Lecture 1 Antibiotic resistance:

Testing methods for antimicrobial susceptibility testing:

1-Disk diffusion procedure Sensitive, Intermediate, Resistant

2- Etest Quantitative (MIC) and qualitative

Resistant bacteria

- Are not inhibited by the usually achievable systemic concentrations of the normal dosage

Testing methods

typically used for antimicrobial susceptibility testing (AST):

Description: A qualitative method where antibiotic-impregnated paper disks are placed on an agar plate inoculated with the test organism.
How it works: Bacteria grow on the plate.
If the bacteria are sensitive to the antibiotic, a zone of inhibition (clear area) appears around the disk.
The size of this zone is measured in millimeters

- Disk diffusion procedure
  - Sensitive, Intermediate, Resistant

Sensitive (S): Likely to respond to treatment with the antibiotic.
Intermediate (I): May respond if high doses are used or if the drug concentrates at the infection site.
Resistant (R): Unlikely to respond to the antibiotic.

(Epsilometer Test)

- Etest

A quantitative method that determines the Minimum Inhibitory Concentration (MIC) of an antibiotic.
The lowest concentration of an antimicrobial that will inhibit visible growth.

  - Quantitative (MIC) and qualitative

how it works ?
A plastic strip containing a gradient of antibiotic concentrations is placed on an agar plate.
After incubation, an ellipse-shaped inhibition zone appears.
The MIC is read where the zone edge intersects the strip.

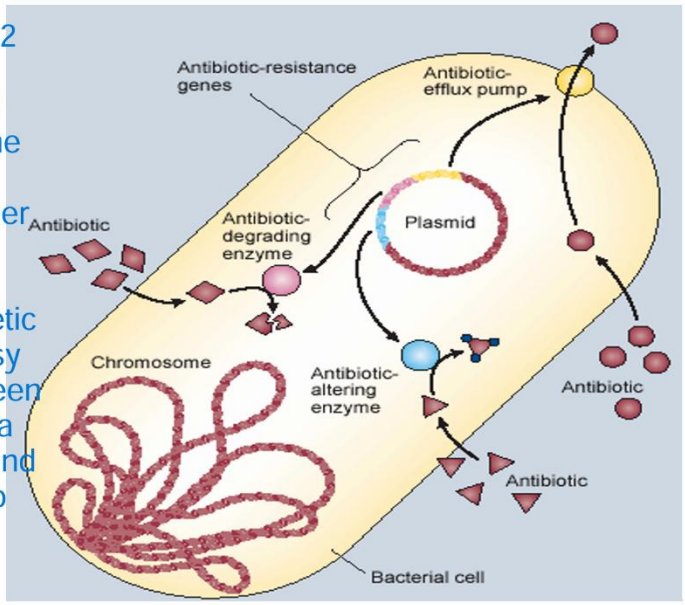
may be considered as resistance

Intermediate strains

- MIC approaches attainable blood levels and response rate may be lower than susceptible bacteria

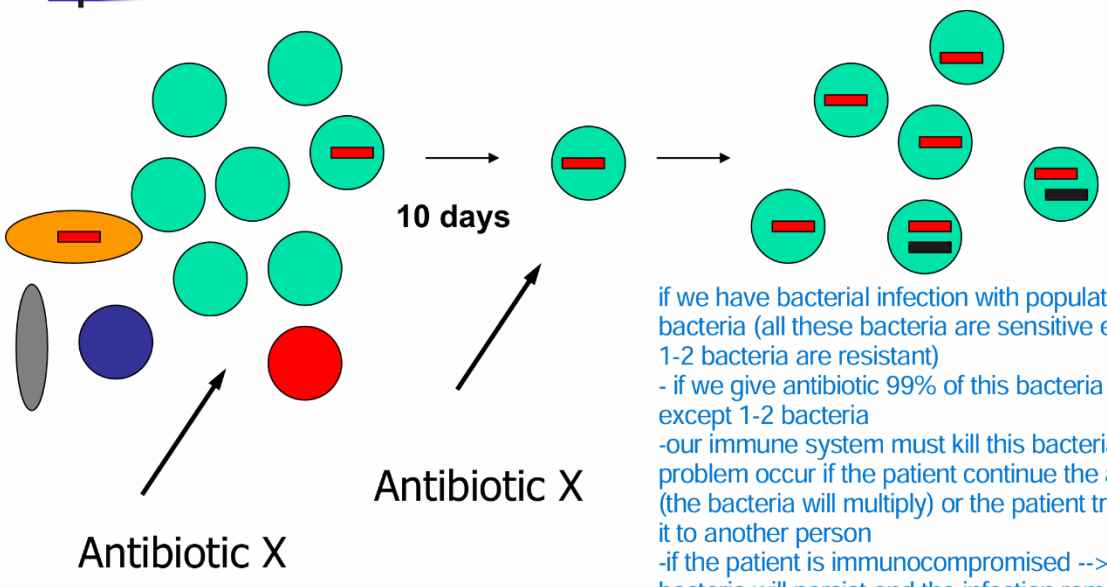
Mechanisms of resistance

the antibiotic have 2 genetic materials :
1-chromosomal (it has a resistant gene but its difficult to transferee to another bacteria
2-plasmid (extra chromosomal genetic material)/ very easy transferrable between bacteria and have a resistance genes and may transferee it to another bacteria



1-antibiotic degrading enzyme (like Beta-lactamase degrade beta-lactam)
2-clindamycin , erythromycin work on certain ribosome receptor (if these receptors change then the antibiotics will be ineffective)
3-bacteria secrete a substance (efflux pump)

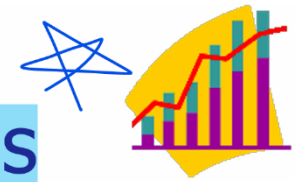
Resistance selection



if we have bacterial infection with population of bacteria (all these bacteria are sensitive except 1-2 bacteria are resistant)
- if we give antibiotic 99% of this bacteria are died except 1-2 bacteria
-our immune system must kill this bacteria but the problem occur if the patient continue the antibiotic (the bacteria will multiply) or the patient transferee it to another person
-if the patient is immunocompromised --> the bacteria will persist and the infection remain or the next infection the patient will have high resistant bacteria

for antibiotic resistance

Surveillance systems



- SENTRY (Longitudinal national and international program)
- EARSS (European Antimicrobial Resistance Surveillance System)
- NNIS (National Nosocomial Infection Surveillance)
- SCOPE (Surveillance and Control of Pathogens of Epidemiologic Importance)
- ICARE (Intensive Care Antimicrobial Resistance epidemiology)

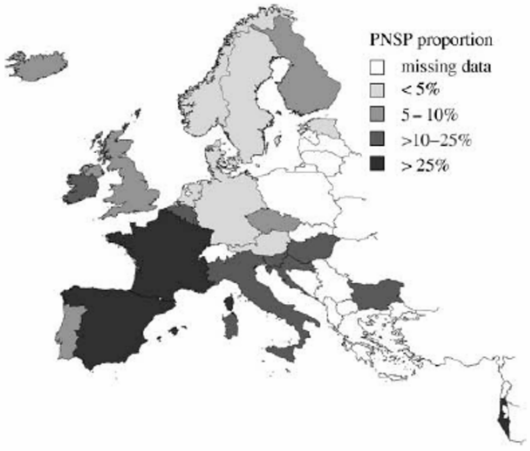
SENTRY 1997-2002

- Blood Stream Infections
- 81,213 isolates
- North America, Europe, Latin America
  - Gram +ve in US vs. Gram –ve in Europe
  - R more common in nosocomial and ICU than community settings

EARSS Program 1999-2002

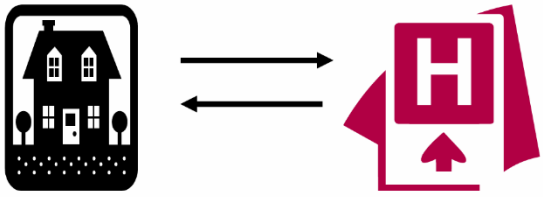
Invasive *S. pneumoniae* resistance trends

- 26 European countries
- 22 277 isolate
- Blood 93%, CSF 7%
- R highest in Mediterranean

