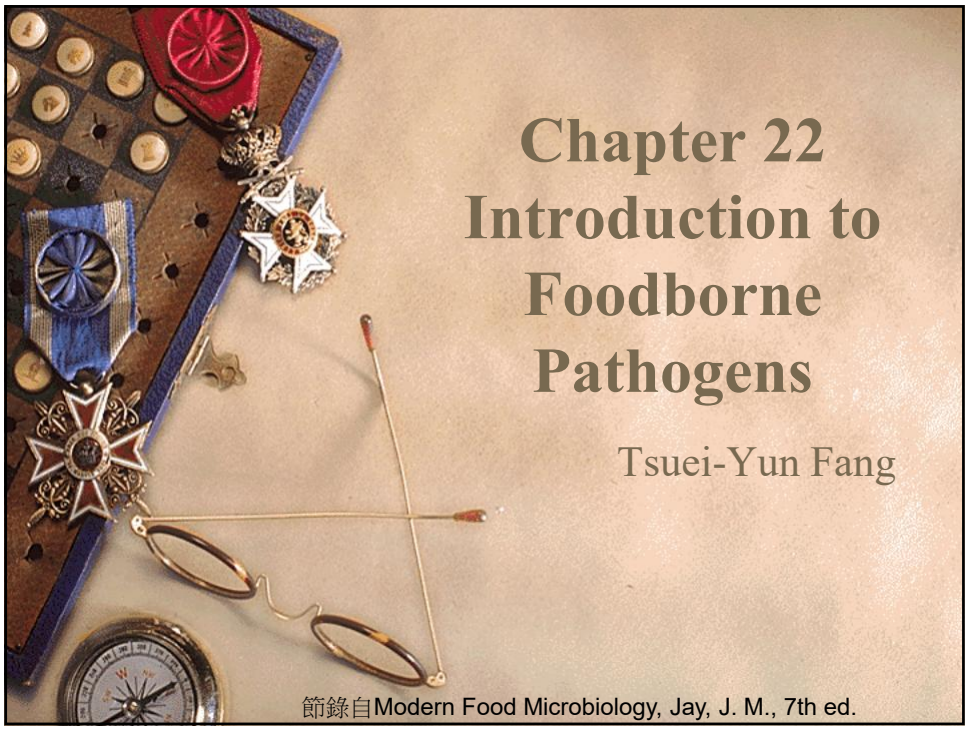
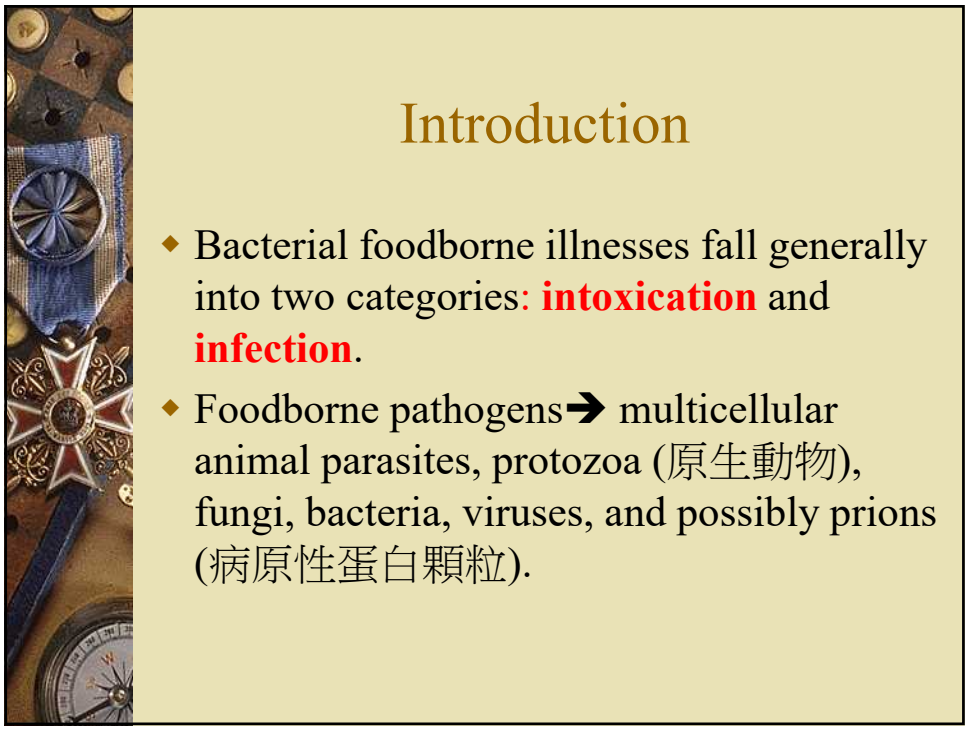

