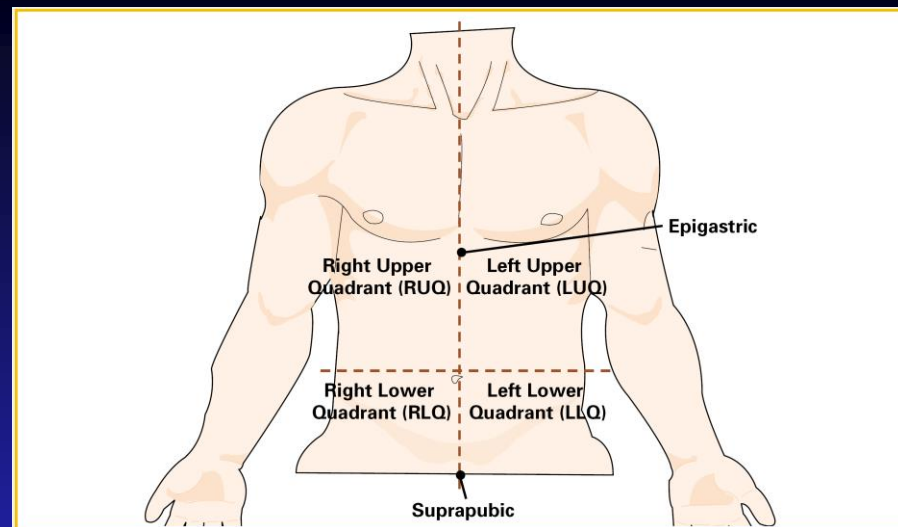


# The Clinical Impact of IAI

IAI is a major cause of morbidity and mortality.

- Intra-abdominal infections are among the most common infections in general surgery.
- Surgery, supportive care, and antibiotic therapy are key in managing IAI.
- In a retrospective study of 604 patients, **morbidity rates of 59% and mortality rates of 21%** were reported.

# IAI的臨床診斷



- 以腹痛表現
- 理學檢查(視、聽、觸、敲)：異常部位、腹部僵硬
- 實驗室檢查：血球數異常、驗尿 (pyuria)、serum amylase、血液pH值、腔液穿放術(paracentesis)含白血球或化膿、細菌染色暨培養
- 影像學檢查異常：X光、超音波檢查、CT電腦斷層檢查、腹腔鏡檢查

# Abdominal Pain

- Although abdominal pain is common and often trivial, acute and severe pain nearly always is a symptom of intra-abdominal disease. It may be the sole indicator of the need for surgery.
- Textbook descriptions of abdominal pain have severe limitations because individuals react to pain differently.

# Physical examination

Abdomen:

- Shape
- peristasis
- tenderness
- rebounding pain
- ascites
- liver, Spleen, kidney, Hernia,
- digital examination

# Lab examination

- CBC
- Biochemistry (amylase, cpk, alk. Phosphatase, T. bil., r-GT, AST, ALT, Glu, Cr,)
- Image study:
  - Sonography of abdomen
  - CT Scan
  - MRI
  - Angiogram
  - Nuclear image exam

# IAI的分類

## ORGAN-SPECIFIC SYNDROMES

Appendicitis

Diverticulitis

Cholecystitis

Cholangitis

Infected pancreatic necrosis

Typhlitis

Focal infection in female pelvis

## INTRA-ABDOMINAL ABSCESS

Intraperitoneal (free) or retroperitoneal

Visceral (pancreas, liver, spleen, kidney, etc.)

## PERITONITIS

### *Primary*

Spontaneous peritonitis of childhood

Spontaneous peritonitis in adults

Tuberculous peritonitis

### *Secondary*

Diseases of the gastrointestinal tract

Injury to the gastrointestinal tract

Diseases of the genitourinary tract (female)

Injury of the genitourinary tract

Secondary to chronic ambulatory peritoneal dialysis

Rupture of intraperitoneal or visceral abscess

# Flora of GI tract

- In health, the **stomach and duodenum are sterile** or only sparsely populated with gram-positive organisms, lactobacilli, and occasionally *Candida*.
- **Gram-negative** organisms are encountered in the **proximal small bowel**
- **Anaerobes** are encountered in the **distal small bowel and colon.**

