Pathology of bacterial infection

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มหาวิทยาลัยนเรศวร

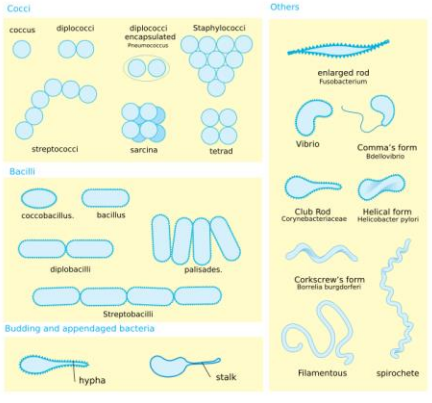
- Bacterial pathogenesis
- Classification of bacterial diseases
- Diseases and pathology

Bacterial Infection

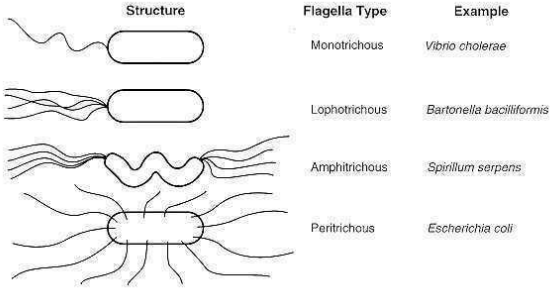
- แบคทีเรียเป็นเชื้อก่อโรคที่สำคัญและพบบ่อย

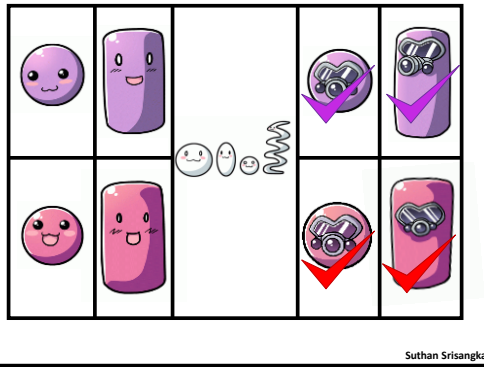
Basic morphology

- รูปร่างกลม (cocci)
- รูปแท่ง (bacilli)
- รูปเกลียว (spirochete)
- Gram's stain
  - Gram positive (แกรมบวก)
  - Gram negative (แกรมลบ)

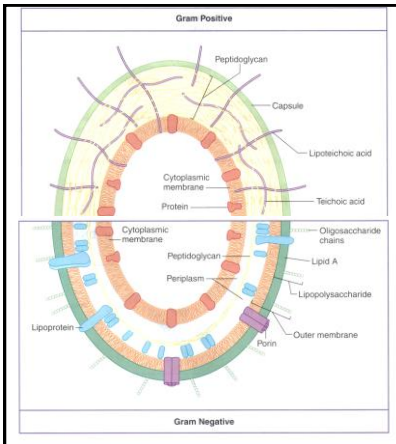


http://cellbiology.med.unsw.edu.au/units/images/Bacterial_morphology_diagram.png

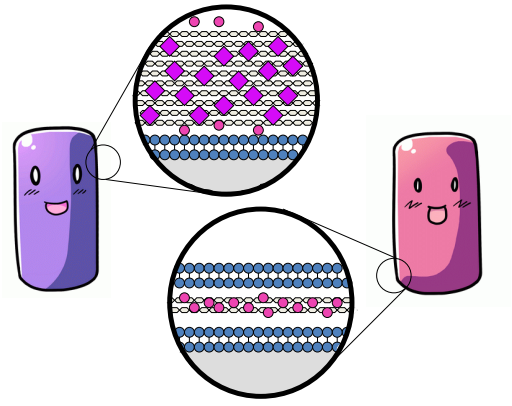




Suthan Srisangkaew, M.D.



แบคทีเรียแกรมบวกจะมี outer membrane ทำให้การย้อมสีแกรมต่างกัน และยังส่งผลต่อกลไกของเชื้อโรคอีกหลายประการ และยังใช้ในการจัดจำแนกเชื้อแบคทีเรียก่อโรคได้



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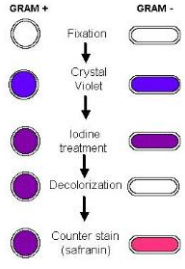
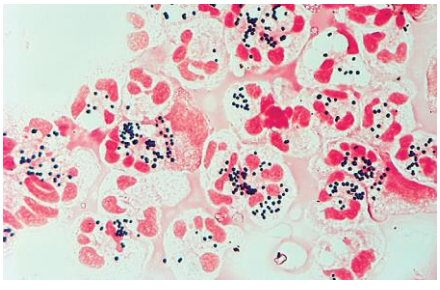


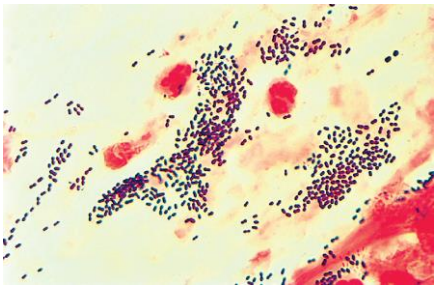
ขั้นตอนการย้อม gram stain

1. ทำการตรึงสไลด์ด้วยความร้อน
2. ย้อมด้วยสี crystal violet ประมาณ 1 นาที
3. ล้างด้วยน้ำสะอาด
4. ย้อมด้วยสีแกรม Iodine 1 นาที (เพื่อทำให้เกิดสารประกอบขนาดใหญ่กับ crystal violet ทำให้ติดกับผนังเซลล์แบคทีเรียแกรมบวก)
5. ล้างสี (decolorize) ด้วย น้ำยา decolorizer (ethanol, ethanol-acid or alcohol-acetone)
6. ย้อมด้วยสี safranin นาน 1-2 นาที
7. ล้วยด้วยน้ำสะอาด ปล่อยให้แห้ง

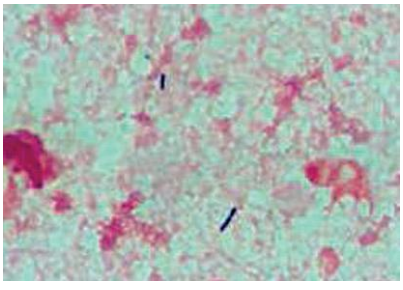
http://spot.pcc.edu/~jvolpe/b/bi234/lab/differentialTests/GramStain.html



- Gram positive cocci in pairs, short chains and cluster suggestive of Staphylococcal infection in cerebrospinal fluid

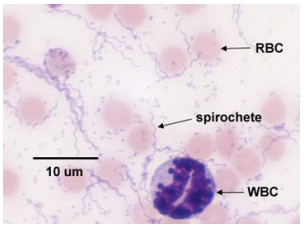


- Gram positive diplococci, suggestive of *S. pneumoniae*



- Gram positive bacilli (*Bacillus cereus* in peritoneal fluid)

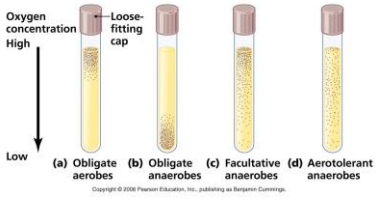
- Gram negative bacilli, suggestive of *Escherichea coli*



Spirochete bacteria; *Leptospira spp.*

Living environment

- Living environment : Aerobic, Anaerobic, Facultative anaerobic, Microaerophilic, Obligate intracellular

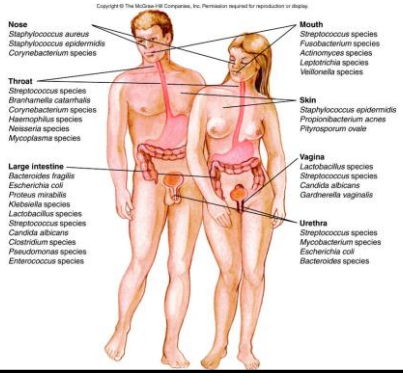


Laboratory identification

- Staining eg Gram's stain, AFB, Modified AFB
- Culture
  - Biochemical method : substrate, enzyme, product
- Molecular method(s) eg PCR
- Immunological method(s)
- Etc.