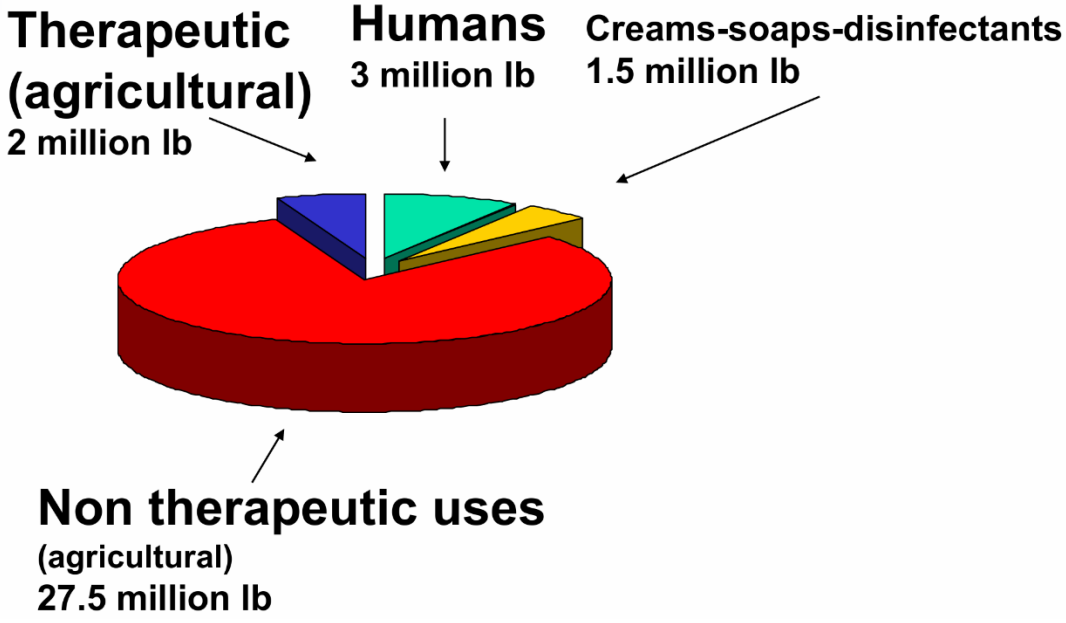


Common resistant bacteria

- MRSA
- CoNS
- *VRE*
- *E. coli*
- *P. aeroginosa*
- *Enterobacter* spp
- *S. pneumoniae*
- *Klebsiella* spp
- *Acinetobacter* spp
- *N. gonorrhea* cause sexual transmitted disease
- *S. typhi*



Antimicrobial consumption



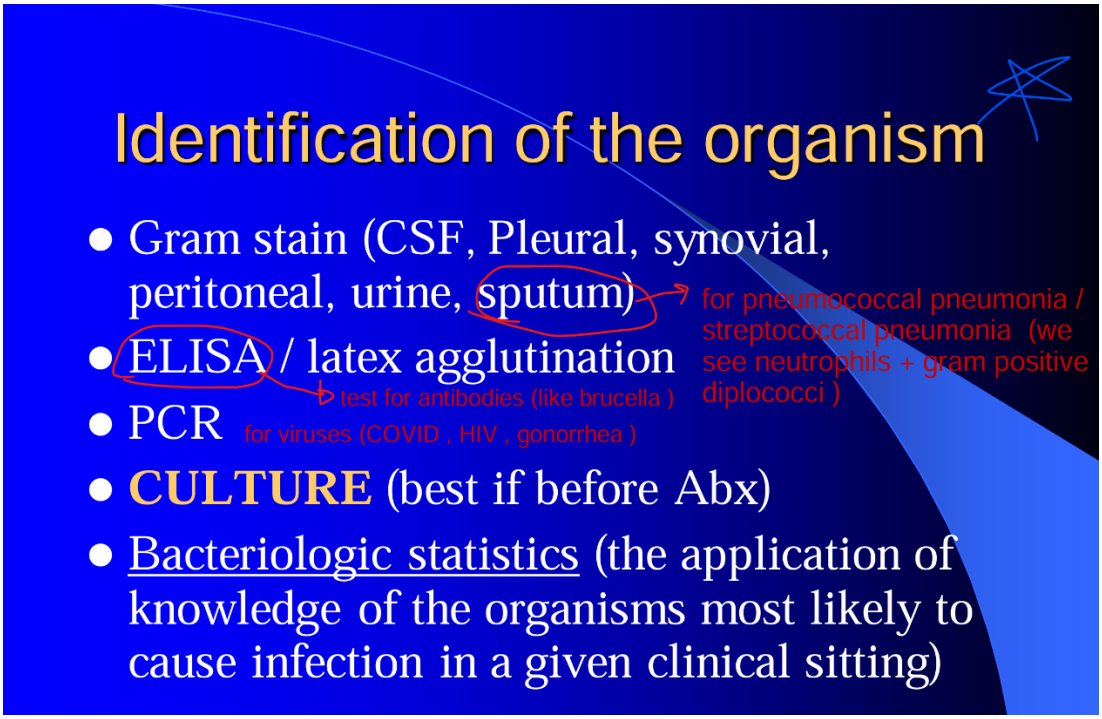
how to differentiate between staph aureus if it is VISA or VRSA ? by MIC

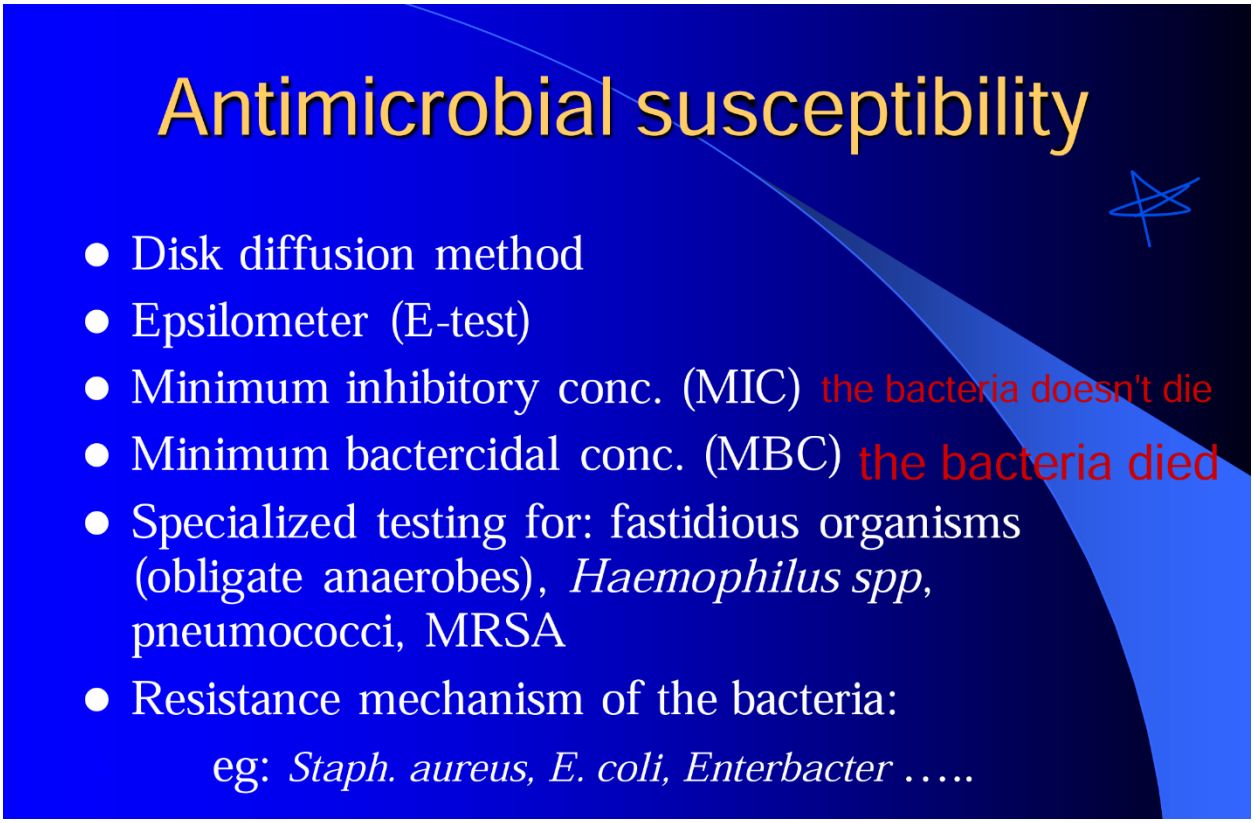
if the MIC >16 or 32 --> VRSA

if the MIC = 4-8 --> VISA

if the MIC = 1-2 --> vancomycin sensitive staph aureus

lecture 2 Principles of antibiotic therapy:





Pharmacodynamic profile

Ratio of total drug exposure over 24 hours (AUC) to the Minimum Inhibitory Concentration (MIC).
Reflects the overall drug exposure the bacteria sees

- Area under the curve / time curve to MIC (AUC / MIC)

Higher AUC/MIC --> better killing
Maximize total exposure for best effect.

