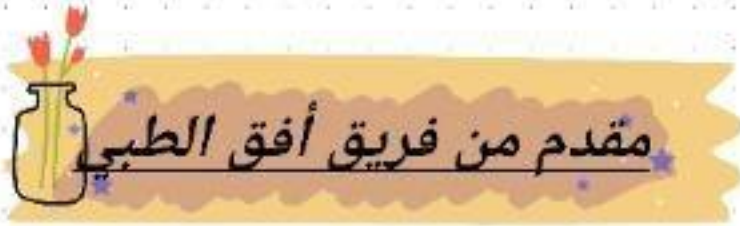

مقدم من فريق أفق الطبي


جامعة الأزهر - غزة
AL-AZHAR UNIVERSITY - GAZA
1412-1991 - ١٤١٢-١٩٩١


حركة الشبيبة الفتحاوية
جامعة الأزهر
Fateh Youth Movement

Ch3 = Growth of Bacteria

- Bacteria ⟹ binary fission ⟹ process by one parent cell divides to form two progeny cells

- exponential growth (logarithmic)
  - ex ⟹ N.O of cell ⟹ 1 → 2 → 4 → 8 → 16
  - after 4 generations

- generation time or duplications time ⟹
  - ex ⟹ escherichia coli "20min"
  - Mycobacterium "24h"

- rapid production of very large numbers of bacteria ⟸ short doubling time

① amount of nutrients ② T ③ PH ④ environmental factors / doubling time

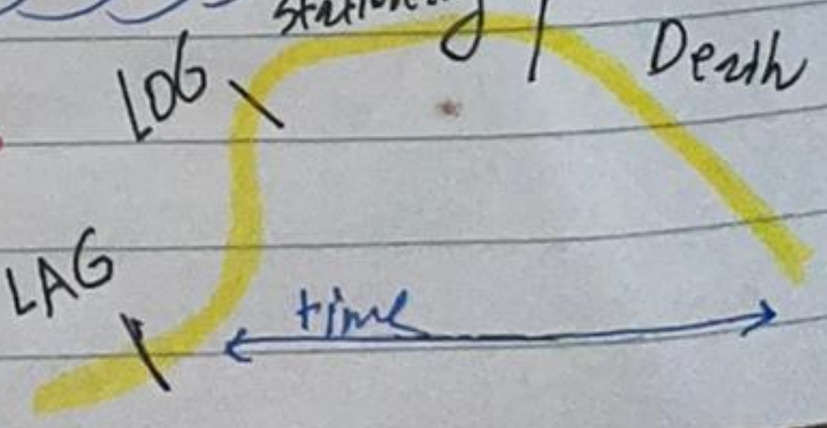
growth curve stage ⟹ 4

① lag phase ⟹ no divide / metabolic activity

② log phase ⟹ rapid cell division
  - ex ⟹ penicillin ⟹ peptidoglycan, cell wall
  - "drug ⟹ effective"

③ stationary phase ⟹ no. of cell new ⟹ no. of cell that die ⟸ balances
  - steady state
  - nutrient depletion / toxic product ⟹ growth to slow

④ death phase ⟹ decline in the N.O of viable bacteria



Aerobic and anaerobic growth

- most organisms ⇒ adequate supply of O_2 metabolism + growth
- oxygen ⇒ hydrogen receptor (final step)
  - cytochromes + flavoproteins
  - energy catalyzed

H_2O_2 hydroperoxide + oxygen ← free radical superoxide O_2^-

superoxide dismutase

toxic

$2H_2O_2 \rightarrow 2H_2O + O_2$

water + H_2O_2 ⇒ catalyzes

O_2 requirements

① ex ⇒ M. tuberculosis ⇒ obligate aerobes ⇒ hydrogen receptor O_2 ⇐ ATP-generating system

② E. coli ⇒ facultative anaerobes ⇒ respiration + O_2 ⇒ ATP / fermentation ⇐ no O_2