Normal flora

Normal flora
VS
Pathogen



Bacterial pathogenesis

- การติดเชื้อ (Infection) หมายถึง
  - A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen or a clinical syndrome associated with a high probability of infection
  - Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g., white blood cells in a normally sterile body fluid, perforated viscus, chest X-ray consistent with pneumonia, petechial or purpuric rash, or purpura fulminans)

Bacterial pathogenesis

- Pathogenicity หมายถึง ความสามารถของเชื้อที่จะทำให้เกิดโรคใน host
- Virulence factors :
  - Exotoxin (gram + and -) : excreted by living cell
    eg neurotoxin, cytotoxin, enterotoxin
  - Endotoxin (gram -) : integral part of the cell wall
    eg. O-specific polysaccharide, lipid A
  - Antiphagocytic factor (capsule)
  - Enzyme (hyaluronidase, collagenase ,deoxyribonuclease, hemolysin)
- Host factor : Immunity, Inflammation, stress, occupation, hereditary

ปัจจัยอื่นที่มีผลต่อการติดเชื้อ

- Tissue affinity
- Microbial adherence
- Invasion of the host
- Infective dose
- Portal of entry
- Communicability via mode of transmission (direct-indirect contact, airborne, foodborne and water borne, animal vector or zoonoses)

Classification of bacterial diseases

- แบ่งตามโครงสร้าง
- แบ่งตามทางติดต่อ เช่น ติดต่อทางเลือด สัตว์เป็นพาหะนำโรค
- แบ่งตามระบบของร่างกาย เช่น ระบบทางเดินหายใจ ระบบทางเดินปัสสาวะ
- แบ่งตามตำแหน่งที่เชื้อเพิ่มจำนวน เช่น ในเซลล์ นอกเซลล์
- แบ่งตามความสามารถในการก่อโรค เช่น high virulent, low virulent
- โรคติดเชื้อฉวยโอกาส (Opportunistic infection)
- โรคติดเชื้อในโรงพยาบาล
  (Hospital acquired/ Nosocomial infection)
- New and Emerging infectious diseases

วิธีการติดต่อ (Mode of transmission)

- การติดเชื้อโดยตรง (Direct transmission)
  คือการติดเชื้อจากคนหนึ่งสู่อีกคนหนึ่งโดยไม่ต้องอาศัยตัวกลาง เช่น น้ำ อากาศ อาหาร เช่น จากการสัมผัส จากละอองเสมหะน้ำลายโดยตรงจากผู้ติดเชื้อ การติดเชื้อจากมารดาทางรก เป็นต้น
- การติดเชื้อโดยอ้อม (Indirect transmission)
  การติดเชื้อโดยอาศัยตัวกลาง เช่น
  การติดเชื้อโรคที่ปนเปื้อนในอากาศ (Air-borne)
  การติดเชื้อจากสิ่งไม่มีชีวิตที่ปนเปื้อน (Vehicle-borne)
  การติดเชื้อจากสิ่งมีชีวิต (Vector-borne)

วิธีการติดต่อ (Mode of transmission)

ชนิดของการติดเชื้อจากคนสู่คน (Type of transmission between humans)

- การติดเชื้อจากระบบทางเดินหายใจ (Respiratory tract) เช่น วัณโรค ไขหวัดใหญ่
- การติดเชื้อจากบริเวณช่องคอและคอหอย (Oropharynx) ผ่านทางน้ำลาย เช่น HSV Epstein-Barr virus, Rabies virus
- การติดเชื้อจากระบบทางเดินอาหาร (Gastrointestinal tract [fecal-oral route]) เช่น ไวรัสตับอักเสบ A
- การติดเชื้อจากระบบสืบพันธุ์ (Urogenital tract) เช่น gonorrhea, HIV,
- การติดเชื้อจากทางผิวหนัง (Skin) เช่น เชื้อกลาก (Dermatophyte)
- การติดเชื้อทางเลือด (blood)
- การติดเชื้อทางน้ำนม (in milk)
- การติดเชื้อตั้งแต่กำเนิด (Congenital transfer)
  - ผ่านทางรก (Transplacenta) เช่น Rubella, CMV, HIV
  - ผ่านทางช่องคลอดเช่น Herpes simplex viruses, gonorrhea

วิธีการติดต่อ (Mode of transmission)

การติดเชื้อจากสัตว์ (Transmission from animals)
Arthropod-borne infection เช่น มาลาเรีย ไทฟัส
Zoonosis (โรคติดเชื้อจากสัตว์สู่คน) เช่น พิษสุนัขบ้า, Q fever

การติดเชื้ออื่นๆ เช่น

- การติดเชื้อเนื่องจากเครื่องมือแพทย์ (Fomite)
- การติดเชื้อจากการกินอาหารที่ปนเปื้อน (Foodborne)
- การติดเชื้อจากเชื้อโรคที่ปนเปื้อนในอากาศ (Airborne transmission)
- และอื่นๆ

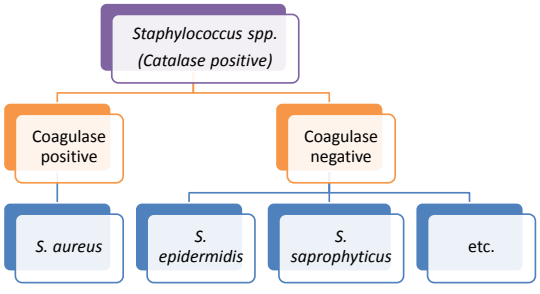
Bacterial infection

Classification
- Pyogenic gram positive cocci
- Bacterial infections of childhood
- Sexually transmitted bacterial diseases
- Enteropathogenic bacterial diseases
- Clostridial infection
- Bacterial infection with animal reservoirs
- Bacterial infection with immunocompromised host
- Filamentous bacterial infection
- Mycobacterial infection
- Mycoplasma infection
- Chlamydial infection
- Rickettsial infection

Pyogenic gram positive cocci

- Staphylococcus
- Streptococcus

Pyogenic gram positive cocci



Staphylococcus aureus

S. aureus is capable of invading almost every organ.
- Furuncles
  - infection around hair follicles
  - common in scalp, face, axilla
- Carbuncles
  - infection around hair follicle
  - and produce draining sinuses
- Hydradenitis suppurativa
  - Infection in sweat gland
- Rx: Penicillins (anti-β-lactamase eg Dicloxacillin, Cloxacillin)
  Macrolides
  Etc.

Furuncle due to *Staphylococcus aureus*.

A carbuncle is a complicated abscess on the nape of the neck.

Staphylococcus aureus

- Osteomyelitis
  - infection in bone
- Septic arthritis
  - Most common in prepubertal children
- Toxic shock syndrome (TSS)
  - infection in eg surgical wound, tampons, nasal packing
  - produce high fever, N/V, and shock
- Food poisoning
  - diarrhea, N/V
  - rapid onset food poisoning within 4-6 hours

Staphylococcus aureus

- Staphylococcal scalded skin syndrome (Pemphigus neonatorum or Ritter's disease)
  - Exfoliatin destroys desmogelin-1
  - The illness begins abruptly with erythema, followed in 2–3 days by the formation of flaccid bullae, which slough, leaving denuded areas that eventually resolve completely
  - Positive nikolsky sign
  - Other organs : lung, heart valve, bone

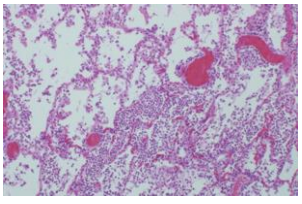
Staphylococcal scalded skin syndrome. Exfoliative phase, during which the upper epidermis is shed.

Nikolsky sign. With slight thumb pressure the skin wrinkles, slides laterally, and separates from the dermis.