Chapter 22
Introduction to
Foodborne
Pathogens
Tsuei-Yun Fang
節錄自Modern Food Microbiology, Jay, J. M., 7th ed.


Introduction
Bacterial foodborne illnesses fall generally into two categories: intoxication and infection.
Foodborne pathogens➔ multicellular animal parasites, protozoa (原生動物), fungi, bacteria, viruses, and possibly prions (病原性蛋白顆粒).

Foodborne illness and food poisoning

- Foodborne illness (食源性疾病) and food poisoning (食物中毒), are often used interchangeably by consumers.
- Foodborne illness can be **an infection** or **intoxication** (中毒) that results from eating food contaminated with **viable (live) microorganisms** or their toxins.
- Foodborne illness also includes allergic reactions where foods act as a carrier of the allergen.

食品中毒定義 (FDA, Taiwan)

- 食品中毒（Foodborne outbreak）：
  二人或二人以上攝取相同的食品而發生相似的症狀，則稱為一件食品中毒案件。
  如因肉毒桿菌毒素而引起中毒症狀且自人體檢體檢驗出肉毒桿菌毒素，由可疑的食品檢體檢測到相同類型的致病菌或毒素，或經流行病學調查推論為攝食食品所造成，即使只有一人，也視為一件食品中毒案件。
  如因攝食食品造成急性中毒（如化學物質或天然毒素中毒），即使只有一人，也視為一件食品中毒案件。
- Outbreak（大量發生）: a sudden rise in the incidence of a disease <an *outbreak* of measles>

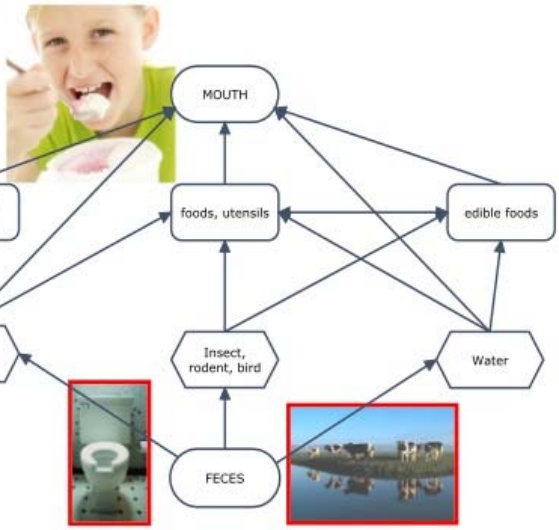
- 依食物中毒的成因可分為以下三大種類：

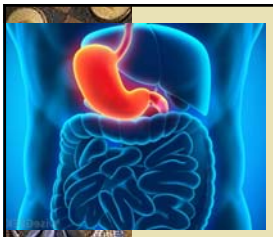
1. 細菌性食物中毒:食物被細菌污染所引發的疾病，其污染的物質可能是病原體，包括細菌、病毒及寄生蟲，或是其產生的毒素。症狀以消化系統障礙為主，尤其是急性腸胃炎之症狀，如嘔吐、腹瀉、腹痛等最常見。
2. 天然毒素食品中毒: 可分為動物性(河豚毒、有毒魚貝類)及植物性(毒菇、發芽馬鈴薯及花生、玉米)兩大類： 潛伏期約20分鐘至3小時。中毒症狀為神經麻痺、嘔吐、頭痛等現象。嚴重時有感覺麻痺、運動失調、血壓下降、繼而肌肉鬆弛、引起之呼吸停止而死亡。
3. 化學性食品中毒: 可分為金屬類農藥、有毒非法食品添加物等。潛伏期(視攝入量之多寡)可分為 ：急性及慢性中毒：潛伏期從數分鐘至數年不等。慢性中毒可引起肝、腎等器官病變