- Maximal serum conc. / MIC (C_{max} / MIC)
- Time during dosing interval that plasma conc. exceed the MIC (*t* / MIC)

Amount of time during the dosing interval that the drug concentration stays above the MIC.
Antibiotic classes:
Beta-lactams (penicillin's, cephalosporins, carbapenems)
Monobactams
Goal: Keep plasma levels above MIC for as long as possible
Longer T>MIC -->better bacterial kill

Antibiotic classes:
Aminoglycosides (e.g., gentamicin)
Fluoroquinolones (also partly AUC/MIC)
Goal: Achieve a high peak for rapid and extensive killing
High Cmax/MIC (>10:1) is ideal for aminoglycosides

Conc. & Time dependent dosing

Fluoroquinolones (FQ) and Aminoglycosides (Ag)

- **Conc. dependent** (FQ, Ag) → increase in conc leads to a more rapid rate of bacterial death (i.e. large dose at long intervals)

- **Time dependent** (β-lactams, vancomycin) →reduction in bacterial density is proportional to the time that the conc. exceeds MIC (i.e. sufficient dose at appropriate intervals to keep conc. above MIC)

Host factors

- Previous history of adverse reactions
- Neutrophil function → neutropenic are treated aggressively
- CLL, MM, asplenia → treated empirically

antibody deficiency , humoral cell deficiency

Age

- Renal function (impaired physiologic function)
- Absorption
- Tetracyclines not for children <3 years
- INH hepatotoxicity
- Nephrotoxicity
- Ag and cochlear toxicity

Genetic / metabolic

- Hemolysis in G6PD deficiency
- DM : sulfa drugs can potentiate the sulfonylurea hypoglycemic agents
  - Dextrose load
  - Poor IM absorption (use IV route)

Pregnancy

Penicillin

- Safe : PCN, cephalosporin, erythromycin base
- Dangerous: **tetracyclines** (hepatic toxicity, dental discoloration)
- ? Teratogenic: **metronidazole**
- **FQ, clarithromycin, erythromycin → Contrindicated**
- ?? rifampin, Ag, azithromyccin, clindamycin, imipenem,vancomycin, TMP

Renal and liver fx

- Vancomycin & Aminoglycosides (gentamicin, amikacin)

Site of infection

- Optimal therapy requires concentrations > MIC at the site of infection
- Meningitis
  Endocarditis
  Osteomylitis
  Chronic prostatitis
  Intraocular infections
  Abscesses
  Foreign body
  UTI

Combinations

- Some physicians use combinations for the sense of security → deleterious effects
- **Indications**: 1) prevention of emergence of resistant bacteria : TB, *staph* endocarditis

  2) polymicrobial infections : abd. sepsis

  3) initial therapy: eg: Ag + piperacillin

  4)Synergism:… One antibiotic enhances the activity of another

Synergism

- For resistant organisms
- Limited data to support their benefit
- e.g.: PCN + Ag → Enterococcal endocarditis
- Oxacillin + Ag → Staph. endocarditis
- Anti-pseudomonal β- lactam + Ag → Pseudomonas bacteremia
- Impaired host

Antagonism

- Too many in vitro reports
- Clinically was seen in : PCN + tetracyclines
- 2 β-lactams → induce β lactamases
- More important in immunosuppressed pts

Route

- Oral → stable , mild infection (reliable pts)
- IV → serious infections (sepsis) + DM

Wrong uses

- Abx for simple gastroenteritis
- Routine use of Flagyl (Metronidazole) to clean bowel
- Abx for common cold and simple bronchitis

Lecture 3 Typhoid Fever & Salmonella Enterocolitis

Most common in India , Bangladesh , Africa ,China , Indonesia , Pakistan ..

Typhoid Fever

Causative Agent --> Salmonella enterica serovar Typhi ((Gram-negative bacillus))

Typhoid fever is an acute generalized infection of the:

- Mononuclear phagocyte system — Includes liver, spleen, bone marrow; Bacteria multiply in macrophages --> systemic spread
- Intestinal lymphoid tissue — Peyer's patches in the ileum; Inflammation and necrosis here may lead to intestinal ulceration, bleeding, or perforation
- Gallbladder caused by Salmonella enterica serovar Typhi.

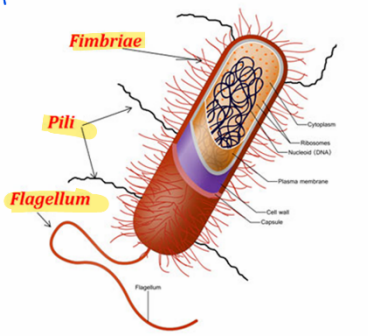
Salmonella

Member of the Enterobacteriaceae family
Strictly human pathogens
Transmitted via fecal–oral route

- Gram-negative motile, nonsporulating, straight-rod bacteria.
- Intracellular facultative pathogens
- *S. typhi* and *Salmonella paratyphi* A, B, and C causes typhoid or paratyphoid (generally milder)
- Salmonellosis-causing serotypes are isolated from humans and animals, including livestock.

Reservoirs: Humans, livestock (cattle, pigs, poultry), reptiles, and contaminated food

- Food poisoning is caused mostly by Serotypes
  - *Salmonella* Typhimurium — Foodborne illness (meat, eggs, poultry)
  - *Salmonella enteritidis* — Contaminated eggs/poultry
  - *Salmonella Newport* — Dairy, beef, produce
  - *Salmonella Heidelberg* — Poultry, meat
  - *Salmonella* Cholerasuis — Invasive disease in pigs; may cause septicemia in humans
  - *Salmonella* Dublin — Associated with cattle; invasive disease in humans



Cell-Surface Appendages of a Bacterial Cell

How It Causes Disease

(virulence) capsular polysaccharide antigen

- The Vi antigen of *S typhi* is important in preventing antibody-mediated opsonization and complement-mediated lysis --> Enhanced survival in the host, especially inside macrophages

- Through the induction of cytokine release and via mononuclear cell migration, *S typhi* organisms spread through the reticuloendothelial system, mainly to the liver, spleen, and bone marrow.

After ingestion (usually via contaminated food or water), the bacteria -->Invade intestinal M cells overlying Peyer's patches --> Are engulfed by macrophages --> Induce cytokine release --> promotes mononuclear phagocyte migration

- Within 14 days, the bacteria appear in the bloodstream, facilitating secondary metastatic foci (eg, splenic abscess, endocarditis).

Spleen--> Splenic abscess
Heart--> Endocarditis
Intestines Ulceration --> bleeding or perforation
Gallbladder--> Chronic carriage
Lungs, bones, CNS --> Less common but possible foci

Humans are the Reservoir

Unlike non-typhoidal Salmonella (which can be found in animals)

- Defined as the habitat in which the agent normally lives, grows, and multiplies) of *Salmonella* Typhi.
- *Salmonella* Typhi has a limited capacity to multiply outside of the human host, but it may survive for extended periods in the environment
  - on contaminated water
  - On surfaces or produce
  - For days to weeks under favorable conditions
- The case fatality risk of typhoid fever was approximately 10%–30% in the pre-antimicrobial era. With effective antimicrobials, the case fatality risk is usually <1%.

Portal of Exit, Route of Infection, and Source

- Transmission is indirect
- Feces represent the major portal of exit of Salmonella typhi, although shedding in urine has also been documented
- Salmonella typhi may be shed in the stool or urine during and following both clinical and subclinical acute infection.
- Shedding may be temporary or chronic.
  - Temporary shedding may be acute or convalescent
  - A convalescent carrier sheds Salmonella Typhi for ≥3–12 months after the onset of acute illness.
  - A chronic carrier sheds typhoid bacilli for >12 months after the onset of acute illness.
- Chronic carriers are known to be a major source of domestically acquired Salmonella typhi infections in countries with low typhoid incidence

Disease Transmission, and Inoculum?

amount (or dose) of a microorganism (like bacteria, virus, or fungus) that enters the body and may cause infection.

- Hygeine
- The portal of entry for *Salmonella* Typhi infection is the mouth, usually through ingestion of fecally contaminated water or food. Infection occurs in a susceptible human host.
- Large inoculums are also associated with higher rates of illness and shorter incubation periods.
  - In general, about 10^6 bacterial cells are needed to cause infection.
  - Low gastric acidity can decrease the infective dose to 10^3 cells, more susceptible
  - Prior vaccination can increase the number to 10^9 cells. less susceptible