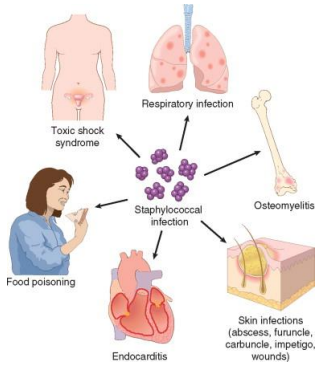
Staphylococcus aureus

- Abscess of skin and soft tissue
- Paronychia
  - Erythema and suppuration
- Breast abscess
  - 2-8 wks old: *S. aureus*, Group B streptococci
  - Minor local trauma may trigger
  - Breastfeeding and breast abscess

- Pneumonia
  - *S. aureus* is an infrequent cause of community-acquired pneumonia but a **common cause of nosocomial pneumonia**, which usually follows aspiration of endogenous nasopharyngeal organisms.



Staphylococcal abscess of the lung with extensive neutrophilic infiltrate and destruction of the alveoli

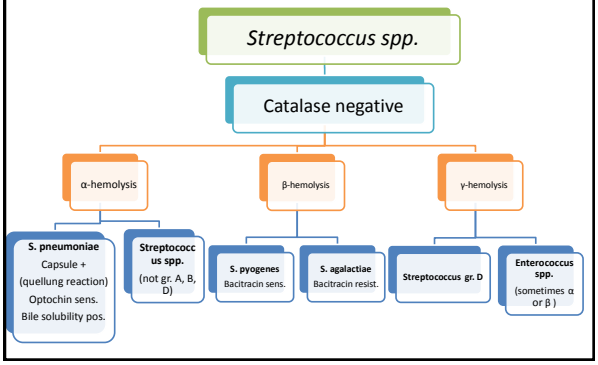


• The consequences of staphylococcal infection

Coagulase-negative Staphylococci

- *S. epidermidis*
  - causes opportunistic infections in catheterized patients, patients with prosthetic cardiac valves, and drug addicts.
- *S. saprophyticus*
  - common cause of urinary tract infections in young women.

Pyogenic gram positive cocci



α-hemolytic streptococci

- *S. pneumoniae*
  - Normal inhabitants of Upper respiratory tract of 5-40% of humans
  - common cause of community-acquired pneumonia and meningitis in adults
  - Sinusitis, Otitis
  - Sepsis in sickle cell anemia and splenectomy
  - Capsule of polysaccharide : Capsule swelling test (The Quellung reaction)

Viridans groups streptococci

- ***S. viridans eg S. mitis***; normal oral flora
  - endocarditis
- ***S. mutans***; synthesis of large polysaccharides
  - dental caries
- ***S. suis***
  - Meningitis, arthritis, endocarditis, pneumonia, and septicaemia with sudden death

β-hemolytic streptococci

- ***S. pyogenes*** (group A)
  - Habitat: throat, skin

- pharyngitis
- scarlet fever
- erysipelas
- cellulitis
- impetigo
- **Acute glomerulonephritis (AGN)**
- **Acute rheumatic fever**

Streptococcal sore throat

- Infant and small children: subacute nasopharyngitis with a tendency to extend to the middle ear, the mastoid and meninges. The cervical lymph nodes are usually enlarged.
- Adult is more acute. Intense nasopharyngitis, tosillitis and intense redness with exudate
- Rx: Penicillins eg Penicillin V, Amoxicillin
  - Cephalosporins, Macrolides, etc.

Streptococcal pyoderma

- Local infection of superficial layers of skin, esp. children, is called ***impetigo***
  - Superficial blisters that breakdown and eroded areas covered by pus or crusts.
  - Some types of M protein: may precede glomerulonephritis but do not often lead to rheumatic fever

Serum and crust about the nostrils is a common presentation for impetigo.

Impetigo in an infant and marked involvement of the face with honey-colored crusts and superficial erosions.

Cellulitis

Cellulitis : Infection in deep dermis
- *S. pyogenes* invade through wound
- Pustule in deep dermis
- Clinical : fever, erythematous skin lesion
- Usu. Clinical diagnosis

Erysipelas : Acute infection of dermis
- A rapidly advacing margin of infection.
- Erythematous rash, rapid distribution at face, particularly both cheek , trunk, extremities (uncommon)
- Most common among elderly, infant and children, diabetes, alcoholism, skin ulcer, impaired lymphatic drainage.

Streptococcal erysipelas.

Cellulitis

Cellulitis of the toe. The infection began adjacent to the nail as a paronychia but spread proximally to involve the shaft of the toe as cellulitis.

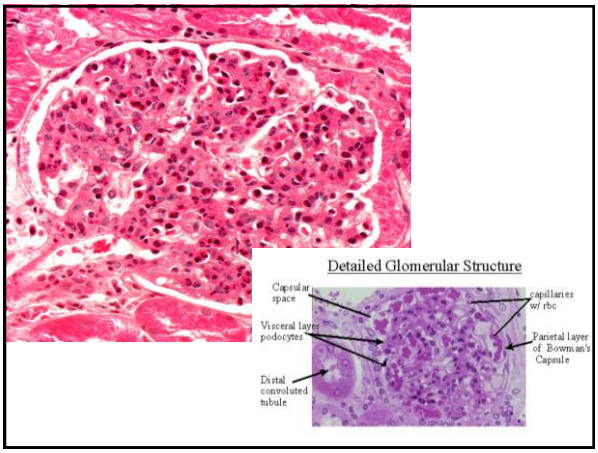
Scarlet fever and Streptococcal toxic shock syndrome

- Scarlet fever
  - Cause by erythrogenic toxin
  - Acute fever, sore throat
  - 1st 1-3 days:
    - Diffuse blanching erythematous rash
    - Sandpapery consistency, Pastia lines
  - White strawberry tongues→ peels off to red strawberry, Desquamation
- Streptococcal toxic shock syndrome
  - Bacteremia, respiratory failure, shock, multiorgan failure
  - Several presentations of soft tissue infection eg necrotizing fasciitis, myositis
  - Strep. TSS and scarlet fever are clinically overlapping diseases

Scarlet fever
Strawberry tongue

Acute glomerulonephritis (AGN)

- Post-Streptococcal Glomerulonephritis
- After infection of the skin (impetigo) or throat (pharyngitis) caused by nephritogenic strains of group A beta-hemolytic streptococci.
  - The **inflammation of the glomeruli** which causes the immunologic mechanism initiated by **antigen-antibody complexes** on the glomerular basement membrane.
  - Histopathologic changes include swelling of the glomerular and infiltration with polymorphonucleocyte.
  - Incubation period is 2 to 3 weeks
  - The majority recover completely



Acute glomerulonephritis (AGN)

- **Signs and Symptoms**
  - **Hematuria**: dark brown or smoky urine
  - **Oliguria**: urine output < 400 ml/day
  - **Edema**: starts in the eye lids and face then the lower and upper limbs then generalized
  - **Hypertension**: mild to moderate

Dx; Anti-streptolysin O, Anti-DNase B

Tx; No specific treatment

Destroy the remaining bacteria eg Penicillin/Cephalexin

Acute rheumatic fever

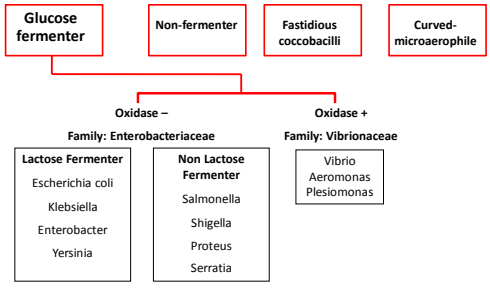
- The most serious sequela : Damage to heart muscle and valves
- Some strains contain cell membrane antigens that cross-react with human heart tissue antigen
- Onset : 1-4 wk
- A marked tendency to reactivated by recurrent Strep. Infection : Prophylactic penicillin administration
- Tx of strep. infection : 10 days of penicillin or erythromycin

Acute and chronic rheumatic heart disease

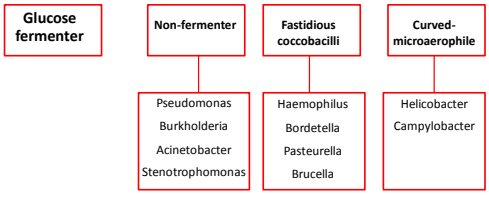
β-hemolytic streptococci

- ***S. agalactiae* (group B)**
  Lab test : Bacitracin resistant
  - meningitis (esp. newborn)
  chorioamnionitis, septicemia
- **Enterococci (group D)**
  normal colonic flora
  - UTI and subacute endocarditis
  - Can be very resistance to antibiotics esp. *E. faecium*
  - Intrinsic resistace to **cephalosporins**, penicillinase resistant penicillins and monobactam