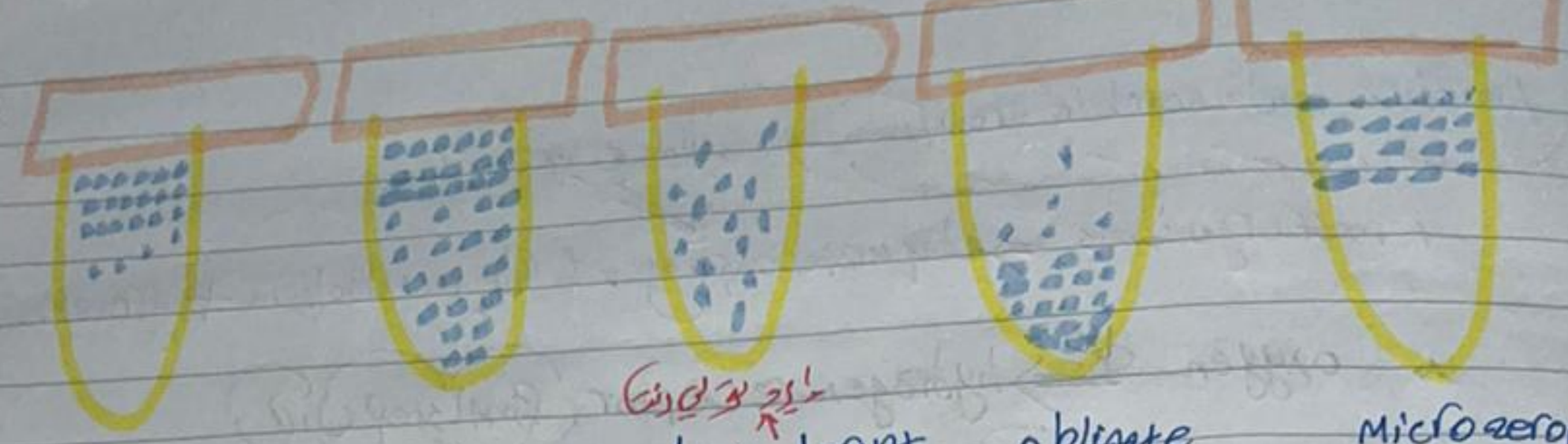
③ obligate anaerobes

↳ cannot growth in presence O_2

superoxide dismutase ⇐ catalase

obligate anaerobe vary in response to O_2 exposure

- killed rapidly
- survive but not able to growth



obligate aerobe

high conc of O_2

presence of enz superoxide dismutase (SOD) + catalase

facultative aerobe

best where most O_2 is present

Aerotolerant anaerobe

Grow equally, O_2 no effect

presence of one enzyme

allows harmful forms of O_2 to be partially neutralized

obligate anaerobe

bottom

no O_2

lacks of enzymes

Microaerophile

Growth when low conc of O_2

produce lethal amounts of toxic

fermentation of sugars ⇒

identification, classification, Differentiation

ex ⇒ Neisseria gonorrhoeae, Neisseria meningitidis

maltose, glucose ✓ fermentation distinguished

meningitides ← fermentation ✓ maltose ✓ ✗ ← neisseria

✗ E. coli ⇒ fermentation of lactose

✗ salmonella + shigella ⇒ non lactose fermentation ⟩ glucose fermentation

(glycolytic)

Def ⇒ Break down of a sugar to pyruvic acid , عكس ⇒ lactic acid
تعريفي ↳ monosaccharide ⇒ glucose/maltose
galactose.

