Introduction;

Basics of bacterial genetics

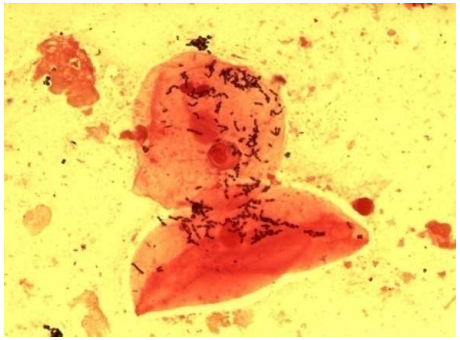
Pavel Drevinek

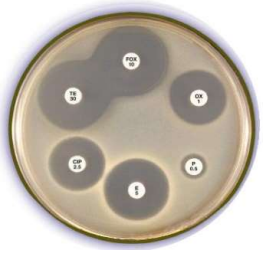
Human body:

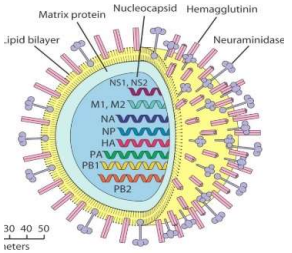
- 10^{13} human cells
- 10^{14} bacterial cells
  (100 trillions)
  ~ 2 kg

Earth:

- 10^{30} microbial cells



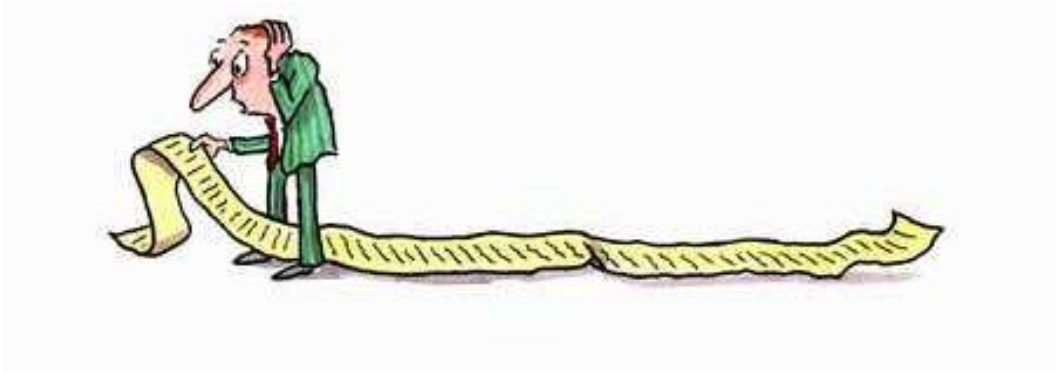




The Subject of Medical Microbiology

- General microbiology
  properties of microorganisms, their pathogenicity, their interaction with a host, pathogenesis of infectious diseases, residential microbiota (flora), antibiotics

- Special microbiology
  individual microorganisms:
  - bacteria
  - viruses
  - fungi
  - parasites



- Clinical microbiology
  microbiological examination, diagnostics of infectious agents in relation to clinical picture, antimicrobial therapy

Lectures summer semester

Molecular microbiology
Bacterial cell structure. Pathogenicity.
Antimicrobial therapy I.
Antimicrobial therapy II.
Staphylococci.
Streptococci and enterococci.
Corynebacteria, listeria, clostridia.
Enterobacteria. Pseudomonads and other G- nonferementers.
Bordetella. Legionella. Meningococci. Haemophilus.
Campylobacter and helicobacter. Anaerobic bacteria.
Atypical bacteria (rickettsia, bartonela, chlamydia, mycoplasma).
Mycobacteria. Spirochetes.

Lectures winter semester

CAVE!

no longer practicals/seminars during winter semester

Medical mycology
General virology
Viral exanthem rash
Herpesviruses
Protosoa
Helminths
Alimentary infections
Respiratory infections
Respiratory viruses
Haemorrhagic fevers
Bloodstream infections. Sepsis.
Healthcare associated infections

Lectures winter semester

CAVE!

no longer practicals/seminars during winter semester

Neuroinfections
Infections in pregancy.
Sexually transmitted infections.
Urinary tract infections.
Virus HIV and hepatitis viruses
Bone and joint infections
Soft tissue infections
Microbiota
Clostridioides difficile infections
MDR bacteria
Vaccination

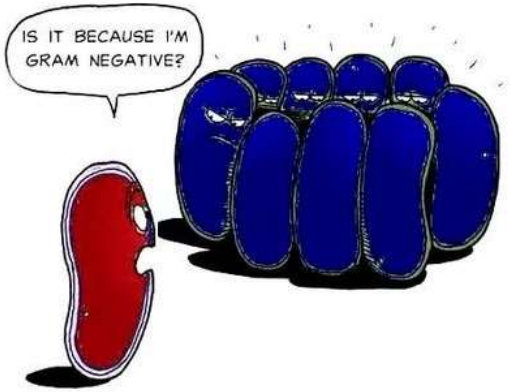
How to not get lost in bacterial classification?

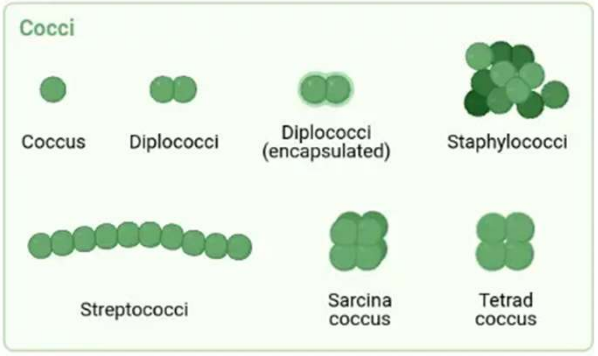
Gram staining:
- Gram positive
- Gram negative

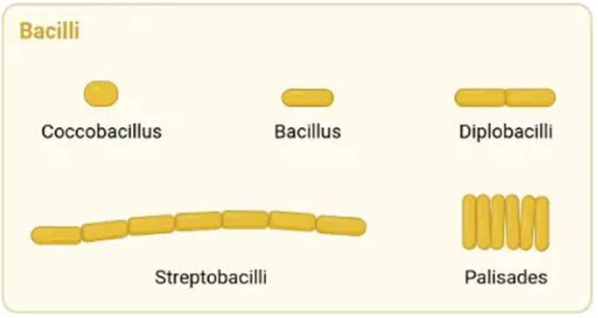
Bacterial cell shape:
- cocci
- rods (bacilli)