Gram negative bacilli



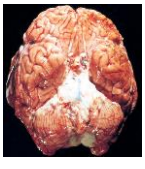
Gram negative bacilli



Bacterial meningitis

community-acquired bacterial meningitis

- *Streptococcus pneumoniae* 50%
- *Neisseria meningitidis* 25%
- Group B streptococci 15%
- *Listeria monocytogenes* 10%
- *Haemophilus influenzae* (type b) <10%



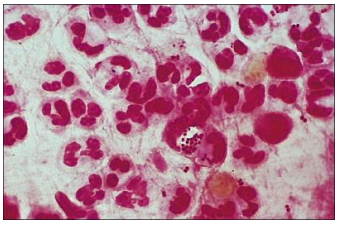
Harrison's Principles of Internal Medicine, 18e

Meningitis

- Incubation periods: 1-10d
- Nuchal rigitdity
- Positive Brudzinski sign
  - Passive flexion of neck
  - Grimace, neck stiffness with flexion
  - Flexion of knees+hips
- Bulging anterior fontanelle

Bacterial meningitis:

- **Neonates (<1 month)**
  - group B *streptococci, L. monocytogenes*
- **Children, young adults (2-20 yrs)**
  - *N. meningitidis*
  - clinical presenting of petechial or purpuric skin lesion
- **Adults (>20 yrs)**
  - *S. pneumoniae*
  - predisposing condition of increase risk infection is pneumococcal pneumonia



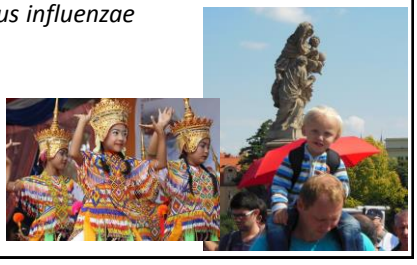
Sputum smear stained with Gram stain shows many neutrophils and intracellular gram-negative diplococci, suggestive of *Neisseria meningitidis* infection

Clinical manifestations of meningococcal disease. **A** and **B,** Macular and petechial rashes of meningococcal bacteremia. **C,**Fulminant meningococcal sepsis with ecchymoses. **D,** Digital necrosis of meningococcemia sepsis. **E,** Hemorrhagic adrenals in fulminant meningococcal sepsis.

Waterhouse-Friderichsen Syndrome : adrenal hemorrhage from *N. meningitidis*

Bacterial infection of childhood

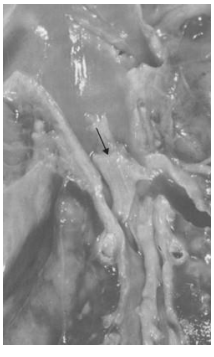
- Diphtheria
- Pertussis (Whooping cough)
- *Haemophilus influenzae*



Diphtheria

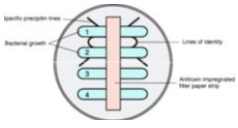
- Toxin-producing *Corynebacterium diphtheriae*
- *Club-shaped appearane (as other Corynebacterium spp.)*
- Transmitted as respiration
- Immunization with diphtheria toxoid (formalin-fixed toxin) **does not** prevent colonization with *C. diphtheriae* but protects immunized people from the lethal effects of the toxin.

- Toxin-mediated **inhibition of protein synthesis**
- Tracheal colonization may lead to
  - Mucosal erosion, Formation of a suffocation, **pharyngeal fibrinosuppurative exudate** (pseudomembrane) → obstruct airway (dirty patches)
- Toxin-mediated damage to the heart, nerves, liver, or kidneys
- Microscopic: necrotic tissue, neutrophil, fibrin, bacteria
- Tx: Antitoxin
  - ABO : penicillin G or erythromycin
  - Neither is a substitution of antitoxin



Membrane of diphtheria (arrow) lying within a transverse bronchus.

Tonsillar diphtheria



Elek test

Pertussis

- ***Bordetella pertussis*** infection (gram negative coccobacilli)
  - B. parapertussis can cause a similar disease
- Common in childhood (<5 yrs)
- Incubation perioid 2 wk
  - Catarrhal stage : mild coughing and sneezing
  - Paroxysmal stage : the cough develops its explosive character 'whoop' , vomiting, cyanosis and convulsion
    - Laryngotracheobronchitis may include mucosal erosion, hyperemia, and copious mucopurulent exudates
  - Rarely, followed by fatal encephalitis

Haemophilus influenzae infection

- Gram negative coccobacilli
- 6 serotype (a-f), **type b** causes as severe disease
- Caused by

  - pneumonia

  - meningitis (common in children)

  - upper respiratory infection (otitis media, sinusitis, epiglottitis)

- **Mechanism**

  - pilli of bacteria attached to respiratory epithelium→ secrete agent interfere cilia function, destroy IgA → hematogenous spreading

  - peptidoglycans destroy vascular and BBB → meningitis
- Dx : stained smear and culture. Immunological methods for *H. influenzae* are available.

Sexually Transmitted Diseases (STDs)

- Gonorrhea
- Chancroid
- Syphilis
- Granuloma inguinale

Gonorrhea

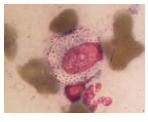
- ***Neisseria gonorrhoeae*** **(gram negative diplococci)**
- Male : urethritis, epididymitis
- Female : Cervicitis, salpingitis, endometritis, pelvic inflammatory disease (PID)
- Neonate : conjunctivitis (can lead to blindness)
- Septic arthritis, septicemia, proctitis, pharyngitis
- Tx : gram's stain and bacterial culture (Thayer-Martin agar)
- Rx : Ceftiazone (tetracycline and quinolone resistance are seen with increasing frequency)

Chancroid (soft chancre)

- *Haemophilus ducreyi* (gram negative bacilli)
- Clinical feature:
  - Painful multiple genital ulcer and dirty based ulcer
  - 50% inguinal lymphadenitis
  - suppurative inguinal lymphadenitis (bubo)
- DDx : from syphilis, herpes simplex infection and lymphogranuloma venereum (LGV)
- Tx : eg IM ceftriaxone, oral erythromycin

Granuloma inguinale

- Uncultivatable gram-negative coccobacilli *Calymmatobacterium granulomatis*
- A Painless papule that enlarge slowly. Inguinal lymphadenopathy is rare (pseudobulbo)
- Giemsa stain of tissue smear shows the black, intracellular Donovan body.



Syphilis

- *Treponema pallidum* (spirochete)

chancre : painless papule → a clean based ulcer and regresses 3-6 weeks. It occurs up to 1 yr after infection.

- inguinal lymphadenopathy
- microscopic: chronic inflammation (plasma cell, lymphocyte, macrophage) and organisms

Syphilitic chancre in the scrotum

Condylomata lata in secondary syphilis

- **Secondary syphilis**
  - systemic dissemination to many organs eg. skin,LN, meninges, liver, mucous membrane
  - common presentation: rash at trunk, extremities, palm, sole appears from 2 wks to 6 months after chancre heals

Secondary syphilis. Ham-colored palmar macules on an adolescent with secondary syphilis.

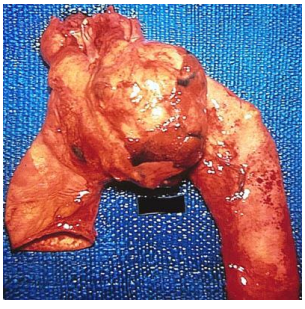
Perianal condylomata lata.

- **Tertiary syphilis**
  - 1/3 of untreated patient develop tertiary syphilis
  - syphilitic aortitis (80%) → aortic regurgitation, aneurysm
  - neurosyphilis → paralysis, seizure
  - Gumma : granulomatous inflammation in any organs eg. skin, bone, liver

Tertiary syphilis. Gummatous syphilis with destructive lesions on the nose.

Secondary syphilis lesion. Mucous patch lesion of secondary syphilis.