The Fecal-Oral Transmission of Foodborne Pathogens

- Fecal-Oral route ➔ primary route of infection for the foodborne viruses and enteropathogenic protozoa (原蟲) and bacteria (Figure 22-2).
- Pathogens may be transmitted from contaminated feces via the fingers of unsanitary food handlers, by flying or crawling insects, or from water.

The contamination paths of the fecal-oral route are complex





HOST INVASION

In order to cause illness an intestinal pathogen must

1. **Survive passage through the extremely acidic environment of the stomach.**
   - by the **protective effect of food**
   - by the use of their **adaptive acid tolerance mechanisms** (see Acid Tolerance below).

HOST INVASION

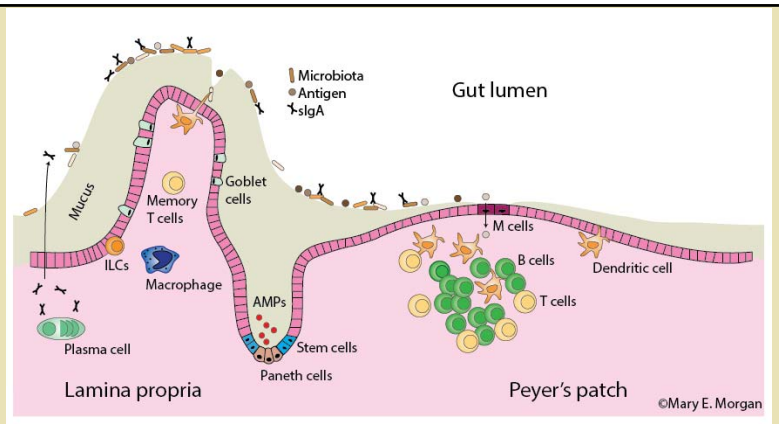
In order to cause illness an intestinal pathogen must

2. **Attach to or colonize the intestinal walls➔** increase in numbers.
   - **The mucus (粘液) layer that covers the intestinal mucosa (黏膜) ➔** the first line of defense encountered by enteric pathogens.
   - *Listeria monocytogenes*（李斯特菌）overcomes the mucus barrier by removing mucus through the aid of **listeriolysin O** (LLO).
   - *Clostridium perfringens*（產氣莢膜梭菌）does not need to attach to intestinal tissues.

HOST INVASION

In order to cause illness an intestinal pathogen must

3. **Possess the capacity to defend itself against host defense mechanisms** such as **gut-associated lymphoid tissue (腸道相關淋巴組織, GALT)**.



Pathogenic microorganisms and other antigens entering the intestinal tract encounter macrophages, dendritic cells (樹突狀細胞 是一種存在於哺乳動物的一種白血球), B-lymphocytes, and T-lymphocytes found in Peyer's patches .

ILCs: innate lymphoid cells, AMPs: anti-microbial peptides, sIgA: secretory IgA, M cells: microfold cells

HOST INVASION

In order to cause illness an intestinal pathogen must

4. **Compete with the large heterogeneous microbiota of the gut.**
   - **competitive exclusion** of the harmless biota➔ once attached to all available sites on the intestinal walls, will exclude pathogens.
   - The gastrointestinal tract is a low-O_2 environment➔ predominant organisms are **anaerobes**.