(note) lactose ⇒ disaccharide ~ glucose + galactose

جل علامة E. coli في B-galactosidase عشان اسمه cleaved من لازم اول

* process by facultative bacteria generate ATP (يعني ان الاكسجين)
↓
grow faster in the presence of O_2

Acid PH ينتج
↑
facultative + anaerobic ⇒ fermentation علطول / aerobic ⇒ fermentation الزائد

deamination تسوي (pseudomonas) e.x
Alkaline PH

* تحديد نوع البكتيريا sugar حسب بكتيريا، فيه مادة PH indector phenol red يعطي لون yellow

(fermentation) لما يصير
red بعطي اللون ← fermentation لما يصير

fermentation بنستخدمه ⇒ clinical laboratory
نتيجة ↳ pyruvate + lactate acid turns the medium acid

iron metabolism

important for production of enzymes + growth factor

iron in form of ferric ion => growth

- iron mostly sequestered ~ transferrin
- siderophores (new) => capture iron (chelating agent)

Ch-4 *Genetics*

single circular DNA
wight ⇒ 2×10^9
basepairs ⇒ 5×10^6 ⟷ escherichia coli (1)

بيحتوي على gene 2000 عشان هي خلية بكتيرية وحيدة
MW ⇒ 50,000 , 2000 protein بيصنع

human

MW 5×10^8 (mycoplasma) ⇐ DNA of the smallest
cellwall نقص ال

100,000 gene code → 100,000 protein
+ base pairs 3×10^9

(2n) two sets of chromosomes

* bacteria ⇒ haploid "كروموسوم واحد" / eukaryotic "diploid" نسختين
recessive متنحي / dominant سائد
لو حصل mutation في جين واحد يبقى الجين التاني شايل الصفة.

(n) * haploid ⇒ mutation في جين واحد مش هيبقى في جين تاني يعوضه، اللي هيحصل انه
→ not expressed بالتالي ⇒ cell ⇒ lost that trait.
one set of chromosomes

Def ⇒ mutation ⇒ change in the base sequence of DNA ⇒ insertion of different amino acid into a protein, appearance of an altered phenotype

* mutations result from three types of molecular changes.

(1) Base substitution ⇒ base مكان base / insertion مش
DNA replication في غلط بيحصل في ال "one base is inserted in place of another"
base لأن ال hydrogen bonding بيحصل فيها تغير في mutagen , error نتيجة DNA polymerase في خطأ
وبالتالي بيحصل wrong base is inserted.

* missence mutation ⇒ base substitution ⇒ codon that simply cause a different A.A to be inserted
يعني حصل A.A مكان A.A تانية وده حصل بسبب تغير في one base وبالتالي تغير ال codes لـ A.A جديد.

UAA UAG UGA

⇒ stop codon

- nonsense mutation ⇒ when a base substitution generates ⟹ termination codon ⟹ stop protein synthesis

- silent mutation ⇒ mutation ⇒ / ⇒ لا يغير

GUU ⇒ CAA (VAL)

GUA ← CAT ⇒ (VAL)

point mutations

- no mutation
- silent
- Nonsense
- missense
  - non-conservative
  - conservative

TTC	TTT	ATC	TGC	TCC	DNA level
AAG	AAA	UAG	ACG	AGG	mRNA Level
LYS	LYS	stop	Thr	Arg	protein level

AGA

② frameshift mutation ⇒

↳ when one or more base pairs are added or deleted

↳ shift reading frame on the ribosome ⇒ incorporation of the wrong A.A "downstream"

from the mutation + production { inactive protein }

TAA CTG CAG GT ⇒ original sequence

TAA CCT GCA GGT ⇒ insertion

insertion of T

③ transposons

↳ transposons or insertion sequences are integrated in to the DNA.

insertion of new genes ⇒ profound change

mutations can be caused by chemicals/radiation/viruses

(1) nitrous acid + alkylating agent ⇒ hydrogen bond هتعمل تغيير في existing base بحيث تكون الـ hydrogen bond غير متوافقة شكل تفضيلي
بحيث preferentially تعمل wrong base ← e.g. ← Adenine بدل ما ترتبط مع thymine ترتبط مع cytosine.