Tertiary syphilis



syphilitic aortitis with aneurysm

Congenital syphilis

- Intrauterine infection of fetus
- Common in primary and secondary syphilis (many organisms) of pregnant women
- Organisms transferred to fetus by placenta
- Causes late abortion, stillbirth, or death soon after delivery
- 2 stages
  - early syphilis
  - late syphilis

- **early syphilis (< 2 yrs)**
  - extensive cutaneous rash containing many spirochetes
  - Osteochondritis with collapse of the bridge of the nose (saddle nose)
  - Periostitis with bowing of the tibia
- **late syphilis (> 2 yrs)**
  - Hutchinson triad
    - eighth nerve deafness
    - interstitial keratitis (blindness)
    - notched central incisors (hutchinson teeth)

Hutchinson's teeth

Saddle nose in a newborn with congenital syphilis

- **Nontreponemal antibody test**
  - detect Ab against cardiolipin in blood
  - RPR, VDRL
  - screening test, follow up
  - positive in secondary syphilis
  - false positive : SLE, acute infection, leprosy, hypergammaglobulinemia
  - cure → negative result

- **Antitreponemal antibody test**
  - detect Ab againt *T. pallidum*
  - FTA-Abs, MHATP
  - positive after infection 4-6 wks and continuous positive until cure

stage	Lesion	Laboratory diagnosis
Primary	Chancre	Serological tests may be negative Dark ground microscopy of exudate
Secondary	Maculopapular rash	TPHA usually positive, VDRL raised
Tertiary	Aortic aneurism, neurosyphilis, gumma	FTA-Abs positive TPHA, VDRL may be negative

Tx : Benzathine penicillin (alt : tetracycline or erythromycin)
Follow-up serology (VDRL) at 1,3,6 and 12 months

Enteropathogenic bacterial infection

Common pathogens : gram negative bacilli

- Enterobacteriaceae
  - Salmonella
  - Shigella
  - *E. coli*
- Vibrionaceae
  - Vibrio

Salmonella enterocolitis

- More than 1,400 serogroup of samonellae
- Eg *Salmonella* Typhimurium, *Salmonella* Enteritidis
- N/V, profuse diarrhae with few leukocytes
- Resolves in 2-3 days
- Bacteremia is rare except in immmunodeficiency person.

Typhoid fever (enteric fever)

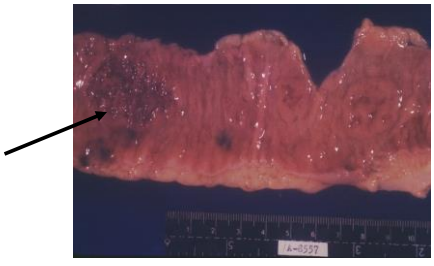
Salmonella typhi is the most important

- contaminated food and water. organisms contaminates in feces of carrier human
- -1 wk : septicemia, fever (gradual, then high plateau with typhoidal stage)
- 2 wks: bacterial replication in macrophages of Peyer patches of terminal ileum → intestinal nodule, abdominal pain

Salmonella Typhi (typhoid fever)

- 3 wks: bacteria invades in intestinal epithelium → ulcer along the intestine → mucous bloody diarrhea → shock
- Preantibiotic era : Intestinal hemorrhage and perforation
- Microscopic: necrotic epithelium, erythrophagocytosis
- Rose spots, usu on skin of abdomen and chest, are briefly seen in rare case.

Typhoid fever



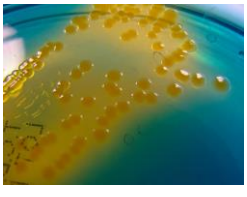
- Rose spots: 2- to 4-mm pink grouped papules on trunk or generalized erythema "erythema typhosum."

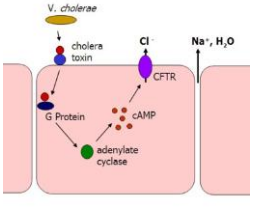
The isolation of *Salmonella sp.*

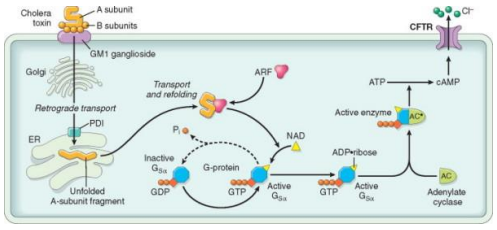
Cholera

- *Vibrio cholerae* (comma shaped, flagellated gram negative)
- V. cholerae serogroup O1 and O139 : Endemic and pandemic cholera
- Incubation period : 1-4 days
- Sudden onset of N/V, profuse diarrhea with abdominal cramps **(Rice water stool)**
- Heat labile enterotoxin subunit A and B

- Dx : Phase contrast microscope may show the rapidly motile vibrio, bacterial culture
- Tx: Tetracycline







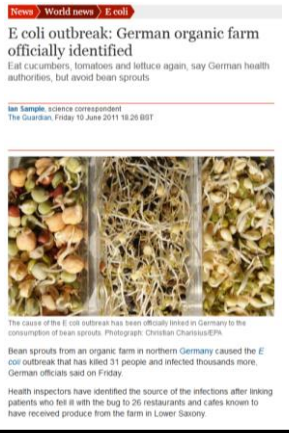
This leads to adenylate cyclase (AC) activation, and the cAMP produced opens CFTR (Cystic fibrosis transmembrane conductance regulator) to drive chloride secretion and diarrhea.

Escherichia coli

- Gram negative bacilli
- Normal flora in colon
- Cause several intestinal and extra-intestinal infections eg. urinary tract infections (UTI), meningitis, pneumonia, abdominal pain and diarrhea

- Enterotoxigenic E.coli produce cholera-like toxin (ETEC)
- Enterohemorrhagic E.coli produce shiga-like toxin, E. coli O157: H7 causes hemolytic uremic syndrome (EHEC)
- Enteropathogenic strains attach and efface epithelium, do not invade (EPEC)
- Enteroinvasive strains like shigellosis
- All cause **"Traveler's Diarrhea"**

Organism	Pathogenic Mechanism	Source	Clinical Features
Escherichia coli			Traveler's diarrhea, including:
• ETEC	Cholera-like toxin, no invasion	Food, water	Watery diarrhea
• EHEC	Shiga-like toxin, no invasion	Undercooked beef products	Hemorrhagic colitis, hemolytic-uremic syndrome
• EPEC	Attachment, enterocyte effacement, no invasion	Weaning foods, water	Watery diarrhea, infants and toddlers
• EIEC	Invasion, local spread	Cheese, water, person-to-person	Fever, pain, diarrhea, dysentery


News › World news › E coli

E coli outbreak: German organic farm officially identified

Eat cucumbers, tomatoes and lettuce again, say German health authorities, but avoid bean sprouts

Ian Sample, science correspondent
The Guardian, Friday 10 June 2011 18.26 BST

The cause of the E coli outbreak has been officially linked in Germany to the consumption of bean sprouts. Photograph: Christian Charisius/EPA

Bean sprouts from an organic farm in northern Germany caused the E coli outbreak that has killed 31 people and infected thousands more, German officials said on Friday.

Health inspectors have identified the source of the infections after linking patients who fell ill with the bug to 26 restaurants and cafes known to have received produce from the farm in Lower Saxony.

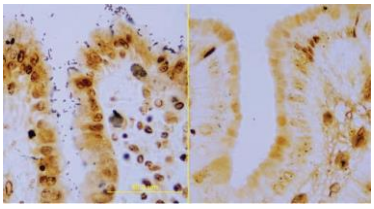
Outbreaks of E. coli O104:H4 infection

Campylobacter infection

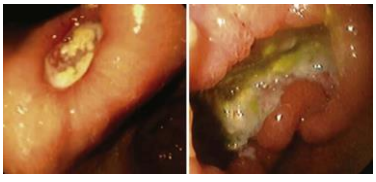
- Comma shaped, flagellated gram negative
- Common pathogen: *C. jejuni*
- Transmitted by contaminated food
- s/s: diarrhea, fever
- Microscopic: ulcer, neutrophils
- Abundant fecal leukocytes
- Complication: reactive arthritis, Guillain-Barre syndrome

Helicobacter pylori

- Curvilinear gram negative bacilli
- Strong producer of urease
- Associated with antral gastritis, duodenal (peptic) ulcer disease, gastric ulcer, gastric carcinoma and gastric lymphoma
- About 90 % of DU Pt and and 50-80% of GU Pt have *H. pylori* infection.
- Dx : Rapid tests to detect urease from fresh tissue are widely use.
  - Other tests : eg serologic tests, special silver stains from biopsy
- Tx : common regimen is triple therapy (PPI eg omeprazole, amoxycillin, clarithromycin)



Steiner stain of gastric antral biopsies from an H. pylori–positive patient (left) and an H. pylori–negative patient



Benign (left) and malignant (right) gastric ulcer.