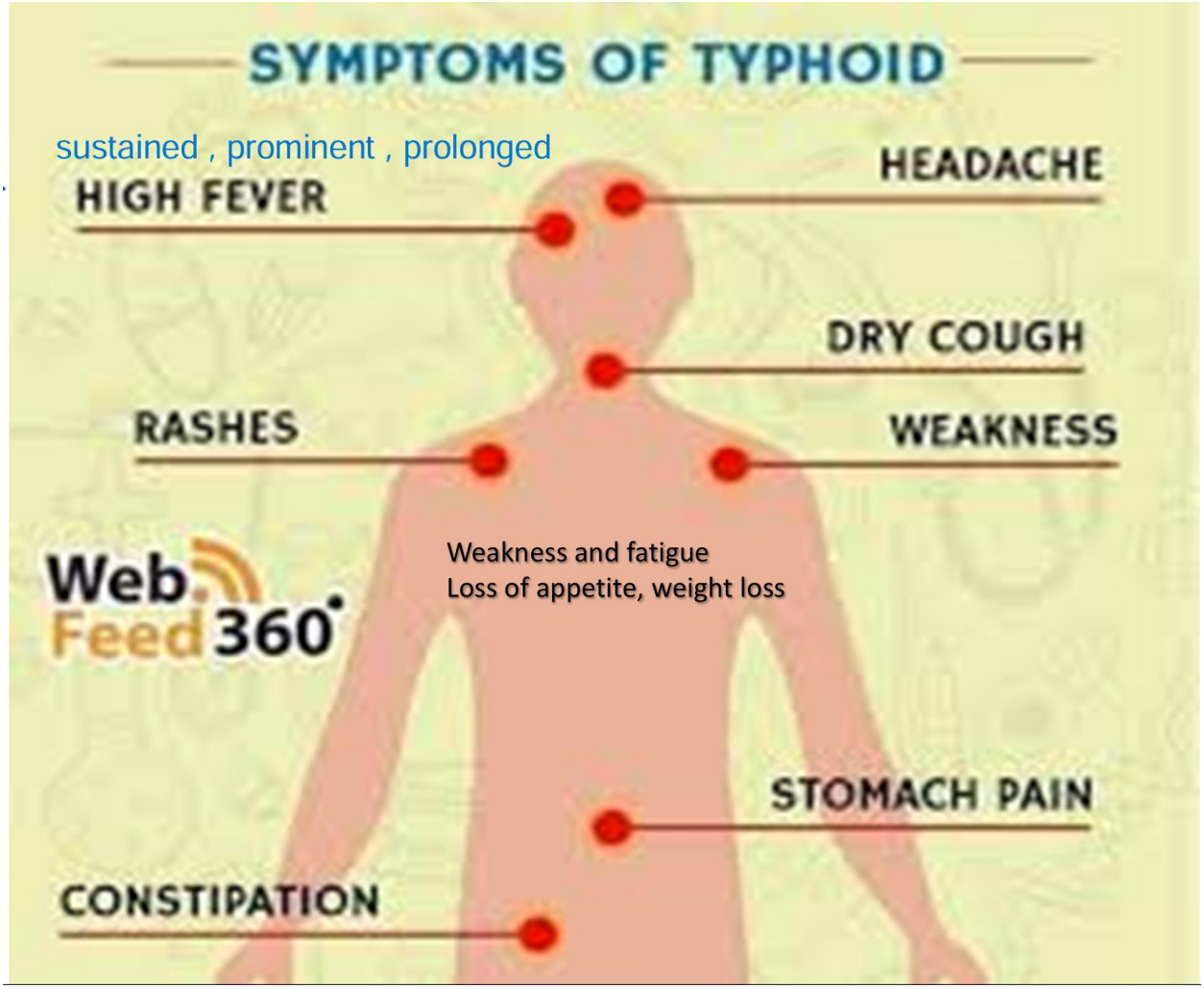
Clinical Presentations; History and Examination

GI symptoms

Nontyphoidal enterocolitis

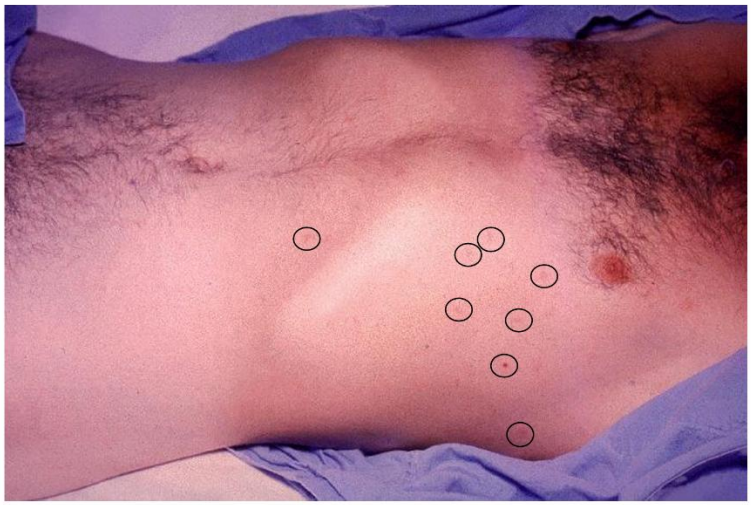
- Symtoms
  - Acute onset of fever
  - Acute abdominal pain
  - Acute diarrhea
  - Nausea, sometimes vomiting.
- The onset of disease symptoms occurs 6–72 hours (usually 12–36 hours) after ingestion of *Salmonella*, and illness lasts 2–7 days.

- Nontyphoidal focal disease
  - Kidney
  - Brain
  - Bone
  - … etc



Note !!!!
Nontyphoidal enterocolitis → cause acute diarrhea
BUT typhoid → cause constipation

Incubation period of 10-14 days



Typhoid fever Signs

Fever
Prolonged low-grade fever
Relative bradycardia
Splenomegaly

The Pattern of Typhoid Fever

Temperature curve from a case of typhoid fever, the first nine days there was no fever but widen daily fluctuation. On the tenth day, the fever started.

The fever may progress in a stepwise manner to become persistent and high grade by the end of the second week.

If left untreated, it can last up to 4 weeks, then return to a normal temperature.

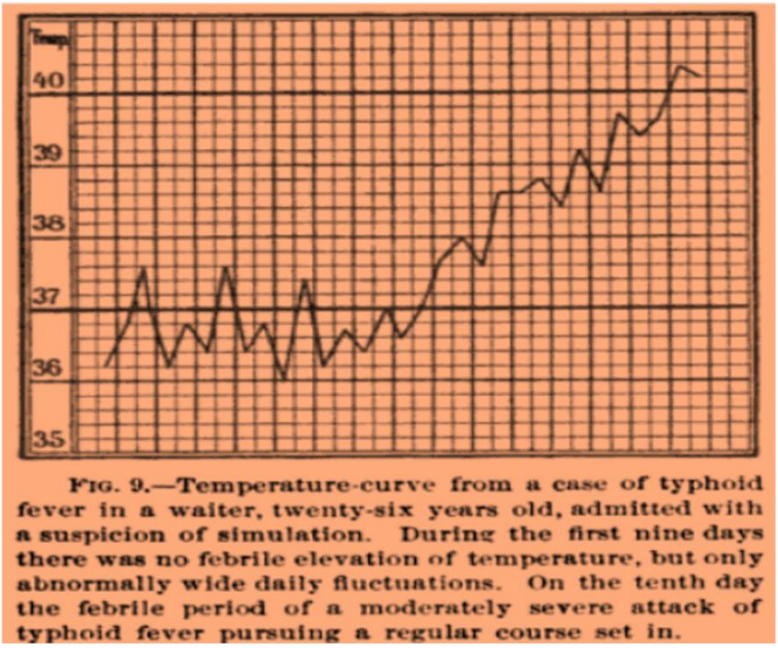


FIG. 9.—Temperature-curve from a case of typhoid fever in a waiter, twenty-six years old, admitted with a suspicion of simulation. During the first nine days there was no febrile elevation of temperature, but only abnormally wide daily fluctuations. On the tenth day the febrile period of a moderately severe attack of typhoid fever pursuing a regular course set in.

Differential Diagnoses

- Campylobacter Infections
- Cryptosporidiosis
- Cyclospora Infection (Cyclosporiasis)
- *Escherichia coli* (*E. coli*) Infections
- *Listeria Monocytogenes* Infection (Listeriosis)
- Shigellosis
- Vibrio Infections
- *Yersinia Enterocolitica*

Frequency and Prevalence a of Specific Typhoid Fever Complications Reported From a Meta-analysis (1990–2018)

In 10%–15% of hospitalized patients

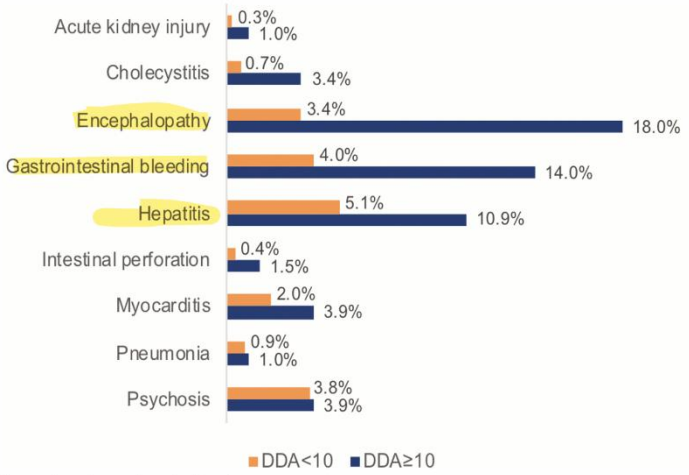
27% (95% CI, 21%–32%) of all blood culture–confirmed typhoid fever cases resulting in complications

- Perforation
- Hemorrhage
- Pneumonia
- AKI
- Encephalopathy
- Hepatitis
- Myocarditis
- Osteomyelitis
- Sever anemia
- Meningitis

- Bone marrow suppression
- Hypothermia
- Pleural effusion
- Paralytic Ileus
- Psychosis
- SIADH
- Stupor, Coma
- Seizure
- Sepsis Syndrome
- Secondary infections
- Carrier status
- Persistent *Salmonella* infection can lead to the development of other severe diseases such as inflammatory bowel disease (IBD) and cancer.
- Infective aortitis, which is characterized by high morbidity and mortality.
- Other Organs abscesses

Clin Infect Dis, Volume 69, Issue Supplement_6, 15 November 2019, Pages S435–S448, https://doi.org/10.1093/cid/ciz477

Frequency (pooled across the studies reporting the complications and illness duration at hospitalization) of typhoid fever complications (1990–2018).