Relation to oxygen:
- aerobes
- anaerobes

Hans Christian Gram
1853 - 1938



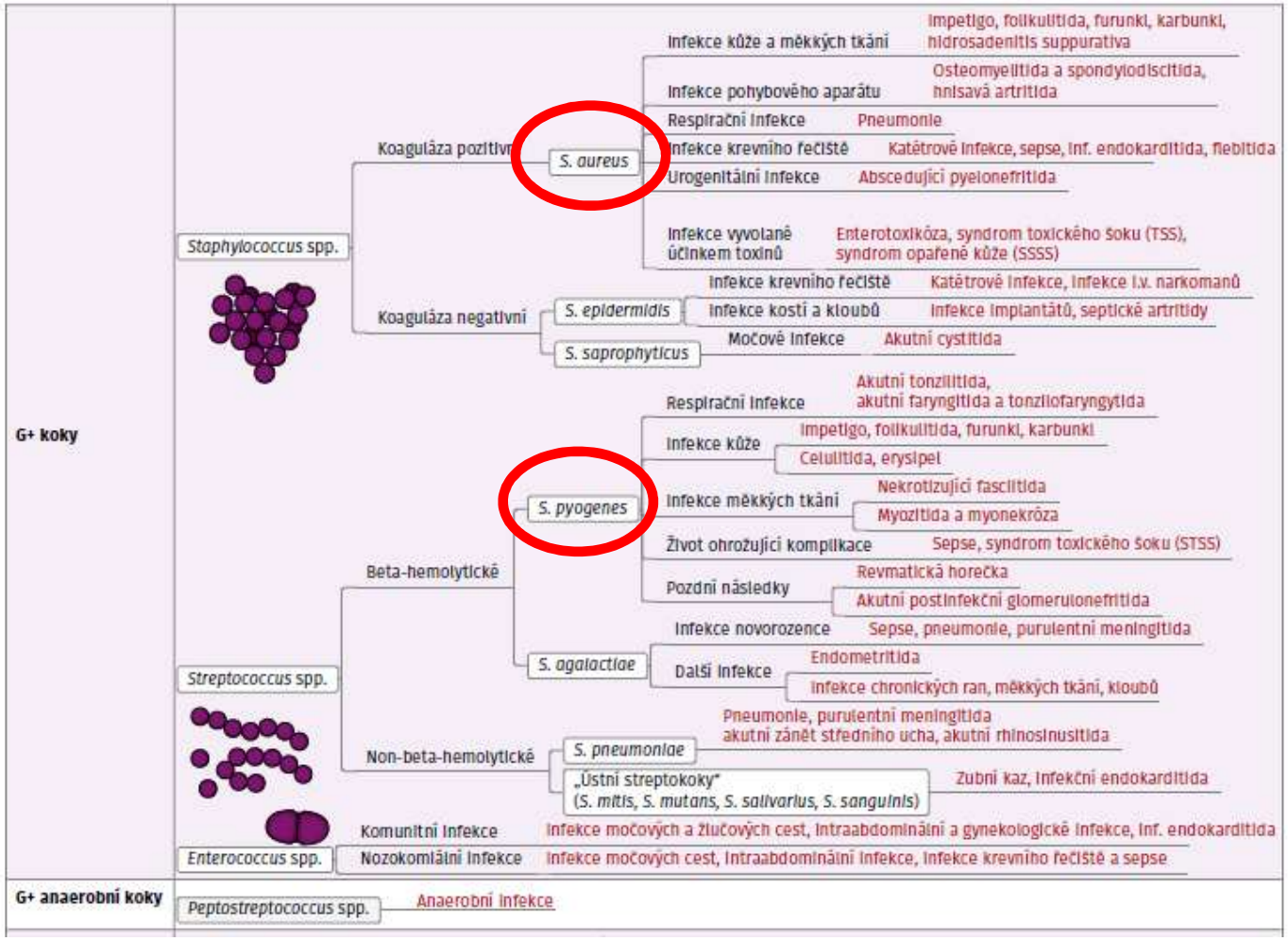




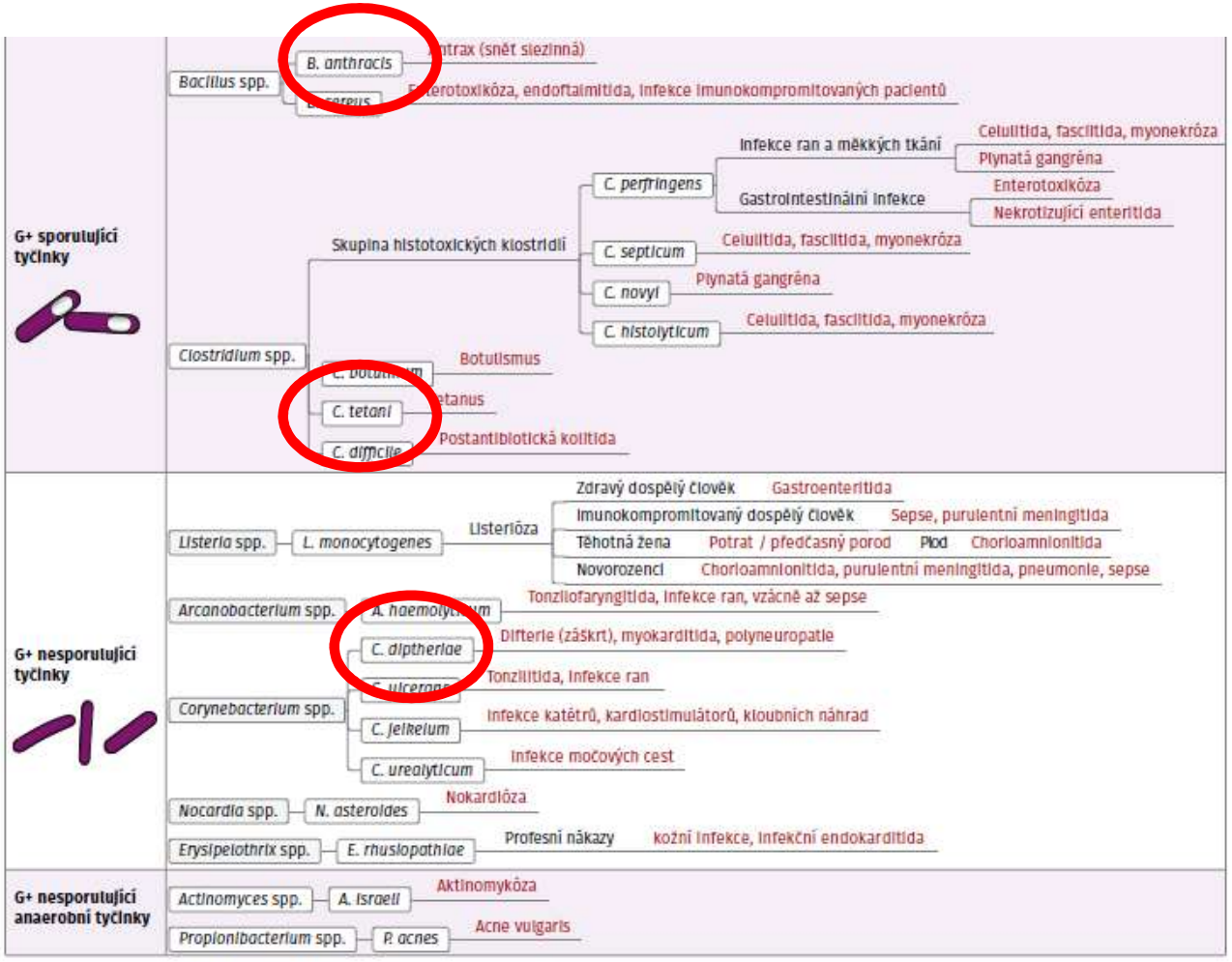
... always a grey zone can be found

- not stainable with Gram
- coccobacilli and other shapes
- facultative anaerobes

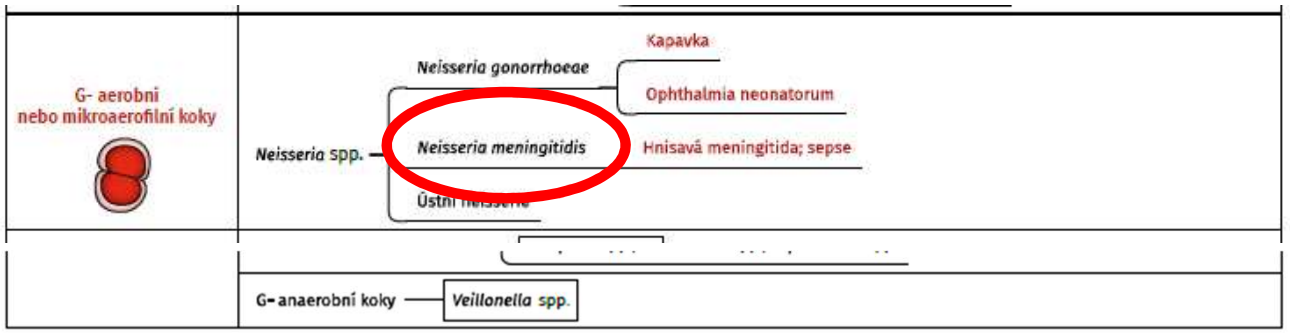
G+ cocci


G+ koky
Staphylococcus spp.
Koagulóza pozitivní
S. aureus
Infekce kůže a měkkých tkání
Impetigo, folikulitida, furunkl, karbunkl, hidrosadenitis suppurativa
Infekce pohybového aparátu
Osteomyelitida a spondylodiscitida, hnisavá artritida
Respirační infekce
Pneumonie
Infekce krevního řečiště
Katétrové infekce, sepse, inf. endokarditida, flebitida
Urogenitální infekce
Abscedující pyelonefritida
Infekce vyvolané účinkem toxinů
Enterotoxikóza, syndrom toxického šoku (TSS), syndrom opařené kůže (SSSS)
Koagulóza negativní
S. epidermidis
Infekce krevního řečiště
Katétrové infekce, infekce i.v. narkomanů
Infekce kostí a kloubů
Infekce implantátů, septické artritidy
S. saprophyticus
Močové infekce
Akutní cystitida
Streptococcus spp.
Beta-hemolytické
S. pyogenes
Respirační infekce
Akutní tonzilitida, akutní faryngitida a tonziofaryngytida
Infekce kůže
Impetigo, folikulitida, furunkl, karbunkl
Celulitida, erysipel
Infekce měkkých tkání
Nekrotizující fasciitida
Myozitida a myonekróza
Život ohrožující komplikace
Sepse, syndrom toxického šoku (STSS)
Pozdní následky
Revmatická horečka
Akutní postinfekční glomerulonefritida
S. agalactiae
Infekce novorozence
Sepse, pneumonie, purulentní meningitida
Další infekce
Endometritida
Infekce chronických ran, měkkých tkání, kloubů
Non-beta-hemolytické
S. pneumoniae
Pneumonie, purulentní meningitida akutní zánět středního ucha, akutní rhinosinusitida
„Ústní streptokoky"
(S. mitis, S. mutans, S. salivarius, S. sanguinis)
Zubní kaz, infekční endokarditida
Enterococcus spp.
Komunitní infekce
Infekce močových a žlučových cest, intraabdominální a gynekologické infekce, inf. endokarditida
Nozokomiální infekce
Infekce močových cest, intraabdominální infekce, infekce krevního řečiště a sepse
G+ anaerobní koky
Peptostreptococcus spp.
Anaerobní infekce