HOST INVASION

In order to cause illness an intestinal pathogen must

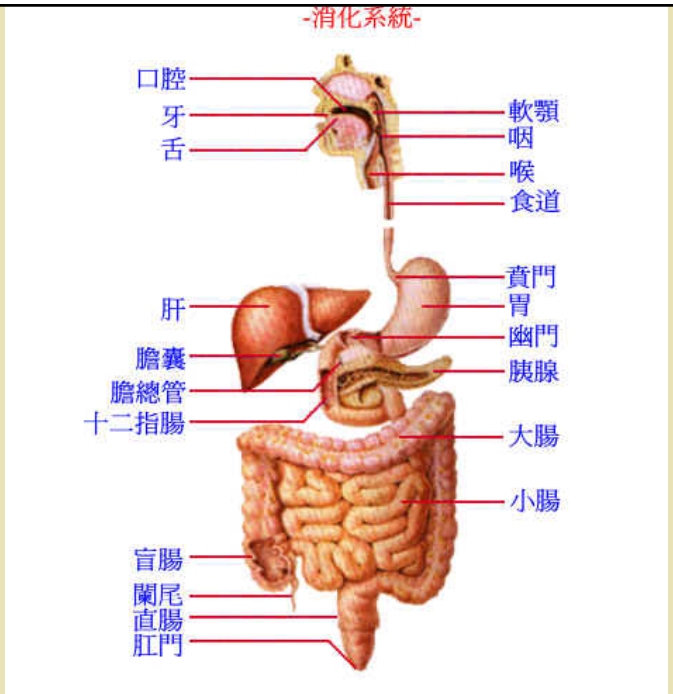
5. Once attached➔ **elaborate toxic products** (e.g., *Vibrio cholerae*霍亂弧菌 non-01) or **cross the epithelial wall and enter phagocytic or somatic cells** (e.g., *L. monocytogenes*).

補充:

- **Epithelium** (上皮細胞) is one of the four basic types of animal tissue, along with connective tissue, muscle tissue and nervous tissue. Epithelium lines both the outside (skin) and the inside cavities and lumen of bodies.
- The **intestinal epithelium** is the epithelium that covers the small and large intestine.

Attachment Sites

- Human digestive System (Figure 22-3).
- A list of pathogens that can adhere to or enter at each site (Exhibit 22-2).
  - Skeletal muscles
  - Stomach
  - Liver
  - Small intestine
  - Large intestine/colon



Sigma Factors and the Acid Tolerance Response

- Some foodborne pathogens use at least **two strategies to survive under low-pH** conditions.
- The ***rpoS* gene** which encodes the **alternate sigma factor** (A sigma factor is a subunit of bacterial RNA polymerase).

Sigma Factors and the Acid Tolerance Response

- RpoS is regarded as being a sigma factor that specifically **affects stationary phase events in some enteric bacteria**, especially *Escherichia coli*, *Yersinia enterocolitica* (耶爾辛氏腸炎桿菌), and *Shigella* (志賀氏菌屬), and it allows them to **survive at pH 2.5 for over 2 hours**.
- RpoS is responsible for the induction of specific sets of genes that can **increase stress resistance**.

Sigma Factors and the Acid Tolerance Response

- The **acid tolerance response** appears to be another survival strategy for pathogens. When ***Shigella*** (志賀氏菌屬)**, *E. coli,*** and ***Salmonella*** (沙門氏菌屬) are exposed to pH <5.9, it induces an acid tolerance response that enables cells to survive at pH 3.3.
  - This response **may lower the number of cells needed to initiate infection**. Salmonellosis may be caused by as few as 10 cells. (**10^7 – 10^9/g** are generally necessary for salmonellosis)
- When *L. monocytogenes* was exposed to pH 3.5 for up to 2 hours at 37˚C ➔ increased lethality (致死率; 殺傷力) for mice.