(2) 5-bromouracil ⇒ base analogues ~ thymine يعني تشابه → (resemble normal base)

بسبب bromine atom اللي نفس نصف القطر radius تقريباً methyl group في الـ 5-bromouracil بيصير
لما يصير insertion يكون بدل thymine ← (5-methyluracil)

note ⇒ 5-bromouracil ≠ thymine ⇒ في hydrogen bonding fidelity
بس عنده ميل إنه يصير ارتباطه مع guanine أكثر.
⇒ A-T base pair تحويلها إلى ⟹ G-C base pair
وبالتالي بيصير فيه mutation في الـ antiviral drug.

(3) benzpyrene موجود ⟹ tobacco smoke
وبيعمل frameshift mutations بدل ما يعدل existing DNA base
لما عملناها بيسمى mutagens, carcinogens
"لأنه ممكن يسبب سرطان أو mutation عليه"

يقحم نفسه بالقوة
to intercalate between the adjacent base → DNA sequence وبالتالي يغير الـ

- Xrays have high energy and can damage DNA in three ways

(1) break down the covalent bond
وبعمل رابط لـ P ribose وبالتالي تحطم DNA

(2) الـ free radical منتجة تهاجم الـ bases

(3) تغير في الـ electrons موجودين في الـ bases وبالتالي تتغير الـ hydrogen bonding

- Ultraviolet radiation

رح ينتج عنه ازدواج في متشابهين
thymine dimer
بتشكل موجود في الـ DNA وبصير عندي dimerisation بين thymine (ribosome وهو بالتالي يؤثر
inability of the DNA to replicate properly بصير فيه مشكلة وبالتالي بصير

وبالتالي بيتم انتاج DNA مشوه بكثرة.

- mutator bacteriophage ⇒ فيروسات الها قابلية كبيرة بصير فيها mutation،

mutation ⇐ bacteriophage تهاجم bacteria وتحقنها بالمادة الوراثية تبعتها

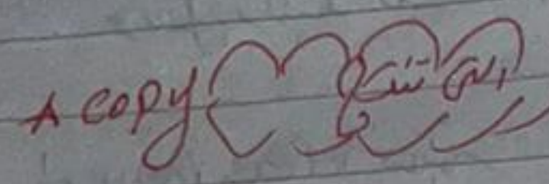
DNA بصير اله عملية insertion في bacterial chromosome والبكتيريا ع تتكاثر من خلال binary fission

مثلاً مكانها وبيغير مكان الـ DNA حسب وين ما أخطأها وبالتالي بصير نوع من الـ mutation
ب various gene ممكن تسبب مشاكل ونقصان بعض صفات حسب مين الجين الـ mutation

frameshift or deletions مثل

- transfer of DNA within Bacterial cells:

transposons
↑ transfer DNA from one site on the bacterial chromosome to be another site or to a plasmid

↑ copy  => inserted in bacterial chromosome or plasmid

↓ medically important ↓ antibiotic resistance

between bacterial cells → conjugation

within bacterial cells → transposons

↑ mechanism
- copy
- paste

- transfer of DNA within bacteria → programmed rearrangements

programmed rearrangements
- Def ⇒ movment of genes from silent stroge site to active expression site.
- e.X ⇒ nesseria gonorrhoae / Borrellia recurrents
- Benefit ⇒ evade immune response.

Transfer of DNA between bacterial cells.

note ⇒ most important consequence of DNA transfer → antibiotic resistance

Def

[1] conjugation ⇒ mating of 2 bacterial cells in which DNA is transferred from donor to recipient.

→ requirments ⇒ f factor in the donor (f⁺)
[redacted] in the recipient (f⁻)
receptor.