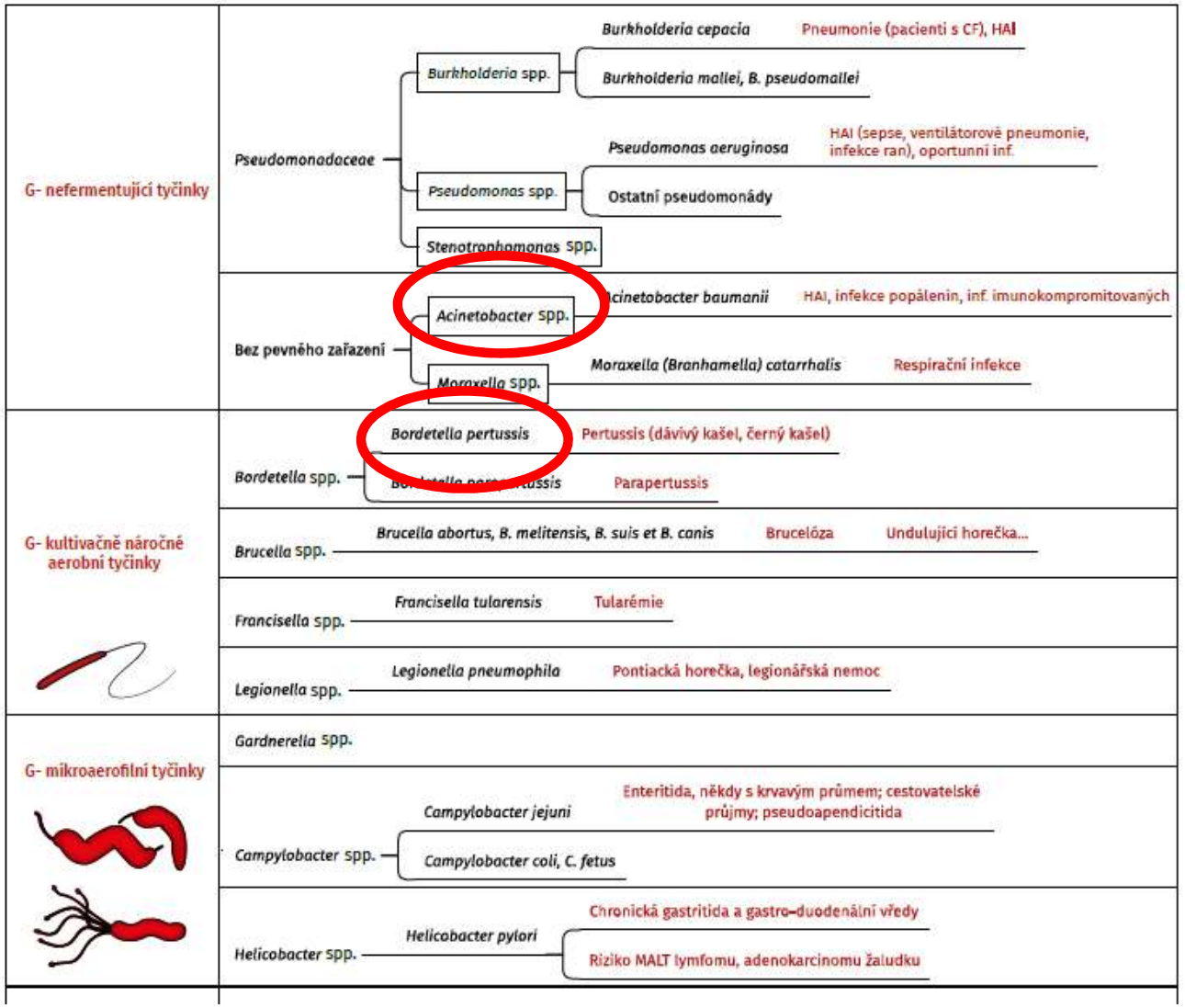
G+ rods (spore forming yes or no)



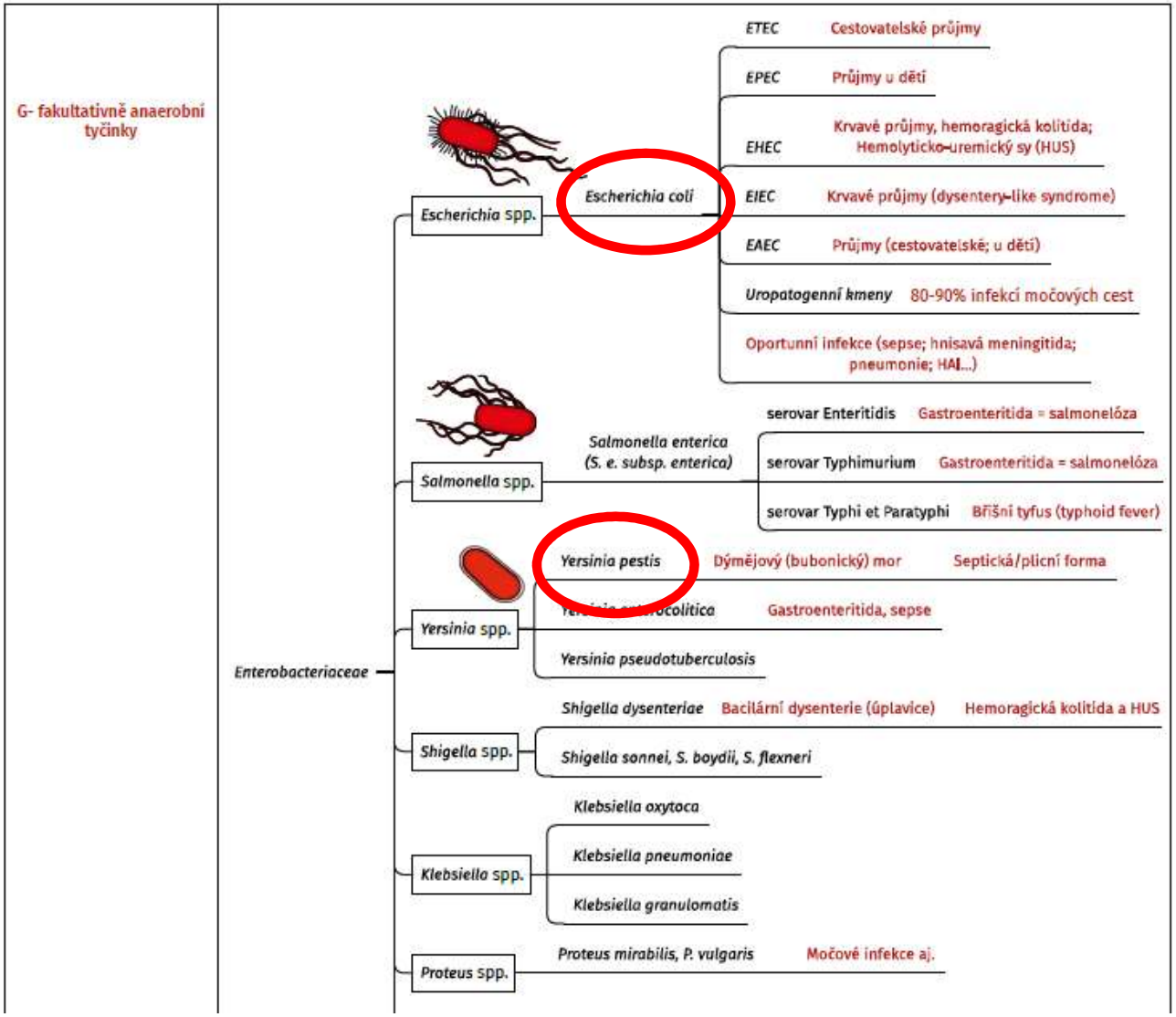
G- cocci


G- aerobní
nebo mikroaerofilní koky
Neisseria spp.
Neisseria gonorrhoeae
Kapavka
Ophthalmia neonatorum
Neisseria meningitidis
Hnisavá meningitida; sepse
G- anaerobní koky
Veillonella spp.