DDA, mean/median illness duration at hospitalization.

Workup?

- Analysis
- Cultures
- PCR??
- Imaging
- Endoscopy never do endoscopy in typhoid!!!! (increase risk of perforation)
- Serological tests (Widal test) useless

Medical Management

Depends on:

- Typhoid (enteric) fever (Ciprofloxacin, Azithromycin, Ceftriaxone, ……)
- Nontyphoidal focal disease (Kidney, brain … etc)
  - The Usual Typhoid treatment
  - Certain world Parts has Extensively Drug-Resistant Typhoid Fever

Management

Nontyphoidal enterocolitis or Salmonella enterocolitis

antibiotics not important in Nontyphoidal enterocolitis or Salmonella enterocolitis
-we can give ciproquinolone --> it cuts down fast on the carrier status / reservoir status
-other antibiotics increase carrier status in nontyphoidal

1- hydration
2- hydration
3- hydration
.

Surgical Management

- Gall bladder
- Bone sickle cell disease --> increase risk of salmonella gastroenteritis
- Heart pericarditis
- Bowel perforation , infection
- Splenic Abscess
- Soft-tissue abscess formation

Prevention?

1. Safe hygiene practice
    1. Wash green food before eating
    2. Wash hands
    3. Travel to an endemic area, cooked or canned food
2. Vaccination + hand hygiene , food hygiene

Prevention

Typhoid Vaccines Available

Abbreviated vaccine name (brand name, manufacturer)	How given	Number of doses recommended	When taken	How long to complete immunization before travel	Minimum age for vaccination	Booster needed
Ty21a (Vivotif, Swiss PaxVax)	1 capsule by mouth	4	Every other day	1 week	6 years	Every 5 years
ViCPS (Typhim Vi, Sanofi Pasteur)	Injection	1	Once	2 weeks	2 years	Every 2 years

- Oral vaccine: Can be given to people at least 6 years old. It consists of four pills taken every other day and should be finished **at least 1 week** before travel.
- Injectable vaccine: Can be given to people at least 2 years old and should be given at least **2 weeks** before travel.
- Typhoid vaccines are not 100% effective.

cdc.gov/typhoid-fever/typhoid-vaccination.html

Lecture 4 Brucellosis:

cocco bacilli or bacilli

- Bruce first isolated *Brucella melitensis* in 1887
- Gram negative bacilli or coccobacilli
- Intracellular
- 12 species
- Pathogenic species:
  - *B. melitensis* meleta
  - *B. suis* pigs
  - *B. abortus* abortion
  - *B. canis* canine

same treatment regardless of the type

- *B. neotomae*: desert wood rats
- *B. ovis*: ..... sheap

No human infections

- *B. pinipedialis*:
- *B. ceti*

Marine mammals , sporadic in humans

- *B. microti*: wild life
- *B. inopinata*: one case of breast implant wound

Brucellosis in animals
zoonotic infection

- Asymptomatic
- Abortions
- Brucella is shed in large numbers in the animal's
  - Urine
  - Milk
  - Placental fluid

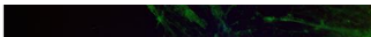
Types

- *B. melitensis*
  - the most virulent and causes the most severe and acute cases
  - the most prevalent worldwide
- *B. suis*
  - A prolonged course of illness, often associated with suppurative destructive lesions
- The type of *Brucella* species involved does not alter treatment.

Pathophysiology

- Only 100 to 1000 organisms are sufficient to cause infection.
- *Brucella* species have a unique ability of invading phagocytic cells

neutrophils and macrophages



Pathophysiology

- Low mortality rate (<5%)
  - Mostly due to endocarditis, a rare complication
  - However, brucellosis can cause chronic debilitating illness with extensive morbidity
- More common in males
  - ratio of 5:2 in endemic areas

Modes of transmission

- **Ingestion** of unpasteurized dairy products is the main route of *B melitensis* transmission to humans
- Slaughterhouse workers
- Veterinarians are infected by inoculation of animal vaccines against *B abortus* and *B melitensis*
- Laboratory workers (microbiologists) are exposed by processing specimens (aerosols) without special precautions

- Macrophages then transport Brucella to the
  - lymph nodes
  - Spleen
  - Liver
  - bone marrow
  - mammary glands
  - sex organs

-CNS
-Heart
-Bone

Signs and symptoms

- Fever is the most common symptom and sign
  - 80-100% of cases
- Fever can be associated with a relative bradycardia
- Anorexia, asthenia, fatigue, weakness, and malaise and are very common (>90% of cases)
- abdominal pain, constipation, diarrhea, and vomiting
- Cough and SOB
  - Dry cough
  - 20% of cases
  - these symptoms are rarely associated with active pulmonary involvement

Presentation

- **Subclinical brucellosis**: A condition where the disease is present, but no obvious symptoms are shown
  - asymptomatic, and the diagnosis is incidental after serologic screening of persons at high risk of exposure
  - Culture is usually unrevealing
- **Acute or subacute brucellosis**: A condition that is between acute and chronic in severity or duration
  - mild and self-limited (eg, *B abortus*)
  - fulminant with severe complications (eg, *B melitensis*)
  - symptoms can develop at 2-12 months prior to diagnosis

Presentation

- **Chronic brucellosis**:
  - The diagnosis is typically made after symptoms have persisted for 1 year or more
  - Low-grade fevers and neuropsychiatric symptoms predominate
  - Results of serologic studies and cultures are often negative; without confirmatory evidence, many authorities doubt the existence of chronic disease
  - Many patients have persistent disease caused by inadequate initial therapy, and underlying localized disease may be present

Presentation

- **Localized complications**
  - In acute disease
  - In chronic untreated infection
  - Sites
    - osteoarticular affect 20-60% / most common complication / sacroiliitis
    - Genitourinary: epididymo-orchitis
    - Hepatosplenic
    - Endocarditis (very rare: 2%)
    - CNS

Presentation

- Osteoarticular
  - symptoms affect 20-60% of patients
  - the most commonly reported complications
  - sacroiliitis is the most common

Diagnosis

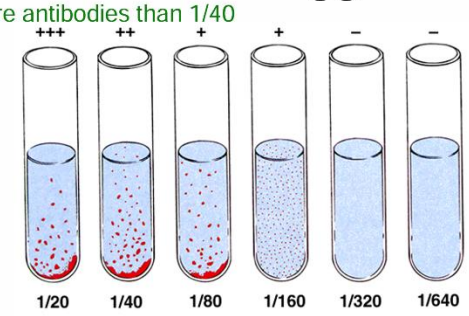
we need positive culture
OR
titer symptoms

- ↓ WBC or normal
- relative lymphocytosis
- Pancytopenia

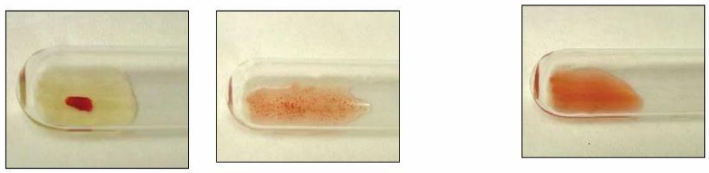
- Elevation in liver enzymes
- Culture — the more the acute disease --> the more the positivity culture
- Serology – titers — look for antibodies against brucella
  - Standard tube agglutination or ELISA
    - More sensitive and specific than agglutination
    - Helps distinguish acute (IgM) vs chronic (IgG) infections
    - more precise than ELISA
- PCR: not yet in clinical practice

Standard tube agglutination

/160 has more antibodies than 1/40



Titer = 1/160



Reaction

No reaction

Treatment

-patient with titer =40 or 80 and the patient Asymptomatic --> no disease --> don't treat them
-if the patient titer =320 or 640 and the patient Asymptomatic --> need treatment

- Multidrug regimens are the mainstay of therapy
  - because of high relapse rates reported with monotherapy
- Doxycycline and rifampin: most commonly used
  - 6 weeks less effective and less toxic
- Doxycycline (6 weeks) + streptomycin (2-3 weeks)
  - more effective but more toxic
- **Children** < 8 years
  - The use of rifampin + (TMP-SMX) for 6 weeks

Trimethoprim–Sulfamethoxazole

- **Pregnant**:
  - Brucellosis treatment is a challenging problem
  - limited studies
  - rifampin alone or in combination with TMP-SMX for 3 months

postnatal --> we give Doxycycline and rifampin

cause bone problems and teeth discoloration

Doxycycline and teeth

don't give it to pregnant ladies or children

Lecture 5 Tuberculosis:

Cause →

1-caseous necrotic granuloma

2- multiple extensive yellow-white nodules on the peritoneal surface

3-large amount of loculated viscous fluid and enhanced diffuse peritoneal thickening

, Posteriorly displaced small bowel loops could be seen (seen on Axial contrast-enhanced CT images)

- TB is the second cause of infectious disease–related mortality worldwide
  - First is COVID
  - Third is HIV
- 2 billion have latent TB
  - a person with HIV is > 15 times more likely to develop active TB (if he has latent TB).