Spore-forming bacilli

- Clostridium
  - *Clostridium perfringens*
  - *Clostridium tetani*
  - *Clostridium botulinum*
  - *Clostridium difficile*
- Bacillus
  - *Bacillus cereus*
  - *Bacillus anthracis*

Clostridial infection

Large anaerobic, gram-positive, motile rods

- *Clostridium perfringens*
- *Clostridium tetani*
- *Clostridium botulinum*
- *Clostridium difficile*

Clostridium perfringens

- **Gas gangrene** (Clostridial myonecrosis)
- Organisms invade through ulcer or contaminated traumatized area (eg soil, feces). The infection spreads in 1-3 days.
- Rapidly progessing necrosis, crepitation in subcutanous tissue and muscle, foul-smelling discharge, fever, shock and death
- Gram negative rods and various cocci occasionally are also usually present
- Toxins
  - α-toxin destroy RBC, platelet, muscle (myonecrosis with gas forming)

Clostridium perfringens

- Food poisoning
- Necrotizing enteritis
  - enterotoxin of *C. perfringens* (type C) induces necrosis and hemorrhage of small intestine
  - abdominal pain, nausea, vomiting, bloody diarrhea, dead (24 hrs)

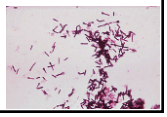
Gas gangrene

Clostridium tetani

- With terminal spore (Drumstick)
- Organism widespread in soil. Wound may be major or minor (a puncture while gardening)
- S/S eg Tetanus (lockjaw), Muscle spasm, hyperreflexia, convulsion
- Tx: Human tetanus immunoglobulin (TIG)
  - Tetanus antitoxin (TAT) : Skin test before use

Tetanus toxoid (formalin-fixed neurotoxin) is part of the diphtheria, pertussis; and tetanus (DPT) immunization.

Antibiotics : metronidazole, penicillin



Mechanism of tetanus toxin

Organisms produces neurotoxin (tetanospasmin)

↓

Toxin travel along peripheral nerve to anterior horn cells of spinal cord

↓

Inhibit neurotransmitter from inhibitory neuron

↓

Continuous muscle contraction

↓

Trismus or lockjaw, risus sardonicus , opisthotonos, dysphagia, dyspnea

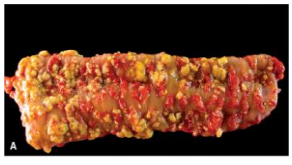
This infant with neonatal tetanus is displaying body rigidity produced by *Clostridium tetani* exotoxin.

Clostridium botulinum

- Produces most potent toxins known to human.
- Grows in improperly processed canned foods (eg home-preserved food) and releases a potent botulinum toxin that blocks synaptic release of acetylcholine and causes a severe paralysis of respiratory and skeletal muscles
- Botulism : Ingesting preformed toxin
- Infant botulism : Organisms produce toxin in infant's gut
- Wound botulism

Clostridium difficile

- Component of normal gut flora
- Hx: Treated by clindamycin or broad-spectrum antibiotics eg. cephalosporin, penicillin causes normal bacterial flora of bowel to be altered. May be spread by fecal-oral route.
- Pseudomembranous colitis (antibiotic-associated diarrhea). Can be fatal.
- Diagnosis by detection of toxins in feces
- Tx : Oral vancomycin or metronidazole



Pseudomembranous colitis

Bacillus

Bacillus cereus - Heat-stable toxin, ***entero***spore

- Food poisoning ; Diarrhea and abdominal pain occurs 8 to 16 hours (Diarrheal type)
  - The emetic form is manifested by N/V, abdominal cramp and occasionally diarrhea
- *B. cereus* is an important causes of eye infection eg severe keratitis, endophthalmitis associated with trauma (foreign body)
- Systemic infection eg endocarditis, osteomyelitis esp. presence of medical device or IV drug use

Bacillus anthracis

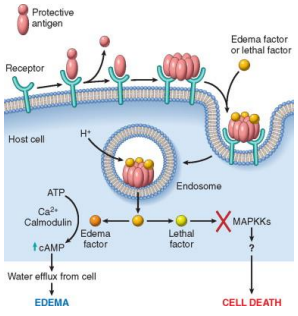
- Reservoirs: goat, sheep, cattle, dog, pig
- Spores form in soil, dead animals
- 3 group
  - cutaneous anthrax
  - inhalational anthrax
  - gastrointestinal anthrax

anthrax

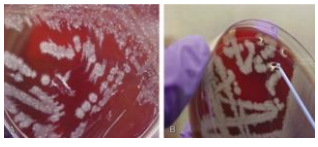
- **Cutaneous anthrax** (95%)
  - spores invade wound→after 1-7 d : painless papule and vesicle → ulcer, regional enlarged LN→ cure (up to 20% of patients can lead to sepsis)
- **Inhalational anthrax**
  - inhaled spores → hemorrhagic mediastinitis → sudden dead
- **Gastrointestinal anthrax** (rare)
  - eating spores contaminated meat → GI symptoms → high mortality rate
- Lab : non-hemolytic colonies aerobically, PCR
- Rx: ciprofloxacin, doxyclycline

Widened mediastinum due to inhalation anthrax.

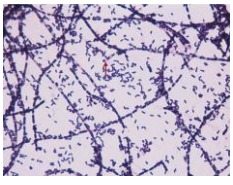
The lesion of cutaneous anthrax.



Mechanism of action of anthrax toxins.



A, Colonies of *B. anthracis* on sheep blood agar demonstrating white-gray colonies and "comet trail" or "Medusa head" outgrowths from colony margins. **B,** "Whipped egg white" appearance of tenacious *B. anthracis* colonies while being removed from sheep blood agar.



Gram stain of *B. anthracis* demonstrating long chains of bacilli that form when grown in culture. The prominent central or paracentral spores do not stain with gram staining and appear as clear areas in many of the bacilli in chains

Bacterial infection with animal reservoirs or insect vectors

- Plague
- Leptospirosis
- Cat-scratch disease
- Human and animal bites
- Anthrax

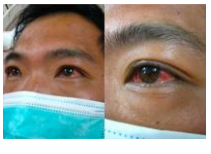
Plague

- *Yersinia pestis* : gram negative rod; bipolar staining with special stain
- Reservoir : flea; The most common vector is rat flea (*Xenopsylla cheopis)*
- Transmission : the bite of flea
  - inhalation of infective droplet : primary pneumonic plaque
- 3 syndrome
  - bubonic plague
  - septicemic plague
  - pneumonic plague

- Bubonic plague
  enlarged LN with hemorrhagic necrosis → involved skin → shock
- Septicemic plague
  septicemia → DIC, no enlarged LN → dead
- Pneumonic plague
  respiratory droplet transmission → pneumonia with hemorrhagic necrosis and pleuritis → dead
- Tx : streptomycin, tetracycline

Leptospirosis

- Leptospirosis is a zoonosis of worldwide distribution
- Human infection : ingestion of contaminated food or water or the organisms may enter through mucus membrane or breaks in the skin.
- Reservoir: rodent, cattle, cat, dog
- Bacteria secrete in animal urination and contamination in environment



- Incubation period : 1-2 wk
- Composed of 2 symptom

1.Anicteric leptospirosis

- leptospiremic phase: fever, headache, myalgia, hepatosplenomegaly
- leptospiruric phase: aseptic meninigitis

2.Severe leptospirosis (Weil's syndrome)