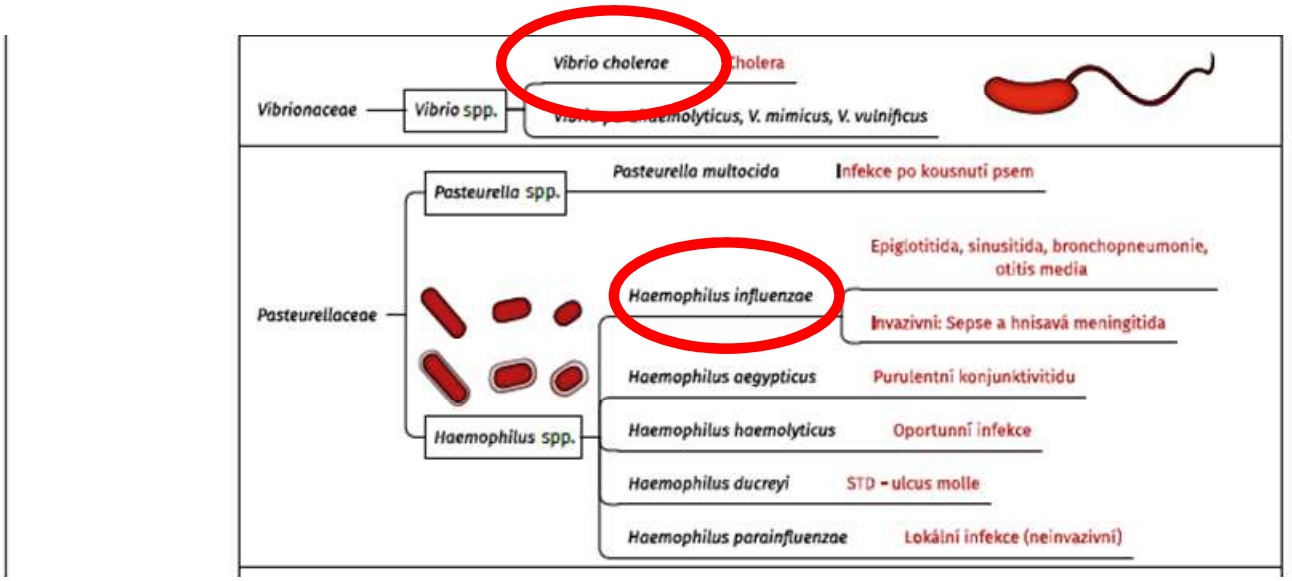
G- rods (part I)

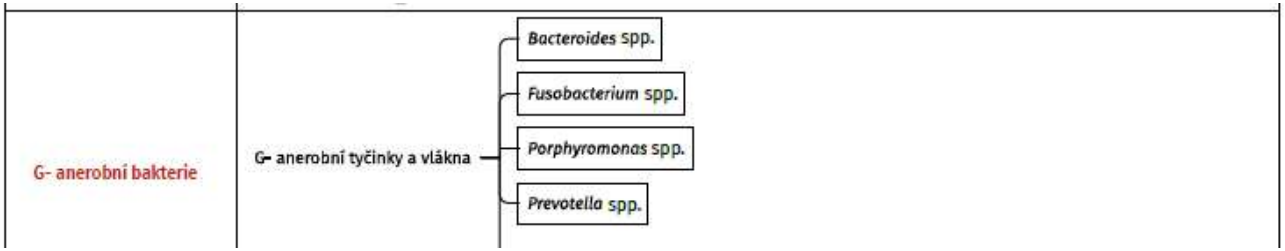

G- nefermentující tyčinky
Pseudomonadaceae
Burkholderia spp.
Burkholderia cepacia
Pneumonie (pacienti s CF), HAI
Burkholderia mallei, B. pseudomallei
Pseudomonas spp.
Pseudomonas aeruginosa
HAI (sepse, ventilátorově pneumonie, infekce ran), oportunní inf.
Ostatní pseudomonády
Stenotrophomonas spp.
Bez pevného zařazení
Acinetobacter spp.
Acinetobacter baumanii
HAI, infekce popálenin, inf. imunokompromitovaných
Moraxella spp.
Moraxella (Branhamella) catarrhalis
Respirační infekce
G- kultivačně náročné aerobní tyčinky
Bordetella spp.
Bordetella pertussis
Pertussis (dávivý kašel, černý kašel)
Parapertussis
Brucella spp.
Brucella abortus, B. melitensis, B. suis et B. canis
Brucelóza
Undulující horečka...
Francisella spp.
Francisella tularensis
Tularémie
Legionella spp.
Legionella pneumophila
Pontiacká horečka, legionářská nemoc
G- mikroaerofilní tyčinky
Gardnerella spp.
Campylobacter spp.
Campylobacter jejuni
Enteritida, někdy s krvavým průmem; cestovatelské průjmy; pseudoapendicitida
Campylobacter coli, C. fetus
Helicobacter spp.
Helicobacter pylori
Chronická gastritida a gastro-duodenální vředy
Riziko MALT lymfomu, adenokarcinomu žaludku

G- rods (part II)



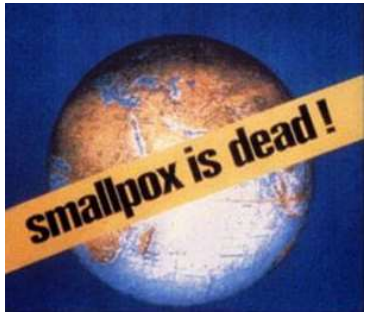
G- rods (part III)





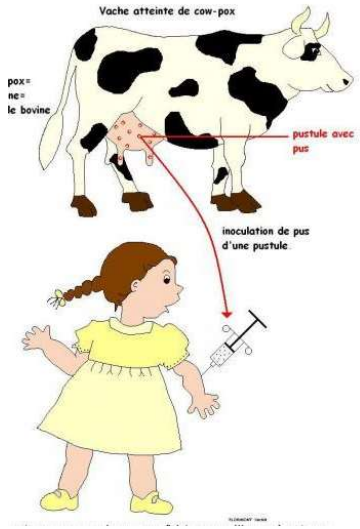
Other big names

Edward Jenner
1749 – 1823



eradication 1980

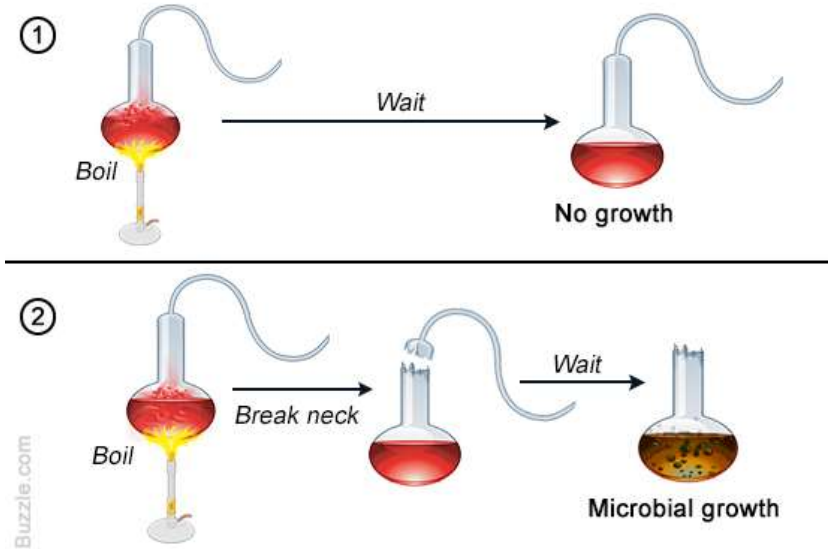
smallpox



vaccination 1796

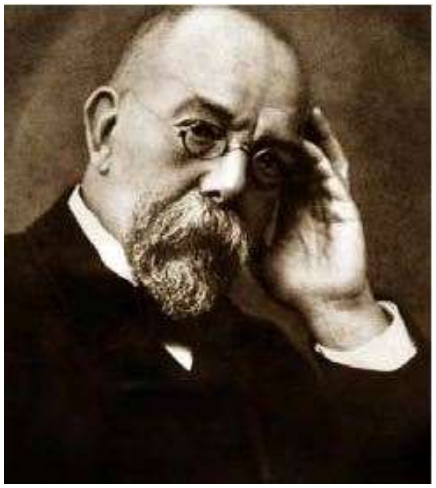
"Greatpox" = Syfilis; one of signs of secondary stage
(ultrarare today)