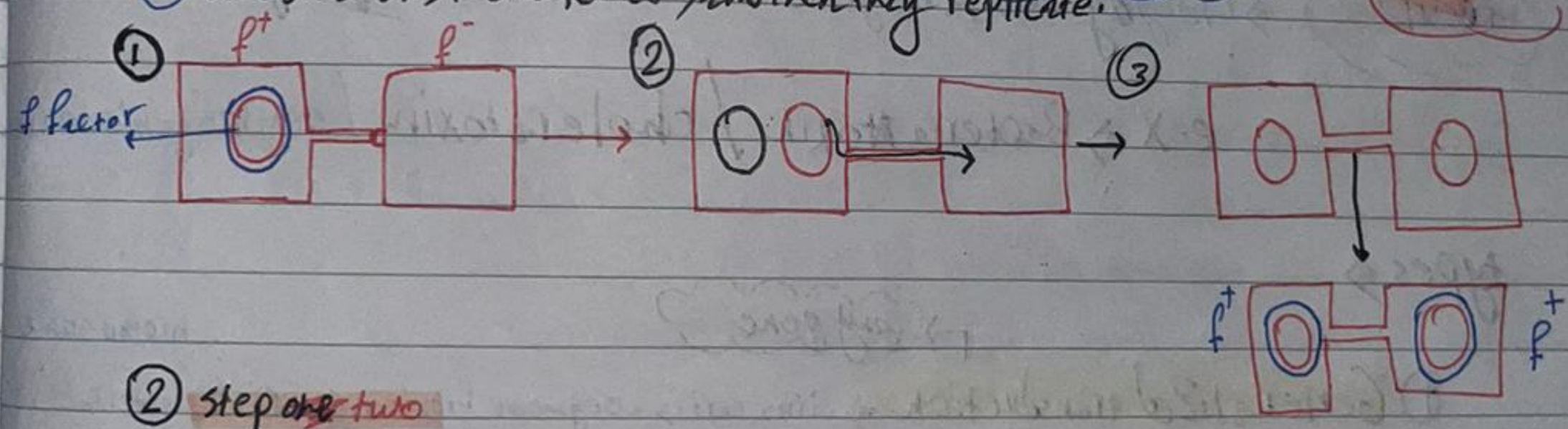
→ f factor ⇒ genes → proteins required for conjugation such as pilin
(sex pili)

nature of DNA transferred ⇐ → types → plasmid transfer ① & ② bacterial chromosomal DNA transfer

Mechanisms for:

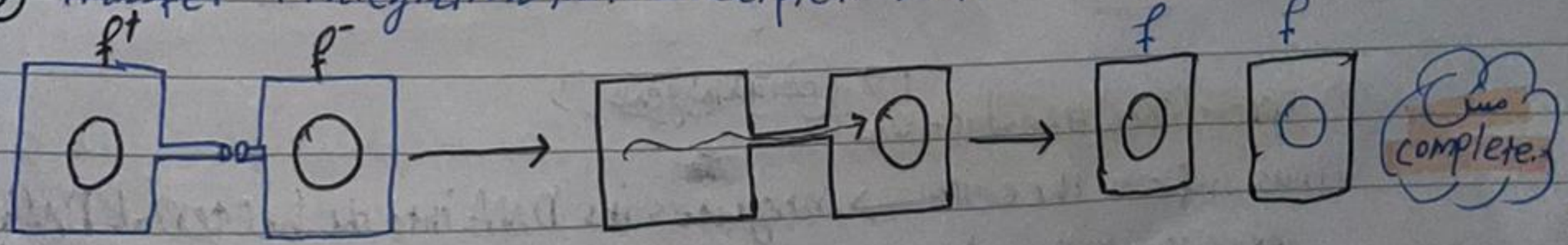
step one

① the polus of f^+ attaches to the receptor of f^-
② enzymatic cleavge of the f factor
③ one strand is transferred, and then they replicate.



② step one two

① pilus of f^+ attaches to the receptor of f
② cleavge of bacterial chromosome.
③ transfer + integration in the recipient DNA.