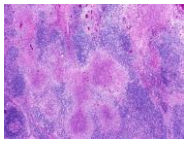
- severe jaundice, hepatosplenomegaly
- acute renal failure (dead)
- bleeding in GI, skin, brain

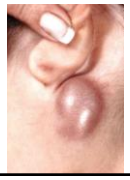
Dx : Dark field examination, Agglutiation antibody, etc

Tx: penicillin, ampicillin, amoxycillin, erythromycin

Cat-scratch disease

- *Bartonella henselae* (gram negative bacilli)
- Transmitted by scratch or bite of cat
- s/s : red papule or pustule skin, enlarged LN (axilla, neck)
- Microscopic: granulomatous inflammation and abscess

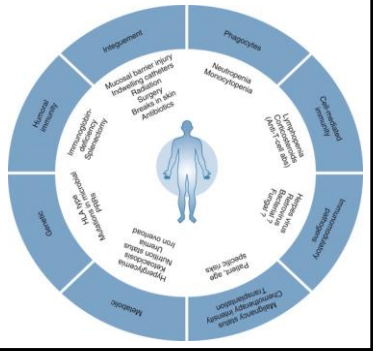




Human and Animal bites

- Dogs , Cats
  - *Pasturella multocida (gram-negative coccobacilli)*
    - ABO : amoxicillin-clavulanate, fluoroquinolones, tetracycline, etc.
- Human
  - Eikenella, anaerobes, strep, staph
- Reptiles
  - Enteric gram negatives (Salmonella)
- Raccoons, Bats, Foxes: Rabies
  - Exposure to saliva is sufficient!

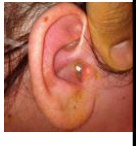
Bacterial infection with immunocompromised host



Constellation of factors contributing to increased risk for infection in immunocompromised hosts.

Pseudomonas infection

- *Pseudomonas aeruginosa* (gram negative bacilli)
- Nosocromial infection
- Common in severe burn, cystic fibrosis, leukopenia, UTI
  - Necrotizing pneumonia
  - Keratitis (contact lens)
  - Vulvular disease (IVDU)
  - Otitis externa (swimming), malignant otitis externa (immunocompromised)
  - Ecthyma gangrenosum (severe burn) (Yellowish – green discharge)



Klebsiella infection

- Gram negative rod with capsule
- Aspiration pneumonia in alcoholics and diabetics
- Community-acquired pneumonia
- Nosocomial infection
- UTI
- Treatment depends on the organ system involved

Neutropenic patients with fever

- Increased risk of bacterial and yeast infection
  - Looking for the signs of
    - Pneumonia
    - UTI
    - Skin sepsis (esp around IV catheter insertion sites)
    - Oral and perianal infection
    - Septicemia
  - Organisms usually come from GI tract (e.g. gram negative bacilli, enterococci) or skin (e.g. staphylococci, corynebacterium)

Splenectomy and sepsis

- Put them at risk of infection with capsulated bacteria particularly
  - S. pneumoniae
  - H. influenzae
  - N. meningitidis
- Opsonic IgG

Filamentous bacteria

- Aerobic actinomycetes
- Anaerobic actinomycetes

Order Actinomycetales (Actinomycetes)

- Aerobic actinomycetes
  - cell wall **with** mycolic acid
    Nocardia(mAFB only), Mycobacterium
    Corynebacterium
  - cell wall without mycolic acid
    Actinomadura, Streptomyces
- Anaerobic actinomycetes
  - cell wall without mycolic acid
    Actinomyces, Propionibacterium, Lactobacillus

* เชื้อที่ cell wall มี mycolic acid จะย้อมติด AFB และ modified AFB

Filamentous bacteria infection

- Actinomycosis
  - Normal flora of the mouth and gastrointestinal tract
  - *E.g. Actinomyces israelii*
- Cervicofacial diseas : mass, erythema in the jaw area fluctuant, producing draining fistulas
- Osteomyelitis, intra-abdominal infection, pelvic inflammatory disease (IUD)
- Gross: sulfur granules (grains) ; yellow color, up to 1 mm in size and are compose of macrophages, tissue cells, fibrin, and bacteria
- Microscopic: organisms surrounded by neutrophils, histiocytes, giant cells
- Special stains (GMS): filamentous shaped bacteria
- Tx : penicillins, tetracyclines, erythromycin, clindamycin, etc.

Actinomycosis

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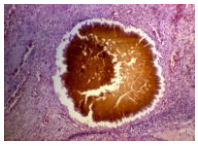
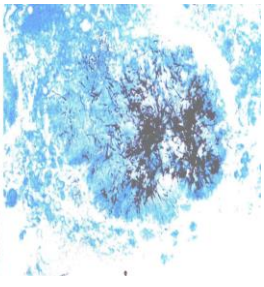


sulfur granules

Actinomycosis

Cluster of filamentous bacteria



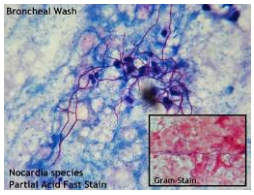
Filamentous bacteria by GMS

Nocardiosis

- An oppotunistic infection associated with impair CMI, AIDS, TB, Organ transplantation, alcoholism, immunosuppression or corticosteroid treatment
- *Nocardia asteroides*
- S/S chronic lobar pneumonia : fever, weight loss, chest pain
- Spread from the lung : CNS abscess
- Dissimination : skin, kidney, etc

Nocardiosis

- Microscopic : neutrophil, macrophage, necrosis, organisms and may be giant cells
- Special stains : modified acid fast stain (red filament or branching)



Mycetoma

- **Actinomycotic mycetoma** : caused by
  - *Actinomadura* spp.
  - *Streptomyces* spp.
  - *Nocardia* spp.
- **Eumycotic mycetoma** : caused by
  - fungi e.g. *Pseudallescheria* spp., *Madurella* spp.

Mycetoma

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Actinomycotic mycetoma

- Localized multiple nodules with sinuses and swelling lesions
- Involving cutaneous and subcutaneous tissues, fascia and bone
- Occurs on foot or hand
- Results from traumatic implantation of soil organisms into the tissues
- Lesions are composed of suppurating abscesses and sulfur granules (grains)

Actinomycotic mycetoma

- Microscopic : organisms surrounded by neutrophils, histiocytes, giant cells
- Special stains (GMS): filamentous shaped bacteria

Mycobacterial infection

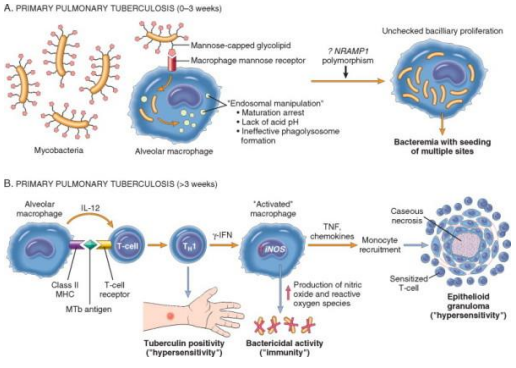
- ***Mycobacterium tuberculosis* complex**
  - *M. tuberculosis, M. bovis, M. africanum, M. microti*
  - causes pulmonary and extrapulmonary TB
- **Nontuberculous mycobacteria (NTM)**
  - *Mycobacterium avium* complex (MAC) (*M. avium, M. intracellulare*)
- **Mycobacterium causes leprosy**
  - *M. leprae*

Pulmonary tuberculosis

- Caused by *M. tuberculosis*
- Classified 2 types
  - Primary pulmonary tuberculosis
  - Secondary pulmonary tuberculosis
- Miliary tuberculosis : The disease of the lung may spread to other sites or proceed to a generalized infection lymphatic or hematogenous spreading (eg liver, spleen, pancreas)

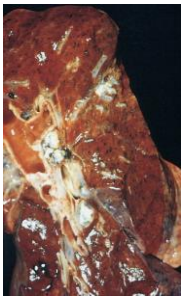
Primary pulmonary tuberculosis

- Primary tuberculosis is usually mild and asymptomatic and in the 90% of cases does not proceed further
- Primary infection at lungs composed of "Ghon complex"
  - Lung infection at lower segment of upper lobe or upper segment of lower lobe → **Ghon focus**
  - **Infection of hilar node**
  - Most of infected persons → healed scar
- Clinical manifestation : Fatigue, Wt loss, fever
  - Infection of the lungs cause a chronic productive cough and sputum may be blood-stained.
- Miliary TB in a small percentage of people (esp. immunocompromised host)