- a disease of poverty
- thrives where social and economic determinants of ill health prevail
- it affects mostly young adults in their most productive years
- 95% of TB deaths are in the developing world

Microbiology

M tuberculosis the human is the only reservoir

- slow-growing organism
  - 4-8 weeks for visible growth on solid medium
- Acid fast bacilli doesn't stain with gram stain
  Ziehl–Neelsen Stain -- > most common technique use
- have been around: 3 million years

M bovis transmitted form cattles to human

- From cattles

Microbiology

- *Mycobacterium tuberculosis*
- *M. bovis*
- *M. microti (rodents)*
- *M. africanum*
- *M. canetti*

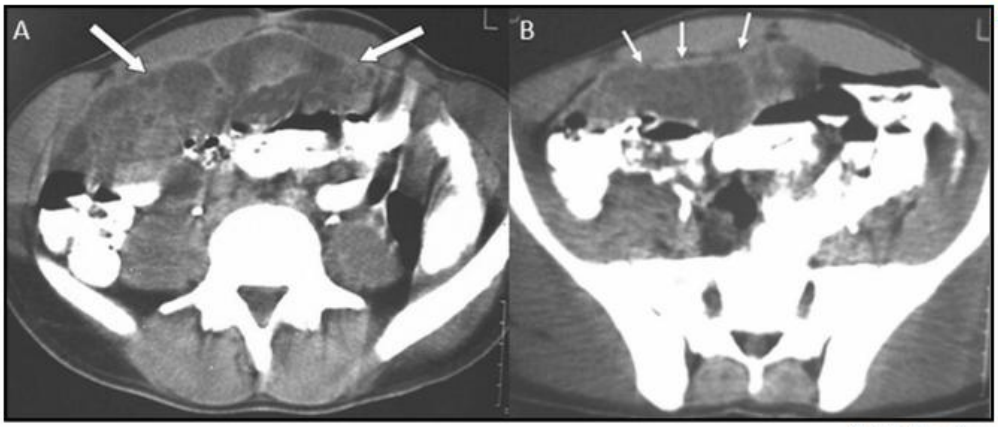
Transmission

- Airborne
- People with active TB can infect 5–15 other people through close contact over the course of a year

Pathophysiology

- Humans are the only known reservoir for *Mycobacterium tuberculosis* (MTB)
- Transmission: airborne droplet nuclei

1. When inhaled, droplet nuclei are deposited within the terminal airspaces of the lung
2. macrophages ingest and transport the bacteria to regional lymph nodes
   A. may be killed by the immune system
   B. they may multiply and cause primary TB
   C. may become dormant and remain asymptomatic
   D. may proliferate after a latency period (reactivation disease)



fluid that has formed into discrete pockets (or "loculated") within the peritoneal cavity

Axial contrast-enhanced CT images showing large amount of loculated viscous fluid (arrows; A) and enhanced diffuse peritoneal thickening (arrows; B). Posteriorly displaced small bowel loops could be seen.

thick and sticky

inflammation of the peritoneum,

due to the mass effect of the fluid collections or due to the thickened peritoneum.

symptoms

Pulmonary tuberculosis (TB)

constitutional symptoms + RS symptoms

- cough
- fever
- weight loss
- hemoptysis
- chest pain
- anorexia, fatigue, and night sweats

symptoms

TB meningitis

- headache that is either intermittent or persistent for 2-3 weeks
- Subtle mental status changes may progress to coma over a period of days to weeks
- Fever may be low-grade or absent

Skeletal TB

tuberculous spondylitis

- most common is the spine (Pott disease)
  - back pain or stiffness
  - Lower-extremity paralysis occurs in 50%
- TB arthritis usually involves one joint
  - the hips and knees are affected most commonly > the ankle > elbow > wrist > and shoulder

Gastrointestinal TB

difficult to diagnose

Any site in the GI may become infected:

- non healing ulcers of the mouth or anus
- difficulty swallowing
- abdominal pain mimicking peptic ulcer disease
- malabsorption
- diarrhea
- hematochezia

Other sites

- TB lymphadenitis (scrofula)
- Genitourinary TB
- Cutaneous TB

Diagnosis

- sputum: in the early morning on 3 days
  - every 8 hours (hospital)
  - Children: early-morning gastric aspirate
- bronchoscopy with biopsy and bronchial washing
- bone marrow Bx
- liver Bx
- ± blood cultures for highly immunocompromised patients
- PCR on smears

Diagnosis

- Obtain HIV in all patients with TB
- CXR
  - may show a patchy scattered, irregularly shaped densities that suggest active infection or inflammation
  - nodular infiltrate
  - upper-lobe involvement is most common
  - in any part of the lung
  - cavity: indicates advanced infection
    - high bacterial load
- Miliary TB: appearance of numerous small nodular lesions that resemble millet seeds on CXR

PPD

(Purified Protein Derivative)

- PPD: tuberculin skin testing (Mantoux test)
  - is the most widely available test for diagnosing TB in the absence of active disease (**Latent infection**)
  - intradermal injection
  - 48-72 hours
  - size of induration, not the erythema
  - Booster effect — may be false negative at the first time if we repeat it may be positive
  - ? Dx role in TB — we diagnose latent TB

PPD

- PPD testing for tuberculosis (TB) is done among persons at **high risk** for the development of TB disease who would benefit from treatment of latent TB infection (LTBI)

- All testing activities should be accompanied by a **plan** for the necessary follow-up medical evaluation and treatment

Groups that should be tested for LTBI

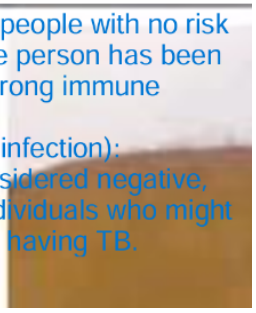
Persons at higher risk for TB once infected

- Illicit drug use
- Certain medical conditions
- HIV
- Recently infected with *M. TB* (2 yrs)

Groups that should be tested for LTBI

- Persons at higher risk for exposure to or infection with TB
  - Close contact of a person known or suspected to have TB
  - Residents and employees of high risk settings
  - HCW
  - Low income populations
  - Children exposed to adults in high risk

-The result of the Mantoux test depends on the size of the induration (the raised, hard area):
-Positive Result (suggests TB exposure or latent infection):
-Induration > 5 or equal mm: In people with high risk (e.g., immunocompromised individuals, close contacts of TB patients, or people with HIV).
-Induration > or equal 10 mm: For people with moderate risk (e.g., healthcare workers, people with recent travel to endemic areas).
-Induration > or equal 15 mm: For people with no risk factors (generally indicates that the person has been exposed to TB and developed a strong immune response).
-Negative Result (suggests no TB infection):
-Induration < 5 mm: Generally considered negative, except in immunocompromised individuals who might still show a negative result despite having TB.



Treatment

- Initial empiric treatment of TB
- Start on a 4-drug regimen
  - INH (ioniazid)
  - Rifampin
  - Pyrazinamide
  - Ethambutol or streptomycin
- Prolonged course > 6 months

Risk for TB in latent TB

- On medicines such as steroids or TNF-a inhibitors
- DM
- Renal insufficiency
- Silicosis

Infection control in hospital

- Respiratory isolation
  - negative pressure room
  - N95 mask

Lecture 6 : Infection Control

-Wash withsoap and water when your hands feel sticky

HBV → transmitted by airborne

Vaccines for HCW

- HBV (Hepatitis B Virus)
- MMR (Measles, Mumps, and Rubella)
- Td (Tetanus and Diphtheria)
- VZV (Varicella Zoster Virus)
- Flu (Influenza)

How HIV / HBV are transmitted

sexual, needles, blood , mucous membrane (eye , nose , mouth) , bodily fluids (except sweat) , damaged skin

1. Sexual contact
2. Sharing needles
3. Mothers to babies
4. A puncture from contact with needle/ glass/ sharp..
5. Contact bet damaged skin and infected bodily fluid and materials
6. Contact bet mucous membrane and infectious bodily fluids and materials

How HIV / HBV are transmitted (cont)

- Damaged skin: cuts, sores, wounds, acne, sunburn, blisters, and abrasions, etc…
- Also mucous membranes
  - Eyes
  - Nose
  - Mouth

eg blood splash into face can enter through eye, nose, mouth

Transmission risk

- HIV 0.3%
- HCV 3%
- HBV 30%

Vaccination

- HBV vaccine
  - 3 doses
  - 0,1,6 months
  - Check titer after 1-2 months from last dose
- HIV, HCV
  - No vaccines

HBV vaccine

- Does not transmit the virus
- The series is administered once
- A booster shot can be given in times of outbreak conditions
- If you are exposed to HBV immediate vaccination is extremely helpful

Isolation

- **Contact** (gowns, gloves, masks)
  - MRSA spread through direct contact with contaminated surfaces or people
- **Respiratory** (negative pressure room, N95 mask)
  - TB, Measles, VZV spread through airborne droplets
- **Droplet** (surgical mask, private room)
  - Meningitis in the first 24hr, non H1N1 influenza
- **Protective** (private room, mask, gown, gloves)
  - Neutropenic pts chemotherapy or with other immune system deficiencies)

Needles, Needle sticks, and sharps

- Never recap a needle If necessary use single hand technique
- Contaminated needles should never be bent, broken
- Contaminated needles should only be disposed in sharps container
- If you need to pick a needle, you can use a tool (forceps …) tools to handle needles. These tools allow you to pick up the needle safely without directly touching it, reducing the risk of injury.