① ⇐ step two, step one الفرق بين
ds DNA هو f⁺ في البلازميد اللي هو ds DNA هو f⁺ في الكروموسوم

* type of cell involved (prokaryotic)

note → The time for complete transfer = 100min → ② only
→ usually the conjugation is broken and only part of the chromosome is transfer
→ newly acquired DNA integrates into the recipient's chromosome DNA, becoming part of genetic material
→ the most frequently transferred gene is the one adjacent to leading piece
الجزء الجاهز للانتقال.

② Transduction ⇒ Def: transfer of cell DNA by bacterial viruses

mechanism: ① during viral growth, bacterial DNA (part) is incorporated into the virus

② in the recepient cell, viral DNA is integrated into bacteral DNA giving it new trait (lysogenic)

result ⇒ changing Non pathogenic bacteria into ~~pathogenic~~ pathogenic ones.

e.x ⇒ Bacteria toxin / cholera toxin / erythrogenic toxin

types ⇒

① Generalized transduction (any gene) ⇒ virus carries segment from any part of bacterial chromosome.
bacterial DNA is fragmented → a fragment is incorporated into virus
the virus infects new bacteria giving it the new traits

② specialized transduction (certain gene)
virus infects the cell → integrates its DNA into the bacterial DNA
excises its DNA and part of the adjacent bacterial DNA
infects new cell giving it new traits.

↳ type of cell involved (prokaryotic)

notes) some virus integrate at specific sites of bacterial DNA, so the adjacent genes that are transferred are specific to that virus.

(3) transformation) transfer of DNA one cell to another

Methods → natural ⇒ the dying cell release its DNA, other recipient cells take it up.

→ laboratory ⇒ extract DNA from one type and introduce it to other types.

transfection

- transformation of DNA from encapsulated to Non encapsulated

→ (Non encapsulated → encapsulated)

non pathogenic → pathogenic

Recombination ⇒ integration of the transferred DNA to the host DNA

→ requirements: ligases + endonucleases.

Types:

DNA

(1) homologus: 2 pieces have extensive homologous regions pair up

exchng piece ⇒ breakage + reunion ← note

(2) Non-homologus: little if any, homolgy is necessary

- type of cell involved (prokaryotic + eukaryotic)
- Nature of DNA transferred (Any DNA.)

ch-5 | Classification of medically important bacteria.

(A) principles of classification.

(1) Cultural characteristics (2) Morphology + staining
(3) Biochemical (4) Molecular (5) serological.

* nature of cell wall
  * Thick, rigid cell wall / flexible, thin cell wall / wall-less cells
    ex: spirochete

(1) Thick cell wall.

↳ extracellular bacteria

(A) free living bacteria ⇒ can Live outside cells in laboratory medium
ex: human + animal cells

(B) non-free living bacteria ⇒ requires cells to survive (obligate intracellular parasites)
↳ ex: Chlamydia / rickettsia.

↳ subdivided according to (shape + staining)
into ↳
- G -ve cocci
- G +ve cocci
- G -ve Bacilli (rods)
- G +ve Bacilli

(+) have different O_2 requirements.
sporing forming abilities -

* G +ve Cocci → Arrangment
  - → sterptococci → catalase -ve
  - → staphylococci → catalase +ve
    ↳ Abscess of skin

ثنين → pneumonia / pharyngitis

* G +ve bacilli ⇒ spore-forming ability

spore forming

O2 requirement

aerobic

Bacillus

Anthrax

anaerobic

Clostridium

tetanus

botulism

non-spore forming

filamentous

Actinomyces israeli

Actinomycosis

Nocardia

Nocardiosis

non filamentous

Corynebacterium

diphtheria

listeria

meningitis

* G ve cocci

Neisseria

Gonorrhea + meningitis

* G ve Bacilli ⇒ O_2 - requirement

Aerobic

ex. Pseudomonas

pneumonia

urinary tract infection & UTI

facultative

shape

straight

curved

Anaerobic

ex. Bacteroides

peritonitis

systemic effected

respiratory

hoemophillis

meningitis

الالتهاب السحائي

zoonotic

Brucella

whooping cough

enteric

E. coli

pneumonia

تابع ورا

للبطن

facultative

shape

curved.