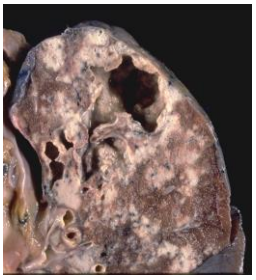
Secondary pulmonary tuberculosis

- Reactivation or reinfection of primary, asymptomatic TB
- Common infection at high O^2 (apex of lung)
- Severe lung damage and produces cavity
- Clinical manifestation : low-grade fever, chronic cough, night sweat, weight loss, anorexia
- Miliary TB in a small percentage of people (esp. immunocompromised host)

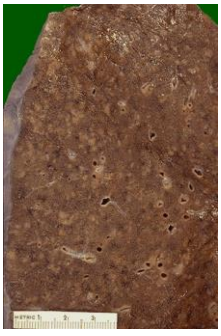


Primary pulmonary tuberculosis, Ghon complex. The gray-white parenchymal focus is under the pleura in the lower part of the upper lobe. Hilar lymph nodes with caseation are seen on the left.

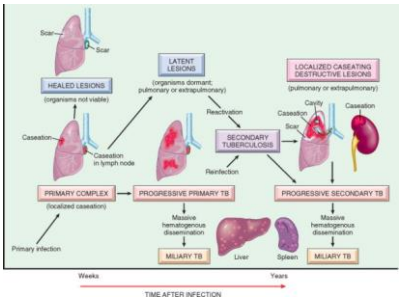
Chest radiograph shows patchy consolidation, nodules, and cavities (arrows) in bilateral upper lung zones.



Secondary pulmonary tuberculosis



The miliary pattern gets its name from the resemblence of the granulomas to millet seeds.



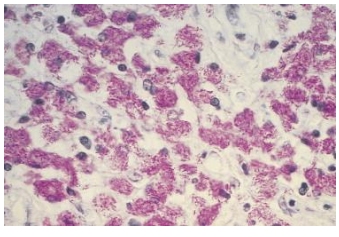
The natural history and spectrum of tuberculosis.

Extrapulmonary tuberculosis

- TB at any organs eg. LN, GI, skin, meninges, bone, liver, spleen etc.
- Tuberculous Lymphadenitis : most common form
- Transmitted by TB lung spreading or direct invasion to any organs
- Gross and microscopic similar to TB lung

Nontuberculous mycobacteria

- *M. avium* complex (MAC or *M avium-intracellulare*)
- Common in immunocompromised host eg. AIDS, leukemia
- Infection in any organs eg: lung, GI, bone
- common among patients with advanced HIV disease and it occurs in people with CD4 counts of <50 cells/µL.
- Gross: non-specific
- Microscopic: clusters of macrophages contain many organisms (AFB stain)
- Rx : eg Clarithromycin or azithromycin plus ethambutol



Photomicrograph of mesenteric lymph node shows histiocytes filled with acid-fast bacilli, stained in red.

Leprosy

- *Mycobacterium leprae*
- Transmitted by respiration
- Causes skin lesion
  - tuberculoid leprosy
  - 'borderline'
  - lepromatous leprosy

Dx: Scrapings from lesions; stained by the Ziehl-neelsen technique

Rx: Dapsone, Rifampin, clofazimine

Tuberculoid leprosy

- Asymmetry erythematous plaque with sharp outer margins fading centrally to a flattened clear zone of healing that is rough, anhidrotic, hairless, hypopigmented, and anesthetic
- Muscle atrophy, ulcer, contracture
- Slow progressive
- Micro: granulomatous inflammation, rare organisms

Lepromatous leprosy

- More severe
- The early lesions of lepromatous leprosy are multiple, symmetrically distributed, erythematous ill-defined macules and papules
- Muscle atrophy
- **Micro:** clusters of macrophages containing organisms (AFB stain)

Tuberculoid leprosy. A single large lesion with irregular, raised, erythematous borders and a depressed, hypopigmented center is shown.

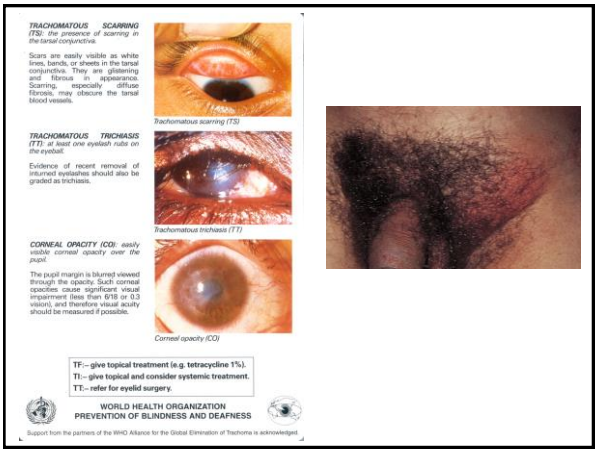
Lepromatous leprosy

Chlamydia infection

- *Chlamydia trachomatis*
- *Chlamydophila psittaci*
- *Chlamydophila pneumoniae*

Chlamydia trachomatis

- Trachoma (Also called granular conjunctivitis) (serovars : A, B, Ba and C)
- urogenital infection, acute inclusion conjunctivitis, newborns infected by the mother (serovars : D-K)
  - Eg nongonococcal urethritis, cervicitis, PID (which can lead to sterility)
  - Dx: Direct fluorescent antibody or ELISA, PCR
    - Neonatal pneumonia: IgM antibody
  - Rx: eg doxycycline, azithromycin
- Lymphogranuloma venereum (serovars : L1, L2, L3)



Chlamydophila psittaci

- Airborne bird excreta to humans
- Incubation period: 10 days
- Mild inapparent infection, UTI, atypical pneumonia to severe pneumonia and sepsis
- Dx : Serology, PCR or antigen detection
- Rx : Tetracycline

Chlamydophila pneumoniae

- Airborne person to person
- Upper and lower respiratory tract disease, atypical pneumonia
- Serology using the microimmunofluorescence test, Direct detection of elementary bodies in clinical specimen
- Rx : macrolides, tetracyclines, some FQs

M. pneumoniae

- No cell wall → no Gram staining
- Transmitted by respiration
- Common in child, young adult
- Caused by
  - pharyngitis
  - sinusitis
  - laryngotrachebronchitis
  - atypical pneumonia

Dx : largely made by clinical recognition
Cold hemagglutinin 1:64
Rx: Tetracyclines or Erythromycins

Rickettsia infection

- spotted fever group
- typhus group
- scrub typhus group

Rickettsia infection

- **Pathology**
  - destroy arteriole and capillary
  - necrotizing vasculitis
- Spotted fever and scrub typhus groups : **eschar**
- Typhus group: **no eschar**

Spotted fever group

- Rocky Mountain spotted fever
  - *R. rickettsii*
  - Tick bite
- Rickettsiapox
  - *R. akari*
  - Mite bite

Rocky Mountain spotted fever

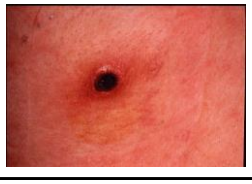
- *Rickettsia rickettsii*
- Tick
- Fever, myalgia, maculopapular rash (palms and soles: **extremities→ centrally**
- Sepsis
- Rx: Doxycycline

Typhus group

- **Epidermic typhus Brill-Zinsser disease**
  - *R. prowazekii*
  - Louse feces
- **Murine typhus**
  - *R. typhi*
  - Rat flea feces

Scrub typhus group

- **Scrub typhus**
  - *Orientia tsutsugamushi*
  - Chigger bite



Scrub typhus

- Presents as an acute febrile illness 7 to 10 days after the bite of an infected larval trombiculid mite (chigger)
- High fever, intense generalized headache, diffuse myalgias
- Some patients develop eschar and/or generalized maculopapular rash.
- The indirect fluorescent antibody (IFA) test is the mainstay of serologic diagnosis.

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