Louis Pasteur
1822 - 1895



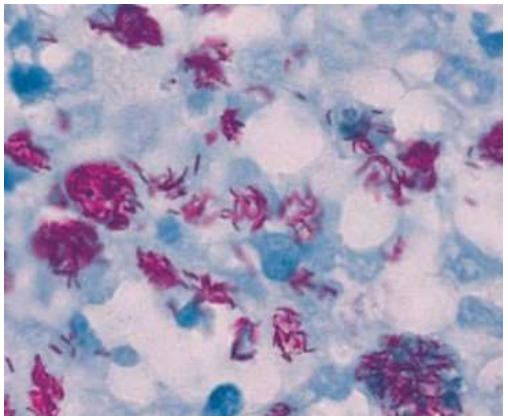
~~Spontaneous generation, miasma~~

Vaccine against anthrax (in animals) and rabies

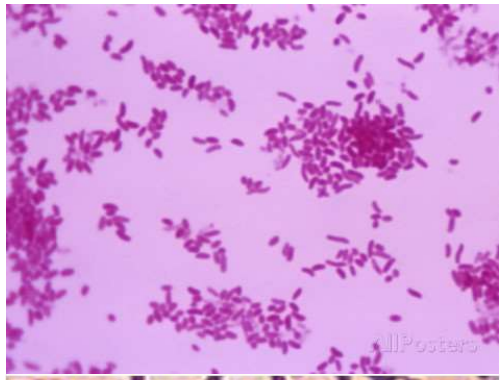


Robert Koch
1843 - 1910

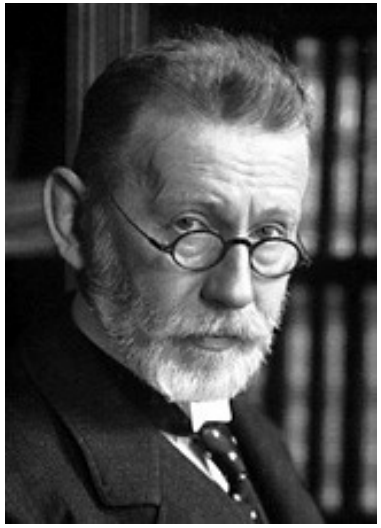
Mycobacterium tuberculosis



Vibrio cholerae

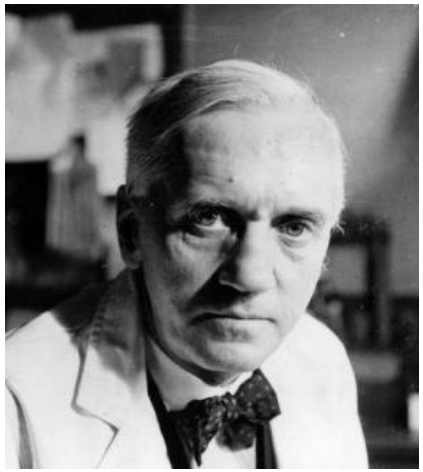


Bacillus anthracis and its spores



Paul Ehrlich
1854 - 1915

- "Magic bullet"
- dawn of chemotherapy era
- Salvarsan: drug against syphilis



Alexander Fleming
1881 - 1955

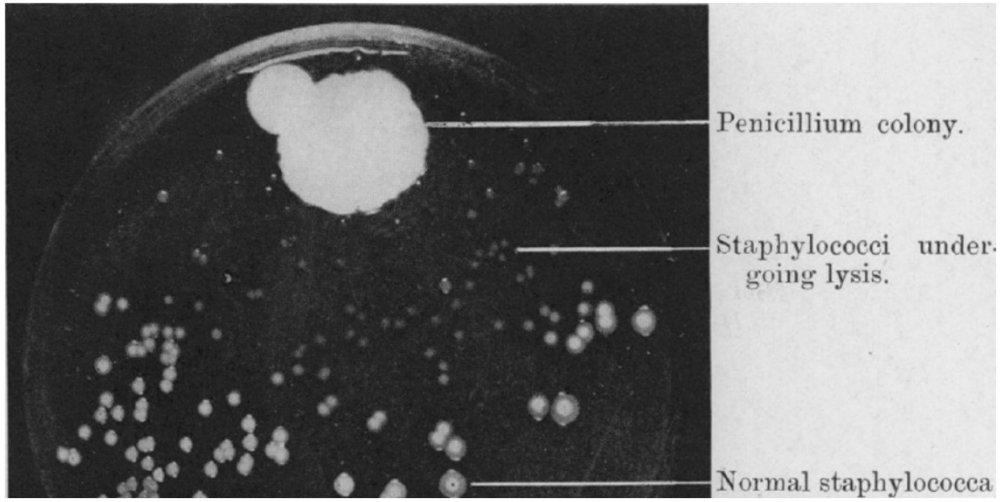
- Discovery of penicillin in 1928
- Go into therapy in 1941
  (Walter Florey, Ernst Chain)

ON THE ANTIBACTERIAL ACTION OF CULTURES OF A PENICILLIUM, WITH SPECIAL REFERENCE TO THEIR USE IN THE ISOLATION OF *B. INFLUENZÆ*.

ALEXANDER FLEMING, F.R.C.S.

From the Laboratories of the Inoculation Department, St Mary's Hospital, London.

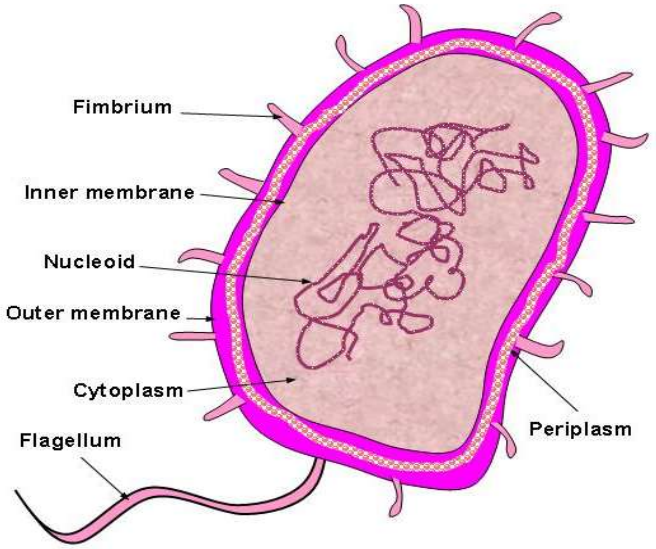
Received for publication May 10th, 1929.



"That's funny"

Bacterial genome

- Its organization
- Its evolution

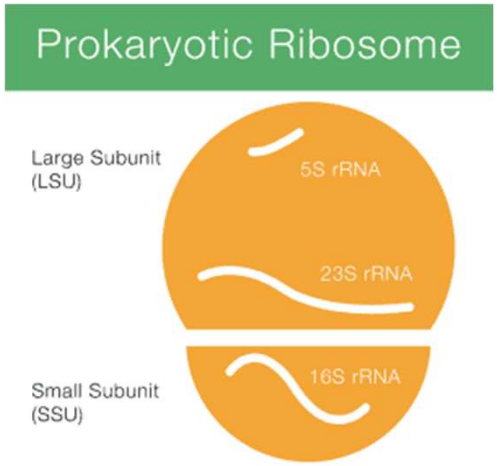


- chromosomal DNA (Mb units)
- extrachromosomal DNA (plasmid - hundreds kb)

Individual genes

- **structural** (protein coding)

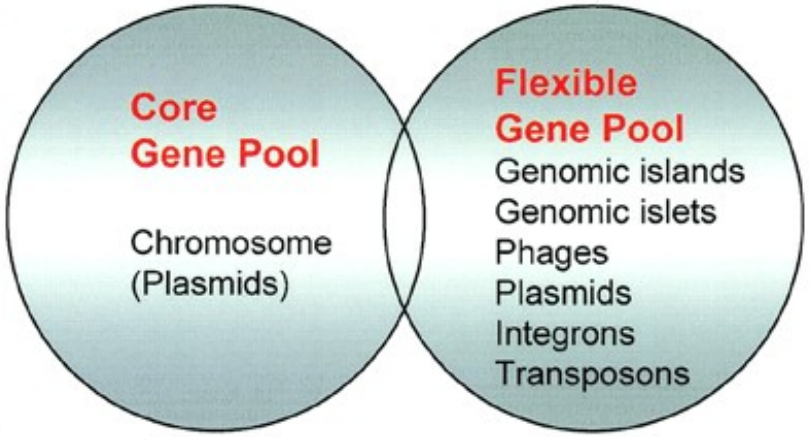
  a gene length ~ 1 kb
  structural genes ~ 90% of genome !