# 腸胃道正常菌叢(GI normal flora) 重要

Site	Commonly Found Bacteria	Approximate Concentration (Log No. Organisms/mL)	
		Aerobes	Anaerobes
Stomach <sup>a</sup>	<i>Streptococcus, Lactobacillus</i>	10–100	Rare
Biliary tract	Normally sterile ( <i>Escherichia coli, Klebsiella, or enterococci</i> in some patients)	0	0
Proximal small bowel	<i>Streptococcus</i> (including enterococci), <i>E. coli, Klebsiella, Lactobacillus, diphtheroids</i>	100	Few
Distal ileum	<i>E. coli, Klebsiella, Enterobacter, enterococci, Bacteroides fragilis, Clostridium, peptostreptococci</i>	10 <sup>4</sup> –10 <sup>6</sup>	10 <sup>5</sup> –10 <sup>7</sup>
Colon	<i>Bacteroides spp., peptostreptococci, Clostridium, E. coli, Klebsiella, enterococci, Enterobacter, and many others</i>	10 <sup>5</sup> –10 <sup>8</sup>	10 <sup>9</sup> –10 <sup>11</sup>

<sup>a</sup>With achlorhydria, H<sub>2</sub>-antagonist therapy, gastric cancer, or gastric outlet obstruction, bacterial counts may rise to 10<sup>5</sup>/mL.



# Microbiology 重要

## Gram-negative aerobic and facultative

*Escherichia coli*

*Klebsiella spp*

*Enterobacter spp*

*Pseudomonas spp*

Other gram-negative enteric bacilli

## Gram-positive aerobic and facultative

*Enterococci*

Nonenterococcal streptococci

*Staphylococcus spp*

## Anaerobic

*Bacteroides fragilis*

Other *Bacteroides spp*

*Clostridium spp*

*Peptostreptococcus/Streptococcus*

# The 4 flora of IAI

## ■ Exogenous flora

- ◆ *S. aureus*, *S. epidermidis*

## ■ Oral gastric flora

- ◆ *Bacteroides*, *Veillonella*, *Actinomyces*, *Streptococcus*, *Peptostreptococcus*

## ■ Biliary flora

- ◆ *Enterobacteriaceae* (*E.coli*, *KP*.....), *E. faecalis*, anaerobes, *Clostridium*, *B. fragilis*, *Peptostreptococcus*

## ■ Fecal flora

- ◆ *E. coli*, *K. pneumoniae*, *Pseudomonas*, *Bacteroides*, *Staphylococcus*, *Peptostreptococcus*, *Clostridium*

# IAI的細菌學 重要

- 可培養出**多重微生物群**。
- 典型是兩種好氧菌(aerobes，常見*E. Coli*)、三種厭氧菌(anaerobes，常見*B. fragilis*)
- Community-acquired IAI: 感染菌株可準確預測(先前未接受抗生素)
- Nosocomial IAI: 較易出現抗藥性菌株的*P. aeruginosa*, *Acinetobacter* spp.
- Opportunistic(伺機性): *Pseudomonas* sp., *Candida* spp., *Staphylococci*.

	出現頻率 (%)
好氧菌	
• <i>Escherichia coli</i>	65
• <i>Proteus</i> sp.	25
• <i>Klebsiella</i> sp.	20
• <i>Pseudomonas</i> sp.	15
• Enterococci	15
• <i>Streptococcus</i> sp.	10
厭氧菌	
• <i>Bacteroides fragilis</i>	80
• Other <i>Bacteroides</i> sp.	30
• <i>Clostridium</i> sp.	65
• <i>Peptostreptococcus</i> sp.	25
• <i>Peptococcus</i> sp.	15
• <i>Fusobacterium</i> sp	20