Needle sticks

- Baseline:
  - HIV, HCV, HBsAg, HBsAb titer
- If no HBV vaccination and low titers
  - Give HBV vaccine ± HBV Immunoglobulin
- If pt has HIV → 3TC + AZT (1 month)
  - Check HIV, HCV, HBV at 1, 3, 6 months
- HCV: no post-exposure prophylaxis

Central line infection pathogenesis

- **Extra-luminal** route: < 10 days
  - Most common mode of infection for non tunneled
  - 4 cm / h by capillary action (Cooper, J Clin Microb, 1988)
- **Intra-luminal** route: > 3 weeks
  - Most common mode of infection for tunneled

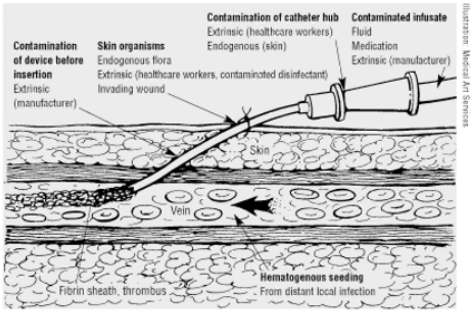


Figure 1. Sources of intravascular catheter–related infection. The chief sources are skin flora, contamination of the catheter hub, contamination of infusate, and hematogenous colonization

Catheter related blood stream infections

-Have high mortality ≈ 25%

-Use **maximum** sterile precautions for central line insertion

- Head cap
- Mask
- Sterile gown
- Sterile gloves
- Large sterile drape

-Avoid vancomycin prophylactic use

Ventilator-associated pneumonia (VAP)

- Most important risk factor
  - leakage of contaminated subglottic secretions around the cuff of the endotracheal tube

Lecture 7 : HIV 1&2

•HIV binding via CD4 & chemokine receptor (cell surface receptor)

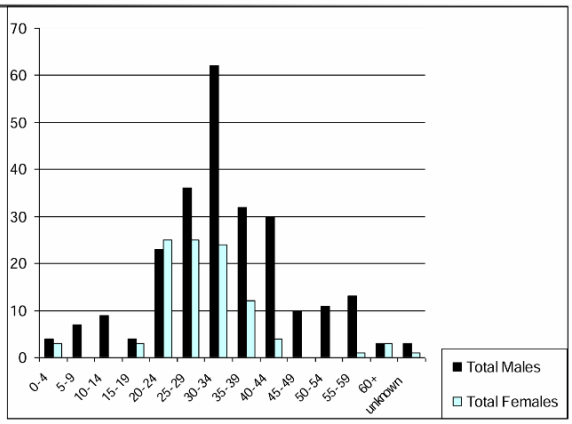
•HIV = destruction of immunity (Destruction of CD4 cells) and Lymph node pathology

Africa, the burning continent

- 8% of adults < 45
- > 80% of prostitutes
- In 2013: **70% of the global total**
- **Life expectancy < 40 years**
- Causes:
  - Multiple sex partners
  - Prostitution
  - STD's sexually transmitted diseases
  - Mother to child transmission

- "…The AIDS epidemic continues to explode in India, China, Russia, and eastern Europe and may be more destabilizing than international terrorism"

HIV in Jordan



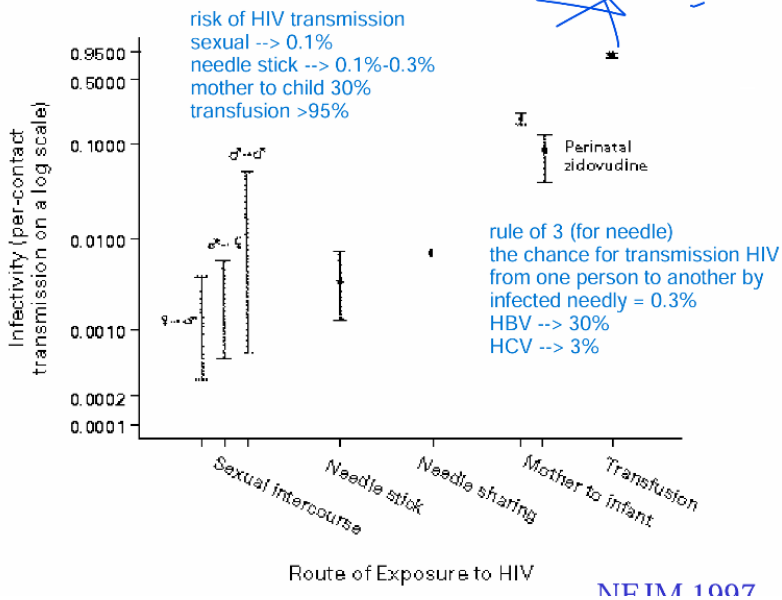
Transmission

- Sexual intercourse
- Mother → child
- IV drug use
- Blood transfusion
- Needlestick injury

All body fluids…

- Blood: PRBCs, FFP, cryo., clotting factors, platelets, IVIG
- Semen
- Vaginal secretion
- Saliva
- Tears
- Breast milk
- CSF
- BAL fluid Bronchoalveolar Lavage fluid,
- Amniotic fluid
- Transplanted organs (liver, kidney, heart, bone)

Transmission risk estimates



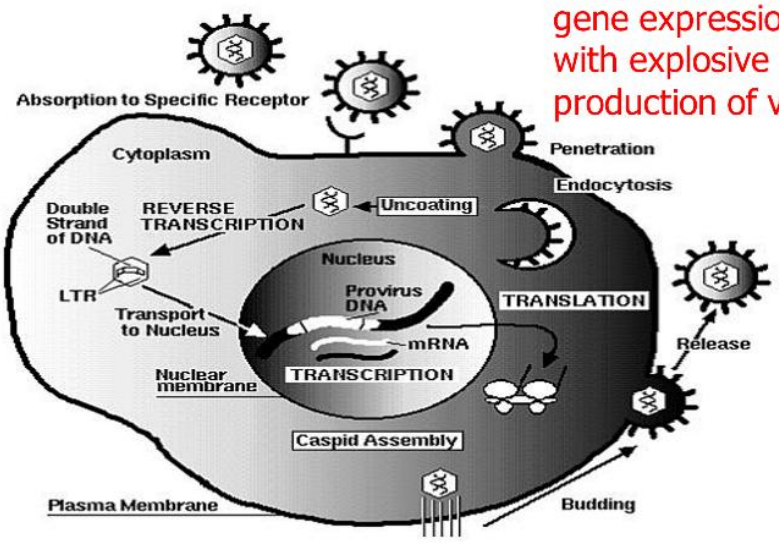
NEJM 1997

Healthcare workers

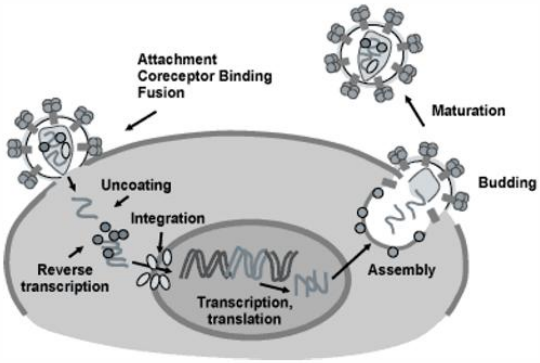
- Low risk
- 0.3% by needle stick
- Universal precautions *****
  - Hand washing
  - Gloves, gowns, masks
  - Sharps
  - Open lesions…

Life cycle of HIV

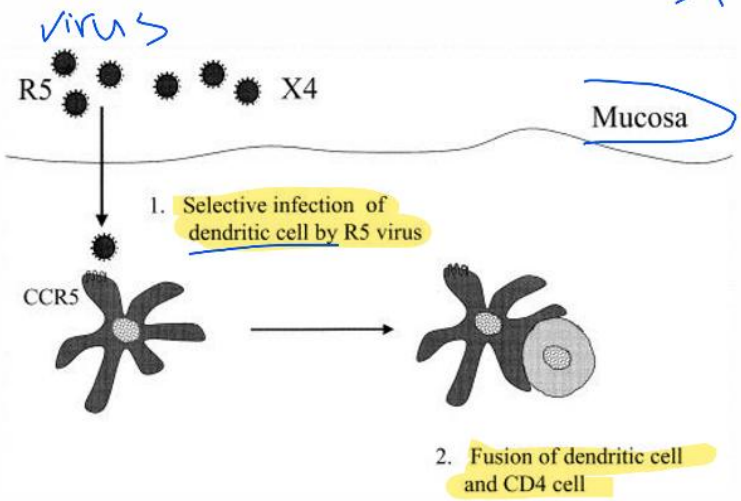
- Transcriptionally latent
- High levels of gene expression with explosive production of virus