stright

system effected

respiratory

haemophillus

meningitis

Bordetella

whooping cough

Legionella

Pneumonia

zoonotic

Brucella

Brucellosis

francisella

tularemia

pasteurella

Cellulitis

enteric

escherichia

urinary tract infection

enterobacter

serratia

Pneumonia

klebsiella

Pneumonia urinary tract infection.

salmonella

shigella

enterocolitis

Campylobacter

enterocolitis

vibrio

Cholera

helicobacter

Gastritis peptic ulcer

Acid fact → Mycobacterium → Tuberculosis ⇒ السل

→ Leprosy ⇒ الجذام

flixibel wall ⇒ spirochetes

→ treponema pallidum ⇒ syphilis ⇒ bacterial disease that can be sexually transmitted

→ Borrdia ⇒ lyme disease

→ Leptospira ⇒ Leptospirosis

Wall-Less cells → Mycoplasma

pleymonia

كانت تسمى سابقاً Pseudomonas الآن from the Burkholderia family because the different between 2 DNA

↓

ايجاد الاختلاف في ال DNA بال molecular test.

: Contents

: Concept of normal Flora

Normal flora is the term used to describe the various bacteria and fungi that are permanent resident of certain body sites , especially the skin , oropharynx , colon , and . vagina

The viruses and parasites , which are the two other major groups of microorganisms , are usually not considered members of the normal flora , although they . can be present in asymptomatic individuals

The normal flora organisms are often referred to as commensals , which are organisms that derive benefit . from another host but do not damage that host

TABLE 6–1 Summary of the Members of Normal Flora and Their Anatomic Locations

Members of the Normal Flora[1]	Anatomic Location
Bacteroides species	Colon, throat, vagina
Candida albicans	Mouth, colon, vagina
Clostridium species	Colon
Corynebacterium species (diphtheroids)	Nasopharynx, skin, vagina
Enterococcus faecalis	Colon
Escherichia coli and other coliforms	Colon, vagina, outer urethra
Gardnerella vaginalis	Vagina
Haemophilus species	Nasopharynx, conjunctiva
Lactobacillus species	Mouth, colon, vagina
Neisseria species	Mouth, nasopharynx
Propionibacterium acnes	Skin
Pseudomonas aeruginosa	Colon, skin
Staphylococcus aureus	Nose, skin
Staphylococcus epidermidis	Skin, nose, mouth, vagina, urethra
Viridans streptococci	Mouth, nasopharynx

The members of the normal flora vary in both Although number and kind from one site to another . of the normal flora extensively populates many areas the body , the internal organs usually are sterile . Areas such as the central nervous system , blood , lower bronchi and alveoli , liver , spleen , kidneys , and bladder are free of all but the occasional . transient organism

*note ⇒ normal flora آخر مكان ممكن يتواجد فيه
skin ③, urogenital tract ②, GIT ①
note ⇒ sterile system لازم يكون normal flora ما فيه
e.x ⇒ CNS, blood.

There is a distinction between the presence of these organisms and the carrier state . In a sense , we all are carriers of microorganisms , but that is not the normal use of the term in the medical context . The term carrier implies that an individual harbors a potential pathogen and therefore can be a source of . infection of others

+ Can transmit infections.
potential pathogen يكون معاه infection
Def ⇒ chronic carrier.