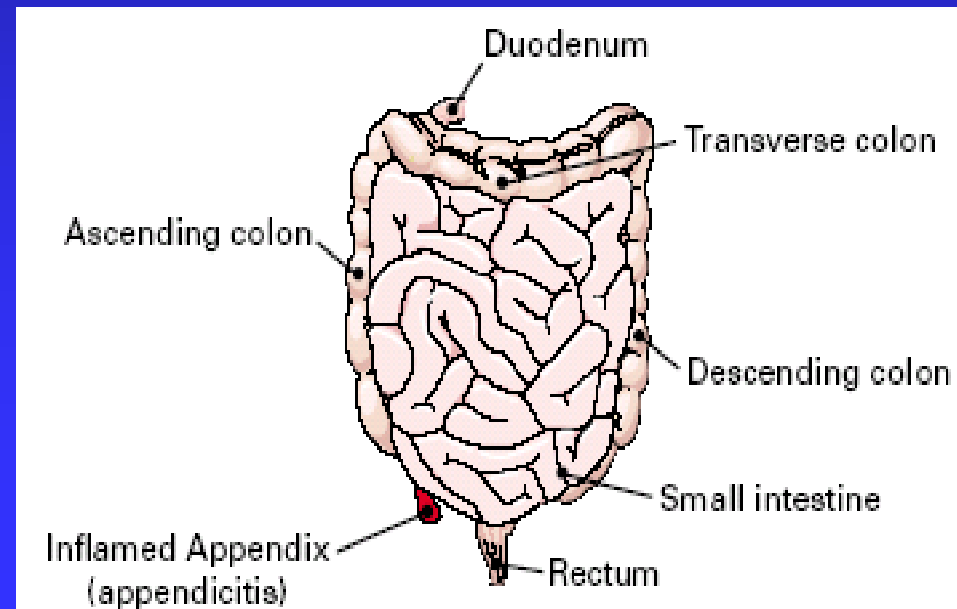
取材自 Reese RE, Betts RF, eds. *A Practical Approach to Infectious Diseases*. 4th ed. New York, NY: Little, Brown and Company; 1996.

# Intra-abdominal infection

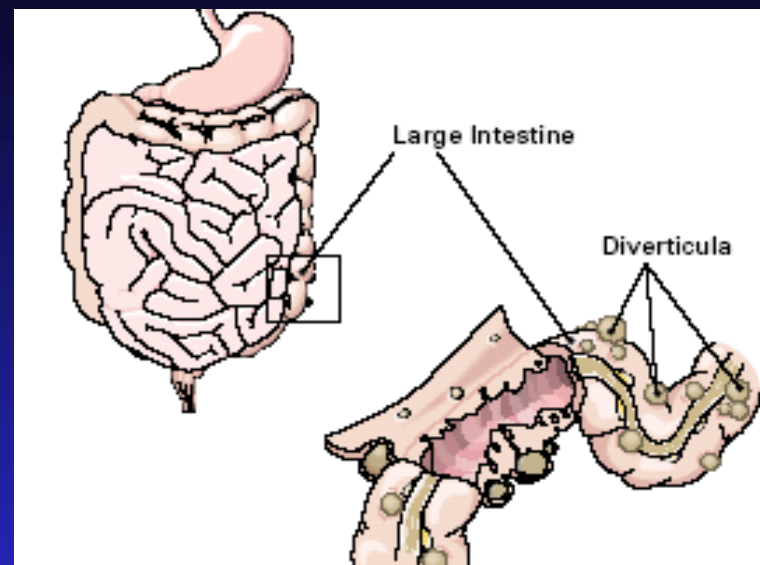
- Acute cholecystitis and cholangitis
- Acute pancreatitis
- Esophageal infection
- Gastroenteritis
- Food poisoning
- Antibiotic-associated diarrhea
- Acute appendicitis
- Diverticulitis
- Abdominal abscess
- Splenic abscess
- peritonitis

# Acute appendicitis

- 外科常見急性腹痛，需求手術中最常見者
- 闌尾管腔阻塞→黏液持續分泌→腔內壓↑腫脹  
→導致動靜脈不通→組織發炎,缺氧壞死→細菌增生  
→穿孔→其他腹腔的感染發炎
- 症狀：右下腹痛、  
噁心嘔吐、厭食、發燒  
以電腦斷層(CT)鑑別