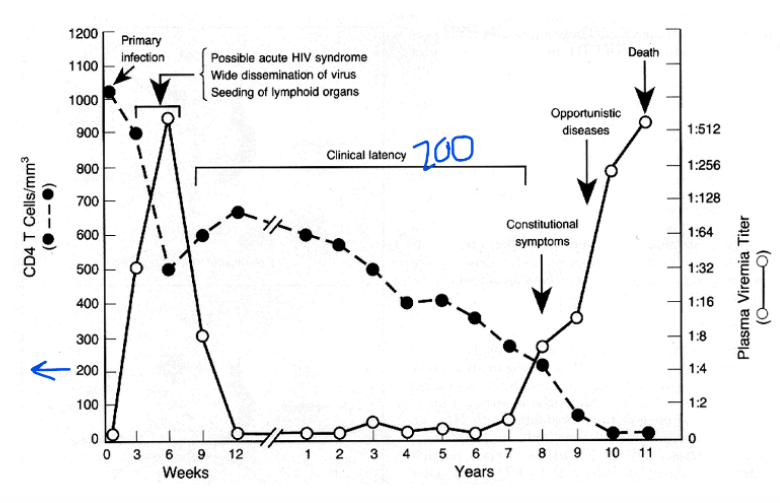
1. Attachment
2. Coreceptor binding
3. Fusion
4. Uncoating
5. Reverse transcription
6. Integration
7. Transcription
8. Translation
9. Assembly
10. Budding
11. Maturation



Transmission



Course of HIV infection



CD4 count
normally =430-1690
>500 is perfect

Acute HIV infection

- Mononucleosis like picture
  - remember secondary syphilis, EBV
- > 70 % of pts present with symptoms,
  - 2 weeks after acquiring HIV but can present as early as 5 days or as late as 3 months after initial infection
- High viremia ≈ 10^8 copies/ml
- Highly infectious
- Dx by PCR followed by serology
  - 4th gneration Ag/Ab test (10-14 days)

Signs and Symptoms of Acute HIV
occur: 2 weeks – 3 months

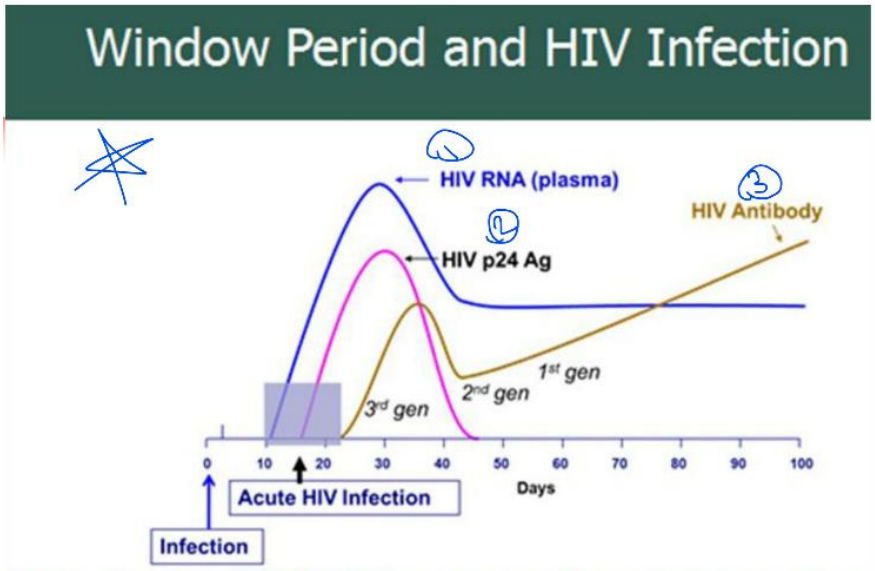
- Fever
- Fatigue/Malaise
- Pharyngitis
- Lymphadenopathy
- Myalgia
- Joint Pain
- Rash
- Diarrhea
- Weight Loss
- Headache
- Vomiting
- Oral or genital ulcer

- **Rare presentation**
- Guillain-Barré Syndrome
- aseptic meningitis
- hepatitis

- completely asymptomatic

RNA test and DX of acute HIV

- Although acute HIV infection with HIV RNA <10,000 copies/mL has been described, such results could also represent false positive tests
  - further lab tests should be performed (eg, additional antibody testing or repeat HIV RNA or both) to confirm cases in which HIV RNA levels lower than 10,000 copies/mL are noted

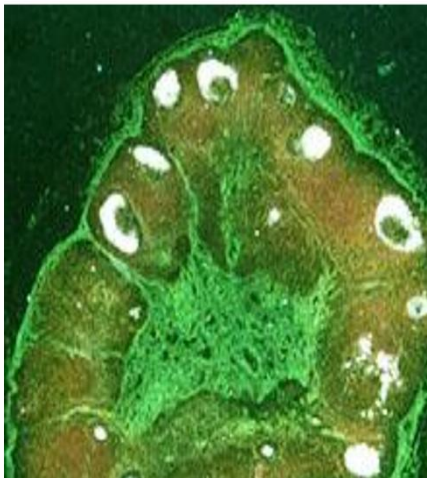


Persons recommended for evaluation of acute HIV infection with available appropriate tests

- All of the following risk groups, ESPECIALLY with **history of an illness with clinical features compatible with acute HIV ("mono" or "flu-like" illness, regardless of severity):**
- recent sexual or needle-sharing exposure with a known HIV-infected partner or a partner of unknown serostatus in the past **2-6** weeks
- Men who report unsafe sexual practices with other men
- A newly diagnosed STD
- Aseptic meningitis
- Requesting HIV testing
- Pregnant and breastfeeding women

HIV = destruction of immunity

- Destruction of CD4 cells
- Evasion of immune response
- Lymph node pathology
- Exhaustion of immunity



HIV Diagnosis

- Viral load (PCR)
  - as early as 7-10 days
- ELISA
- Western blot

the most important one
if it is + --> confirmed HIV
if it is negative --> don't exclude HIE

CDC Classification (1993)

CD4	A Asymptomatic, acute or PGL	B Symptomatic, not A or C	C AIDS indicator
≥500	A1	B1	C1
200-499	A2	B2	C2
<200	A3	B3	C3

AIDS --> if the patient has CD4>500 he doesn't have AIDS unless he has AIDS indicator illness
AIDS --> CD4 <200 or have AIDS indicator illness

CDC classification

diseases indicated low immunity

Bacillary Angiomatosis
Oral thrush
Persistent vulvovaginitis
Fever or diarrhea > 1 month
Hairy leukoplakia
VZV
ITP
PID
Peripheral neuropathy

B Symptomatic, not A or C
B1
B2
B3

CDC AIDS defining diseases (CD4 < 200 cells/ml)

all happen in patients with CD4 < 200 EXCEPT 2 TB + Kaposi's sarcoma

1) Candidiasis
2) Cervical cancer
3) Coccidioidomycosis
4) Cryptococcosis
5) CMV
6) Encephalopathy
7) HSV
8) Histoplasmosis
9) TB
10) Cryptosporidiosis
11) Lymphoma
12) PCP
13) Recurrent pneumonia
14) MAC
15) PML
16) Salmonellosis
17) Brain Toxoplasmosis
18) Wasting
19) Kaposi's sarcoma
20) Isosporiasis

occur in patient with CD4 >200

Antiretroviral agents

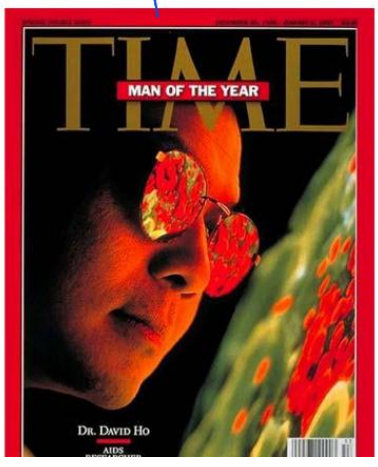
- NRTI dine
  - Ziduvudine (AZT)
  - Didanosine (DDI)
  - Stavudine (D4T)
  - Lamivudine (3TC)
- PI avir
  - Saquinavir
  - Indinavir
  - Ritonavir
  - Nelfinavir
  - Abacavir
- NNRTI pine , renz
  - Nevirapine
  - Efavirenz

Highly Active Anti-Retroviral Therapy (HAART) "Cocktail"

2 NRTI + PI

❑Aim:
- Suppress viral load
- Increase CD4

❑Disadvantages:
- Toxicity
- Cost



Notes:

▪If the mother is infected with the hepatitis B virus during pregnancy, the child must receive the vaccine within the first 24 hours after birth

▪Protection is confirmed when the vaccine titer >10

▪in rubella virus → If a woman is infected with the rubella virus during the first three months of pregnancy, it can cause congenital malformations

-A woman should wait at least two months before becoming pregnant after receiving the vaccine

Done by Haya Khader ❤️‍🩹