- **genes for rRNA** (16S rRNA, 23S rRNA, 5S rRNA)
- **genes for tRNA**
- additional non coding RNA)small RNA)

} not translated

Genome structure



Housekeeping genes:
encoding

- ribosomes
- Cell wall
- Metabolic pathways
- DNA replication
- ...

Additional genes:
encoding

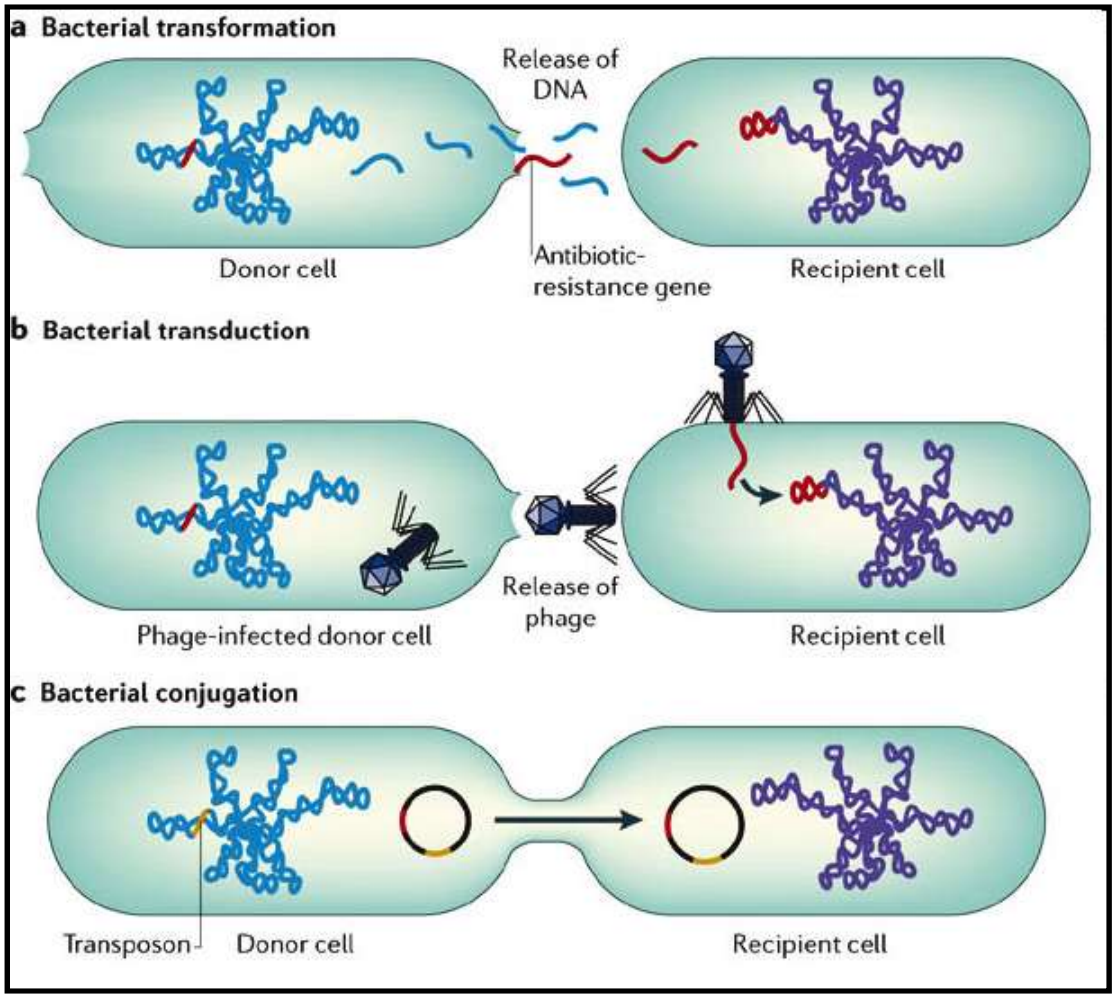
- Pathogenicity
- AB resistance
- Mobile genetic elements
- ...