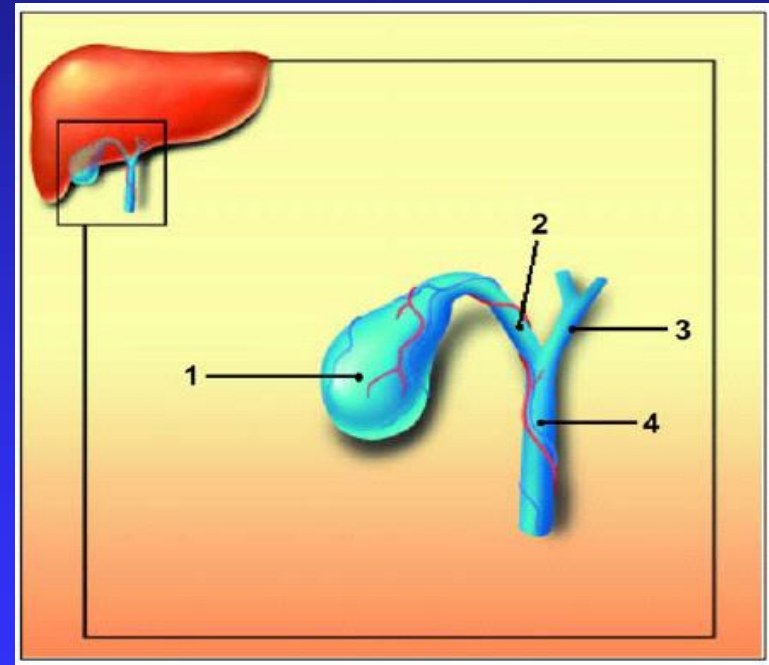
# Diverticulitis(憩室炎)



- 憩室多為後天生成，在降結腸或乙狀結腸
- 大腸壁上或內襯上皮之小凹陷發炎、穿孔
- 穿孔易導致局部生腹膜帶或膿瘡形成
- 左下腹痛、低燒、白血球升高
- 以鋇劑灌腸攝影、電腦斷層(CT)檢查鑑別

# Biliary Tract Infection

- Acute cholecystitis
- Acute cholangitis





# Acute cholecystitis

- The most common cause: gall stone
- RUQ pain, fever, leukocytosis
- 膽石→膽囊口堵塞→囊壞死穿孔
- 症狀:黃疸,發燒,絞痛,  
AST,ALP↑,hyperbilirubinemia
- 膽石→25-30%須手術、經驗性抗生素



# Diagnosis

- History: RUQ pain, fever, more than 12 hours, dark urine
- Physical exam: tenderness over the RUQ
  - Murphy's sign +
  - jaundice
- Lab: CBC: leukocytosis
  - AST, ALT: elevation
  - Lipase
- Sono of abdomen

# Treatment

- Fluid resuscitation
- Bowel rest
- Antibiotic treatment : 線索(院內外？  
有無手術？ 有無膿瘍？)
- Surgical

# Cholangitis

- 肝管、總膽管感染稱之
- 多因膽結石、癌症引起
- 症狀：高燒、黃疸、肝臟部位瀰漫性疼痛
- 廣效抗生素、手術、膽道引流(ERCP, PTCD)

# 急性胰臟炎 (Acute Pancreatitis)

- 由喝酒及膽結石或高血脂引起
- 症狀：腹痛、噁心、嘔吐
- 診斷：腹部電腦斷層，腫大水腫壞死
- 80% 為輕微型，禁食後緩解
- 嚴重型，胰臟壞死併發感染  
(infected pancreatic necrosis)
- **多半非感染**，如果感染多為單一菌種感染，  
75% G(-), 10% G(+), 10% anaerobes. → 擴創術、經驗性廣效性antibiotics

# Liver Abscess

1. Pyogenic liver abscess is usually a polymicrobial infection that has ascended from the gastrointestinal tract.
2. In western countries, the most frequent aetiologic agents of pyogenic liver abscess were *Escherichia coli*, streptococci and anaerobic bacteria.

# Liver Abscess

1. Liver abscess has usually been caused by **a single microorganism, K.P**, presenting in 50% to 88% of pyogenic liver abscesses in **Taiwan**.
2. Approximately, 3% to 7.8% of cases involving this organism have distant metastasis to the eye via the bloodstream causing septic endophthalmitis
3. Previous studies from Taiwan demonstrated that D.M. is the most common underlying condition, with prevalence ranging from 45% to 75% in patients with K.P liver abscess.