PATHOGENESIS (發病機制)

- **The initiation and course of foodborne illness**

Gram-Positive Bacteria

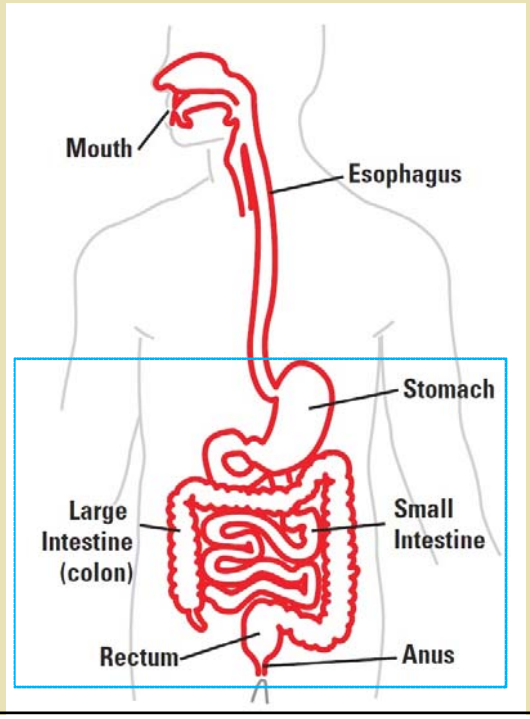
- Virulent strains➔ produce **exotoxic factors (exocellular substances)** that are absent in avirulent strains.
- Staphylococci, *Clostridium botulinum*（肉毒桿菌）, *C. perfringens* (產氣莢膜梭菌), and *Bacillus cereus*（仙人掌桿菌） cause foodborne illness due to **exotoxin**s.

PATHOGENESIS

Gram-Positive Bacteria

- The toxin cause botulism is a potent **neurotoxin** ← *Clostridium botulinum* cells growing in susceptible foods.
- The *C. perfringens* (產氣莢膜梭菌) enterotoxin (CPE) is a **spore-associated protein→ produced during sporulation** (孢子形成) in the **GI tract (gastrointestinal tract)**.

- **GI tract**



PATHOGENESIS

Gram-Positive Bacteria

- ***Listeria monocytogenes*** (李斯特菌)
  - An **intracellular pathogen**.
  - The virulent strains produce the exocellular pore-forming substance **listeriolysin O** (LLO). LLO is a **hemolysin** (溶血素) involved in the **invasion of the gut epithelium**➔ cell-to-cell spread of the organism.

PATHOGENESIS

Gram-Positive Bacteria

- ***Listeria monocytogenes***
- The **ingestion of viable cells** is necessary for listeric infection to occur.
  - What sets this species apart from the nonpathogenic *Listeria* is the capacity to **adhere to and breach (破壞) the mucosal/epithelial barrier, and to spread from cell to cell with the aid of LLO**.

PATHOGENESIS

Gram-Negative Bacteria

- ***Salmonellae*** \ˌsal-mə-ˈnel-ə\
  - Produce **enterotoxin**
  - Virulent strains of *S. enterica* (腸道沙門氏菌) initiate infection in non-phagocytic cells by **attaching to the intestinal mucosa (黏膜)** with the aid of **fimbrial adhesions** (菌毛粘著作用).
  - Virulent strains of *S. enterica* secrete into the cytoplasm a protein (SpiC) that prevents the fusion of vesicles with lysosomes.

PATHOGENESIS

Gram-Negative Bacteria

- ***Escherichia coli*** \ˌesh-ə-ˈrik-ē-ə\\ˈkō-ˌlī\
- **Enteropathogenic (EPEC)** and **enterohemorrhagic (EHEC)**
  - The **pathogenicity island** on the chromosome of EHEC and EPEC contains the gene that encodes the **intimin protein** (黏附蛋白) that is essential for attachment-effacement (A/E, 附著在小腸上皮細胞導致腸內微絨毛消失).
  - The pathogenicity of EHEC is due to the possession of Stx toxins, endotoxins, and host-derived cytokines (**細胞激素**) such as tumor necrosis factor (腫瘤壞死因子) alpha (TNF-α) and interleukin (介白素)-1β. .