→ genome plasticity

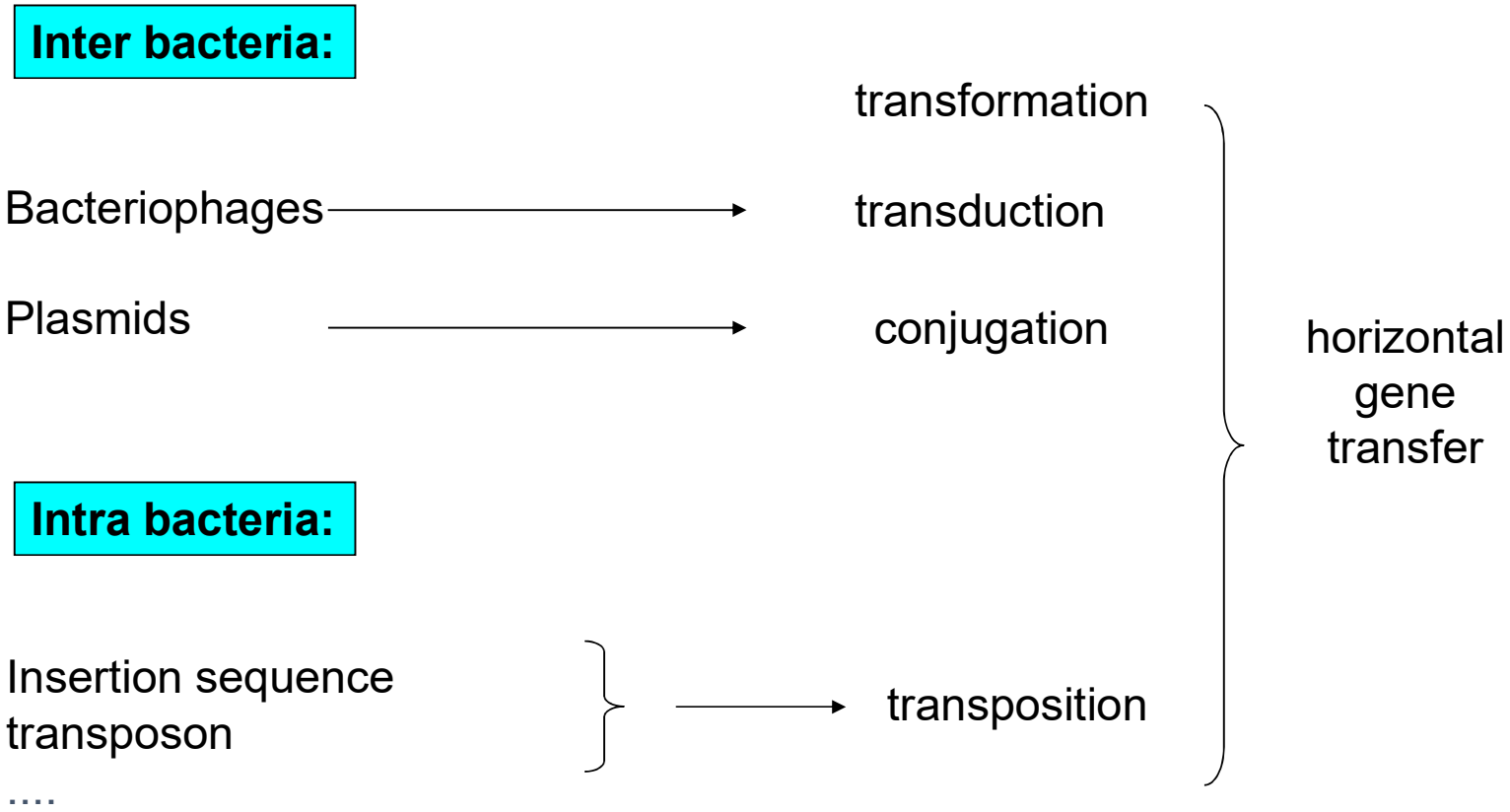
Transformation

Transduction

Conjugation



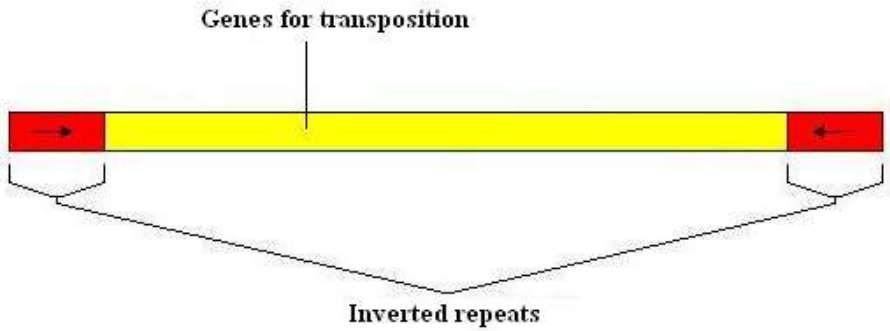
Mobile genetic elements



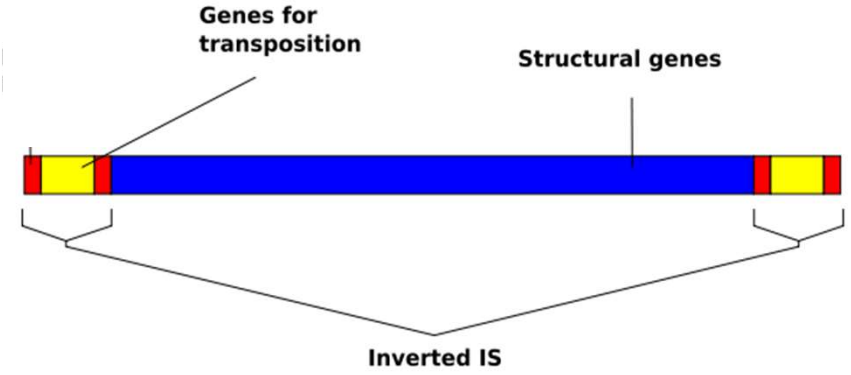
Transposable elements

DNA that is capable of movement within the genome

Insertion sequence
(0,8 - 2,5 kb)

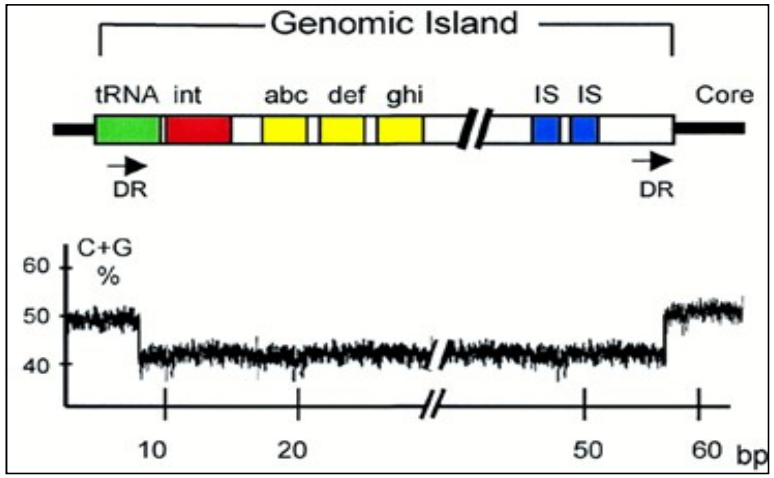


Transposons
(3 - 30 kb)



Genomic islands

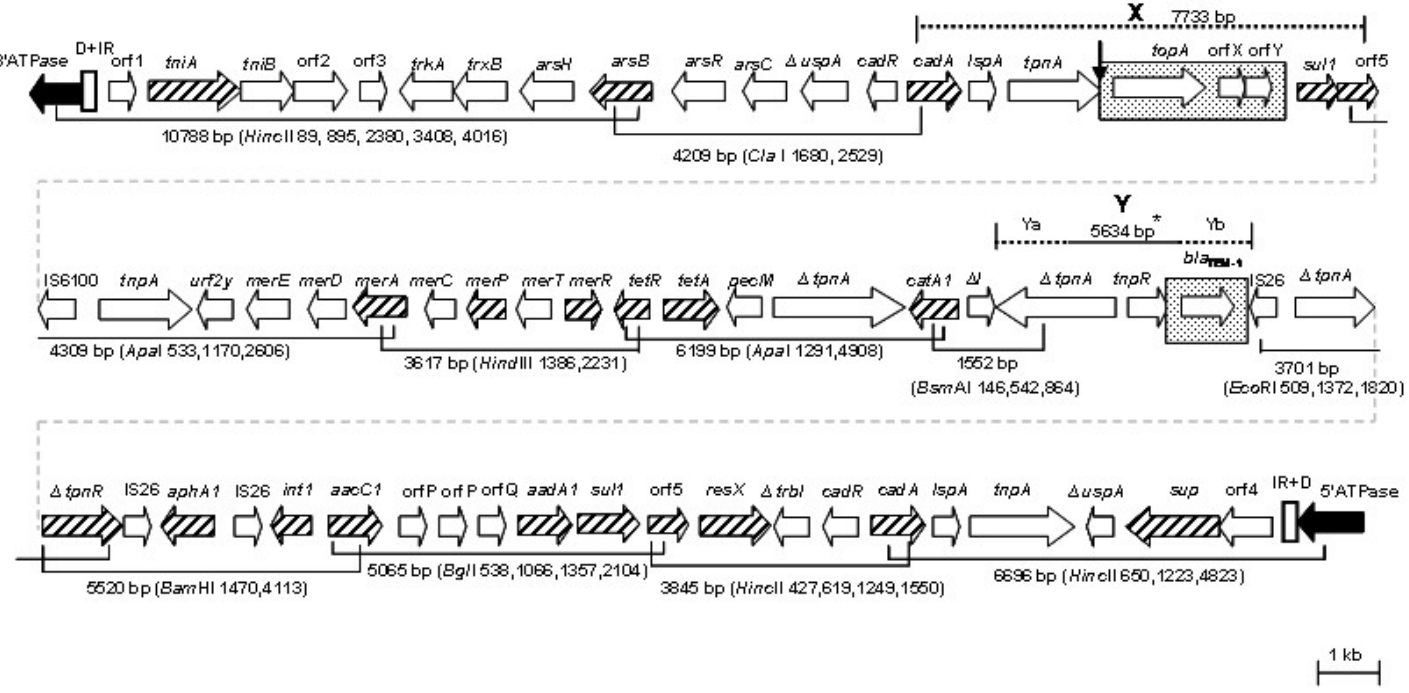
transposition can end up
with the creation of genomic islands
(10 - 200 kb)



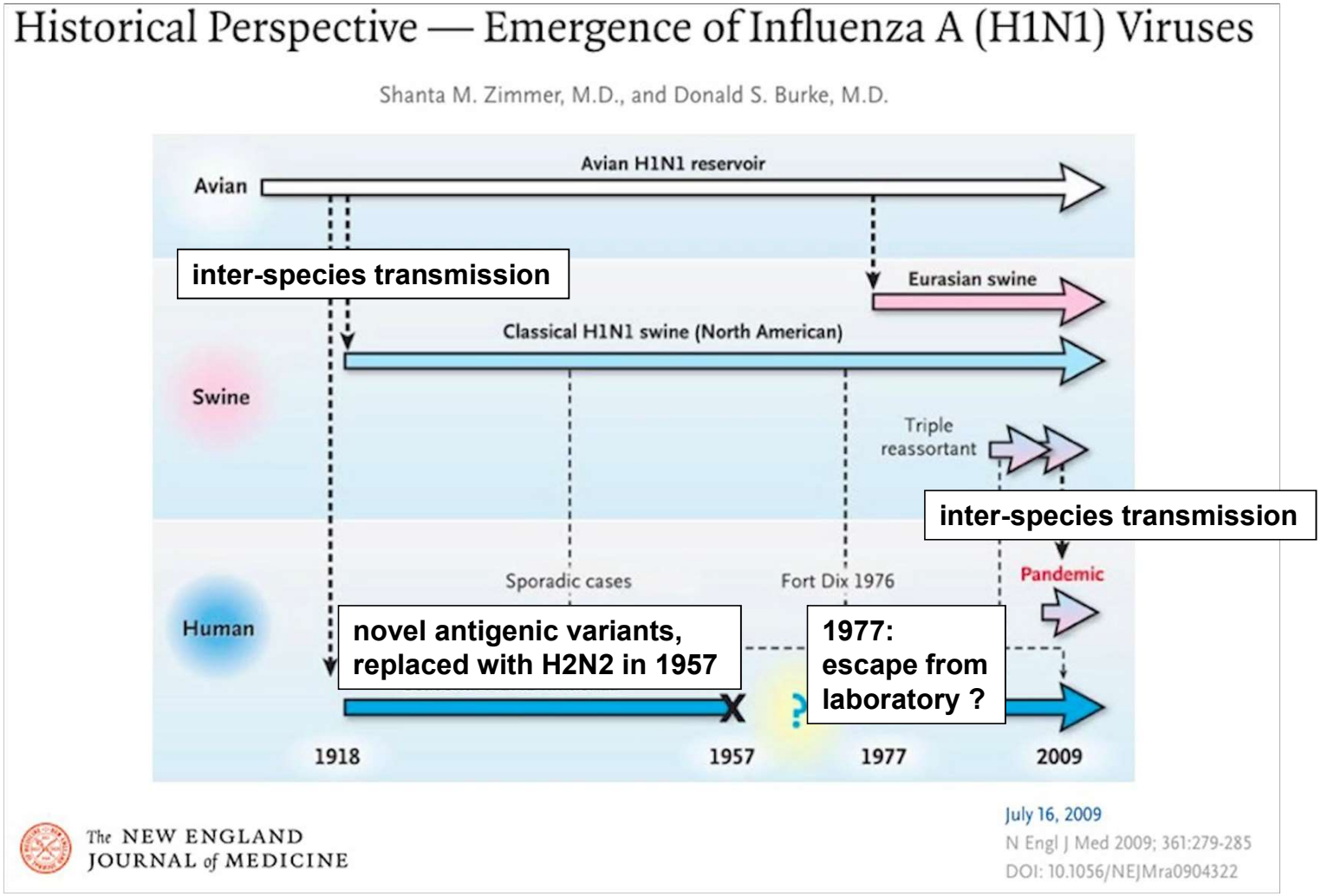
- resistance islands (RI)
- pathogenicity island (PAI)
  (not present on avirulent strains of the same species)