Chang FY et al. J.Formos.Med.Assoc. 1995

Cheng DL et al. J.Formos.Med.Assoc. 1989

Chang SC et al. Diagn.Microbiol.Infect.Dis. 2000

## Clinical differences between patients with *Klebsiella pneumoniae* abscesses and non-*K. pneumoniae* abscesses of the liver

Clinical feature	KP (%) (n=114)	Non-KP (%) (n=32)	P-value
<b>Symptoms</b>			
Fever	111(97)	28(87)	NS
Chills	102(89)	26(81)	NS
Abdominal pain	80(70)	25(78)	NS
<b>Signs</b>			
Pulmonary	25(22)	6(19)	NS
Jaundice	20(18)	8(25)	NS
<b>Underlying disease</b>			
<b>Biliary disorder</b>	<b>24(21)</b>	<b>24(75)</b>	<b>&lt;0.001</b>
<b>Diabetes</b>	<b>75(66)</b>	<b>6(19)</b>	<b>&lt;0.001</b>
<b>Abscess finding</b>			
Monomicrobial	108(95)	16(50)	<0.001
Polymicrobial	6(5)	16(50)	
<b>Solitary</b>	<b>105(92)</b>	<b>21(66)</b>	<b>&lt;0.001</b>
Multiple	9(8)	11(34)	
Size > 5 cm	87(76)	20(62)	NS

NS: not significant

Chang FY et al. J.Formos.Med.Assoc. 1995

**Table .****Outcome and complications in all patients with liver abscess due to *Klebsiella pneumoniae***

No.(%) of patients treated with:

Sever complication	Cefazolin	Extended-spectrum cephalosporin	<i>p</i>
	(n=59)	(n=48)	
Metastatic infections	7 (11.9)	0	0.02
Pulmonary complications	17(28.8)	3(6.3)	<0.01
Death	5 (8.5)	2(4.2)	0.42

AAC . 2003 July Vol.47,7, 2088-2092



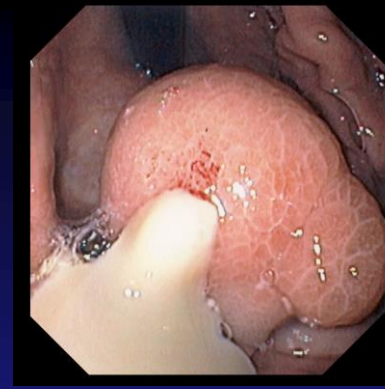
# 腹膜炎(**Peritonitis**)

- 腹膜腔被微生物或刺激性化合物污染

Evans HL et al. 2001; Current Opinion in Critical Care

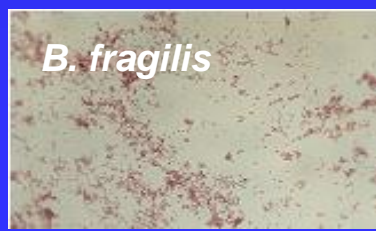
# Definition

- Peritonitis is following the rupture of a hollow viscus, the true definition of peritonitis
- In health, the peritoneal cavity contains 100 mL of peritoneal fluid containing scattered macrophages and lymphocytes.



# Classification of Peritonitis

	1° peritonitis	2° peritonitis	3° peritonitis
Etiology	SBP CAPD-related	Perforation of hollow organ	Post-operative infection (Nosocomial infection)
Infection	Mono-microbial Enteric GNB <i>Enterococci</i>	Polymicrobial Aerobes Anaerobes	CoNS <i>Enterococci</i> <i>Pseudomonas</i> Candida



# Primary or spontaneous peritonitis

- 並無顯而易見感染點，經血液、淋巴、腸壁
- 好發於腹膜透析者、(酒精性)肝硬化者、會產生腹水的疾病(CHF, SLE)
- 常見*E. Coli*, *K. pneumoniae*, *S. pneumoniae*, enterococci, 少見anaerobes
- 發燒、腹痛、反彈痛、腹水白血球升高

# Secondary peritonitis

- Secondary peritonitis is peritonitis occurring as a consequence of gut organisms through a **physical hole** in the gastrointestinal tract or through a necrotic gut wall. Its flora is typically polymicrobial.

# Tertiary peritonitis

- The microbial flora isolated in tertiary peritonitis is dominated by organisms such as coagulase-negative *Staphylococci*, *Pseudomonas*, *Candida*, and the enterococci.
- Enterococci are isolated more frequently in patients with **postoperative peritonitis** than in patients with intra-abdominal abscesses developing outside the hospital.