PATHOGENESIS

Gram-Negative Bacteria

- ***Escherichia coli***
  - Stx1 and Stx2 toxins **inhibit protein synthesis in endothelial cells** (内皮細胞). Human renal (腎臟的) tissue contains large amounts of Gb3 (globotriaosylceramide, **the Stx receptor**) and thus it is highly sensitive to the Stx toxins.
  - EPEC strains require the plasmid-borne **bundle-forming pili (bfp)** for adherence and autoagglutination (自體凝集). Mutants that lacked bfp caused less severe diarrhea and were about 200-fold less virulent in human volunteers.

PATHOGENESIS

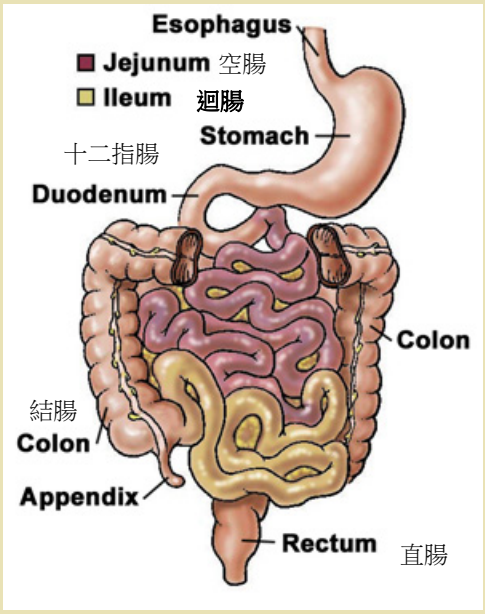
Gram-Negative Bacteria

- ***Yersinia*e**
  - The most significant pathogenic mechanism of *Y. enterocolitica* (耶爾辛氏腸炎桿菌) is contained in the **yersiniae outer protein (Yop) virulon** (see Exhibit 22-3), which is also possessed in *Y. pestis* （鼠疫耶爾辛氏桿菌） and *Y. pseudotuberculosis* (假結核辛氏桿菌）.
  - The **Yop** virulon allows yersiniae to **survive and multiply in host lymphoid tissue**

PATHOGENESIS

Gram-Negative Bacteria

- ***Shigellae***
  - **The M cells (microfold cells,微皺褶細胞是一種免疫細胞) of Peyer's patches in the terminal ileum (迴腸)** are invaded by shigellae as well as some salmonellae, some EPEC, and some viruses.
  - Shigellae invade macrophages of the colonic (結腸的) and rectal (直腸的) M cells ➔the macrophages die by apoptosis (細胞凋亡) ➔ an **acute inflammatory response with dysentery (痢疾的急性炎症反應)**.



PATHOGENESIS

Gram-Negative Bacteria

- ***Shigellae***
  - This invasive strains of *S. flexneri* lead to the loss of blood and mucus in the intestinal lumen. Since **colonic absorption of water** is inhibited, the result is the passage of scanty (稀薄的) dysenteric stools
  - Shiga toxin ➔ may inhibit mammalian protein synthesis

PATHOGENESIS

Gram-Negative Bacteria

- ***Vibrios***
  - The pathogenesis of *V. parahaemolyticus* **(副溶血性弧菌/ 腸炎弧菌)**
  - is associated with the production of a 46-kDa homodimer**—thermostable direct hemolysin (TDH)**.
  - TDH appears to be responsible for the following events: **hemolysis, pore-forming capacity, cytotoxic effects, lethality in small animals, and enterotoxigenicity.**

PATHOGENESIS

Gram-Negative Bacteria

- ***Vibrio*s**
  - The two primary virulence factors of *V. cholerae* (霍亂弧菌) are (1) **toxin-coregulated pili (TCP)** that are required for intestinal colonization, and (2) **cholera toxin (CT)** that is an enterotoxin.
  - Among foodborne pathogens, genes for the following toxins are known to be carried by phages: **CT toxin of *V. cholera*, Staphylococcal enterotoxin A, Stx1 and Stx2 of EHEC strains of *E. coli*, and botulinal toxins.**