Resistance island and *Acinetobacter baumannii*

64 kb in length
23 genes of resistance on various transposable elements disruption of a gene for ATPase
clone of *A. baumannii* with a **multiresistant phenotype**



just a note: Spanish flu H1N1 and its fate



Pathogenicity island and ...

Black death

1. the Justinian plague (542 - 757)
2. Black Death (Europe, 1346 - 1352 and till 18th century)
3. Third pandemics (China, 1860 – 1890s)

over 200 mil people killed

today endemic in Africa, Asia, N. America
in 1997: 5500 cases (and 270 deaths)

- bubonic form
- septicemic
- pneumonic

Black death

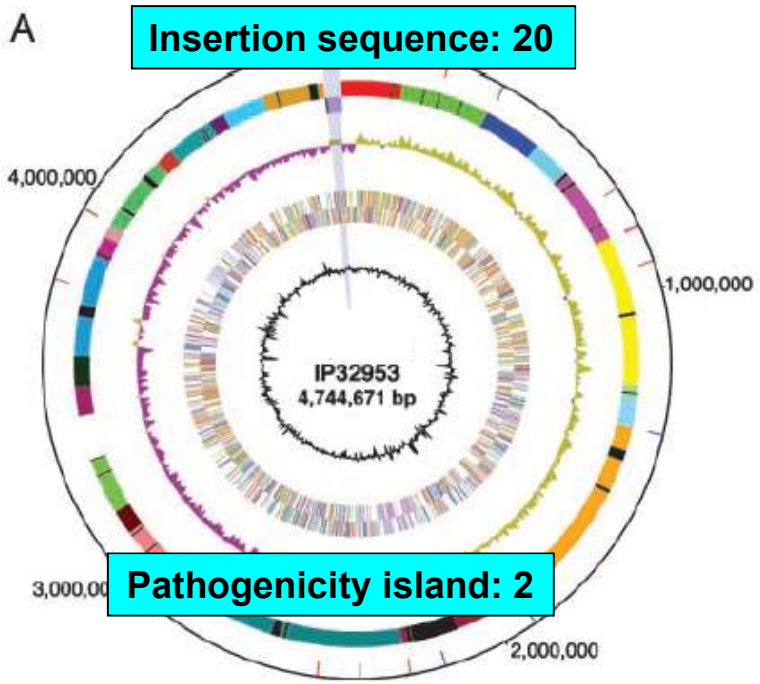
1894: Alexandre Yersin – discovered the cause: *Yersinia (Pasteurella) pestis*
1898: Paul-Louis Simond – discovered the route of transmission
(dead rats as a good hint)

Why pandemics?

- a dense human population cohabiting with infected rats
- low hygiene standards
- a large and susceptible rat population
- development of pneumonic form
- extremely low infectious dose

Pathogenicity island and ...

Yersinia pseudotuberculosis

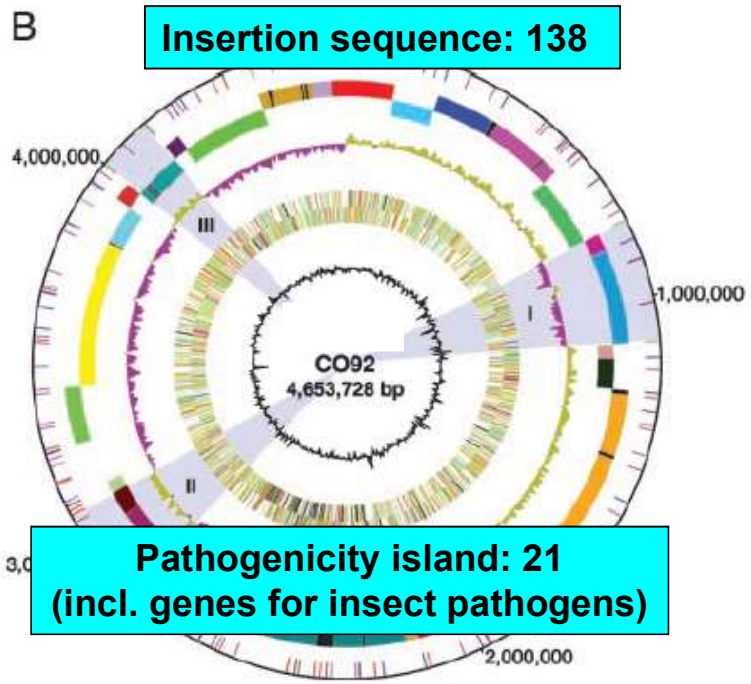


Insertion sequence: 20

Pathogenicity island: 2

Pseudogenes: 62

Yersinia pestis



Insertion sequence: 138

Pathogenicity island: 21
(incl. genes for insect pathogens)

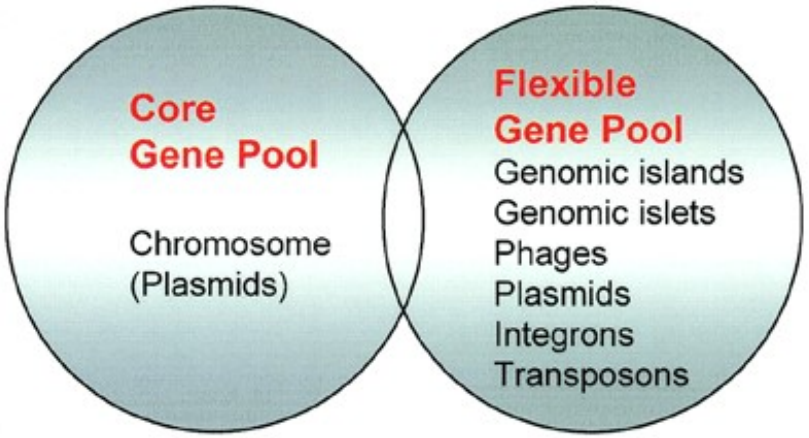
Pseudogenes: 149

Chain et al: Insights into the evolution of Y. pestis ... 2004.

What happens to bacterial genome

- Its flexible part is really in motion

- adaptability of the organism to new conditions
  - random mutations
  - horizontal gene tranfer: acquisition, loss, inactivation/activation
  - intragenomic recombination



Bacterial genome

obligate intracellular pathogens

- *Yersinia pestis*
- *Salmonella* Typhi

opportunistic extracellular pathogens

- *Acinetobacter baumannii*

Typhus

„War Fever“, „Jail Fever“:

- June 1812: Grand Army entering Russia; 500,000 troops
- Sept 7, 1812: battle at Borodino, 130,000 troops
- Sept 14, 1812: seizing Moscow, 90,000 troops
- Dec 1812: on retreat, 20,000 troops, just 1,000 fit for duty

Typhus

1909: Charles Nicolle - discovered the transmission

1916: Henrique Da Rocha-Lima
- discovered the cause of the disease:

Rickettsia prowazekii

† Howard Ricketts
† Stanislaus Von Prowazek

contaminated faeces

Why epidemics?

overcrowded places
low hygiene
body lice