# Microbiology of peritonitis **重要**

Primary Peritonitis	Secondary Peritonitis	Tertiary Peritonitis
單一	多重	院內菌
Gram-negative bacteria	Gram-negative bacteria	Gram-negative bacteria
<i>E. coli</i>	<i>E. coli</i> 32–61%	<i>Pseudomonas</i>
<i>Klebsiella</i>	<i>Enterobacter</i> 8–26%	<i>Enterobacter</i>
	<i>Klebsiella</i> 6–26%	<i>Acinetobacter</i>
	<i>Proteus</i> 4–23%	
Gram-positive bacteria	Gram-positive bacteria	Gram-positive bacteria
<i>S. aureus</i>	<i>Enterococci</i> 18–24%	<i>Enterococci</i>
<i>Enterococci</i>	<i>Streptococci</i> 6–55%	Coagulase-negative
	<i>Staphylococci</i> 6–16%	<i>Staphylococci</i>
	Anaerobic bacteria	
	<i>Bacteroides</i> 25–80%	
	<i>Clostridium</i> 5–18%	
	Fungi 2–15%	Fungi
		<i>Candida</i>

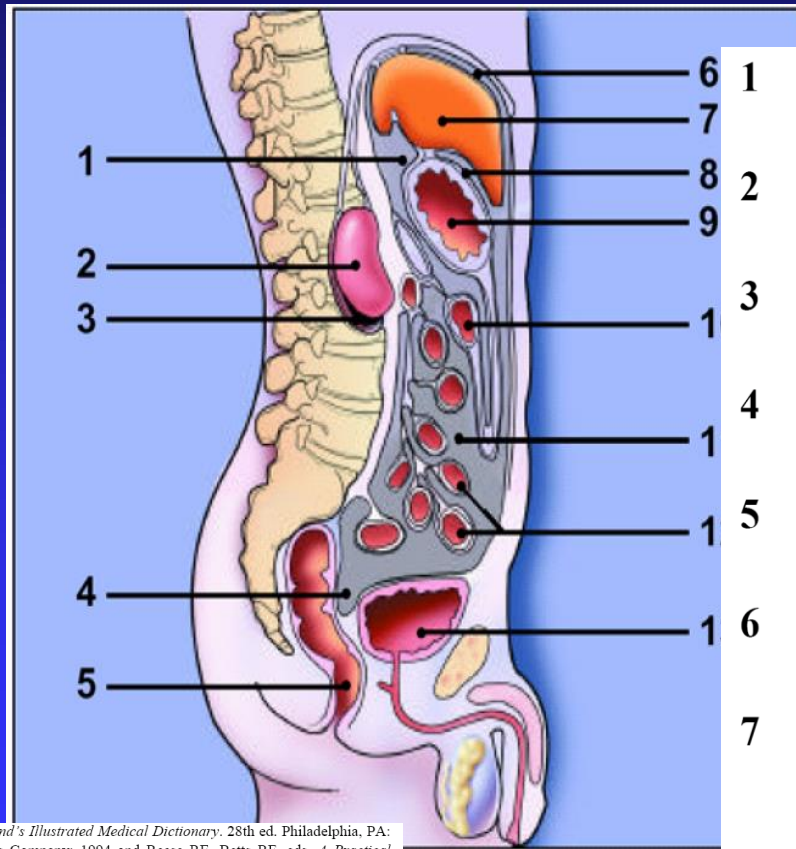


# 腹腔內膿瘍(Intra-abdominal abscess)

- 常發生於腹膜炎、腹部穿透外傷、腹部手術後、膽管病灶、憩室炎、發炎性腸道疾病、胰臟炎、胃潰瘍穿孔
- 產生膿瘍為身體的防衛反應，以限制疾病擴散，但亦提供厭氧菌生長與繁殖環境
- 常為**多重微生物感染**。常見為*B. fragilis*, *Clostridia*, *E. Coli*, *Klebsiella sp.*, *Enterobacter sp.* *Proteus sp.*, *P. aeruginosa*, *S. aureus*, *Enterococci*.
- 以引流、經驗性抗生素療法治療



# 腹膜腔可形成膿瘡處



- |   |                                |    |  |
|---|--------------------------------|----|--|
| 1 | 網膜囊<br>(Lesser sac)            | 8  | 肝下空間<br>(Subhepatic space)                 |
| 2 | 腎臟<br>(Kidney)                 | 9  | 胃<br>(Stomach)                             |
| 3 | 橫隔膜周邊空間<br>(Periphrenic space) | 10 | 橫結腸<br>(Transverse colon)                  |
| 4 | 骨盆空間<br>(Pelvic space)         | 11 | 腸間隙<br>(Interstices between<br>intestines) |
| 5 | 直腸<br>(Rectum)                 | 12 | 小腸<br>(Small intestine)                    |
| 6 | 膈下空間<br>(Subphrenic space)     | 13 | 膀胱<br>(Bladder)                            |
| 7 | 肝臟<br>(Liver)                  |    |  |

# Management of IAI

1. Resuscitation with early fluid requirement
2. Systemic Antibiotics
3. Source control: drainage  
debridement  
definition management

Marshall JC et al. 2003; Crit Care Med.

# Selection of antimicrobial regimens

- Empiric antibiotic therapy should include agent(s) effective against facultative gram-negative enteric bacteria(*E. coli* and other common members of the family Enterobacteriaceae) and obligate anaerobic bacilli(*B. fragilis*)

# Selection of Antibiotics

1. Patient-specific toxicity
2. Cost
3. Local patterns of antimicrobial resistance
4. Site

Marshall JC et al. 2003; Crit Care Med.

# Identification of risk factors

- Age and co-morbid conditions (malignant diseases, liver diseases, and renal diseases)
- Malnutrition
- High APACHE II score 嚴重度
- Antibiotic-resistant organisms 感染的來源 (院內外?)
- Fever and leukocytosis
- Multiple organ failure
- Delay in treatment

Evans HL et al. 2001 Current Opinion in Critical Care

Mazuski JE et al. 2006. Surgical Infections

# Acceptable antimicrobial therapy for intraabdominal infections

Community-acquired infections of mild to moderate severity

- Monotherapy

- ◆ Cefoxitin
- ◆ Cefotetan
- ◆ Cefmetazole
- ◆ Ampicillin/sulbactam
- ◆ Ticarcillin/clavulanic acid

- Combination therapy

- ◆ Anti-anaerobe plus aminoglycoside

# Acceptable antimicrobial therapy for intraabdominal infections

Severe infections/possible of resistant gram-negative organisms

## ■ Monotherapy

- ◆ Imipenem/cilastatin or meropenem
- ◆ Piperacillin/tazobactam

## ■ Combination therapy

- ◆ Anti-anaerobe plus third-generation cephalosporin or aminoglycoside
- ◆ Clindamycin plus aztreonam
- ◆ Ciprofloxacin plus metronidazole

# Recommended agents for treatment of community-acquired complicated intra-abdominal infections.

Type of therapy	Mild to Moderate	Severe
<b>Single agent</b>		
$\beta$ -lactam / $\beta$ -lactamase inhibitor	Amp/ sub, Ticarcillin/ clavulanic acid	Piperacillin/ tazobactam
Carbapenems	Ertapenem	Imipenem/ cilastatin Meropenem
<b>Combination regimen</b>		
cephalosporin based	Cefazolin or Cefuroxime+Metronidazole	Third/ Fourth-generation cephalosporin( cefotaxime, ceftriaxone, ceftizoxime, ceftazidime, cefepime) + Metronidazole
Fluoroquinolone based	(Ciprofloxacin, Levofloxacin, Moxifloxacin, Gatifloxacin) + Metronidazole	Ciprofloxacin+ Metronidazole
Monobactam based		Aztreonam+ Metronidazole



# IAI 抗生素治療----治療多久？

- 一般而言，應持續給予5-7天療程，如果臨床上感染症狀改善了，可考慮停藥。(Wittman DH, et al, Ann Surg 1996;224:10-8.)(Solomkin JS, et al. Clin Infect Dis 2003;37:997-1005.)
- 如果敗血症持續超過7天，應考慮處理是否另存在感染源、及手術處置。

# 結論

- **IAI** 抗生素治療指引考量
  - 是否有適當的感染原處理？
- 經驗性治療（猜細菌很重要）
- 外科手術處相當重要。如無適當引流或擴創、及結構矯正，抗生素療法常無法見效，導致延長治療、抗藥性問題