It is most frequently used in reference to a person with an asymptomatic infection or to someone who has recovered from a disease but continues to carry . the organism and may shed it for a long period

*note ⇒ carrier لازم يكون عنده normal flora
*note ⇒ carrier state ⇒ asymptomatic infections ⇒ e.x ⇒ hepatitis B

There is also a distinction to be made between members of the normal flora , which are the permanent residents , and the colonization of the individual with a new organism . In a sense , we are all colonized by the normal flora organisms , but the term colonization typically refers to the acquisition of a new organism . After the new organism colonize (i.e., attaches and grow , usually on a mucosal membrane) , it may cause an infectious disease or it may be eliminated by our host defenses . Furthermore , the person colonized by a new organism can transmit that organism to others (i.e., .act as a reservoir of infection for others)

Colonization ⇒ Acquisition of new organism that may cause disease or be eliminated or transmitted to others.
pathogeneses. ال new organism

The members of the normal flora play a role both in the maintenance of health and in the causation of : disease in three significant ways

~E.coli in urinary tract → UTI
immune system weakness
change their location

They can cause disease , especially in(1) immunocompromised and debilitated individuals . Although these organisms are nonpathogens in their usual anatomic location , they can be pathogens in . other parts of the body

*note ⇒ colonization يعني normal flora

They constitute a protective host defense mechanism.(2) The nonpathogenic resident bacteria occupy attachment sites on the skin and mucosa that can interfere with colonization by pathogenic bacteria . The ability of members of the normal flora to limit the growth of . pathogens is called colonization resistance

If the normal flora is suppressed , pathogens may grow and cause disease . For example , antibiotics cab reduce the normal colonic flora that allows Clostridium difficile , which is resistant to the antibiotics , to overgrow and . cause pseudomembranous colitis

They may serve a nutritional function . The(3) intestinal bacteria produce several B vitamins and vitamin K . Poorly nourished people who are treated with oral antibiotics can have vitamins deficiencies as a result of the reduction in the normal flora . However , since germ-free animals are well-nourished , the normal flora is not essential for . proper nutrition

TABLE 6–2 Medically Important Members of the Normal Flora

Location	Important Organisms[1]	Less Important Organisms[2]
Skin	*Staphylococcus epidermidis*	*Staphylococcus aureus*, Corynebacterium (diphtheroids), various streptococci, *Pseudomonas aeruginosa*, anaerobes (e.g., *Propionibacterium*), yeasts (e.g., *Candida albicans*)
Nose	*Staphylococcus aureus*[3]	*S. epidermidis*, Corynebacterium (diphtheroids), various streptococci
Mouth	Viridans streptococci	Various streptococci, *Eikenella corrodens*
Dental plaque	*Streptococcus mutans*	*Prevotella intermedia*, *Porphyromonas gingivalis*
Gingival crevices	Various anaerobes (e.g., *Bacteroides*, *Fusobacterium*, streptococci, *Actinomyces*)	
Throat	Viridans streptococci	Various streptococci (including *Streptococcus pyogenes* and *Streptococcus pneumoniae*), *Neisseria* species, *Haemophilus influenzae*, *S. epidermidis*
Colon	*Bacteroides fragilis*, *Escherichia coli*	*Bifidobacterium*, *Eubacterium*, *Fusobacterium*, *Lactobacillus*, various aerobic gram-negative rods, *Enterococcus faecalis* and other streptococci, *Clostridium*
Vagina	*Lactobacillus*, *E. coli*,[3] group B streptococci[3]	Various streptococci, various gram-negative rods, *B. fragilis*, Corynebacterium (diphtheroids), *C. albicans*
Urethra	*S. epidermidis*, Corynebacterium (diphtheroids), various streptococci, various gram-negative rods (e.g., *E. coli*)[3]	

[1]Organisms that are medically significant or present in large numbers.
[2]Organisms that are less medically significant or present in smaller numbers.
[3]These organisms are not part of the normal flora in this location but are important colonizers.

: Normal flora of the skin

The predominant organism is staphylococcus epidermidis , which is a nonpathogen on the skin but such can cause disease when it reaches certain sites , as artificial heart valves and prosthetic joints . It is found on the skin much more frequently than its . pathogenic relative staphylococcus aureus

There are about 10^3 - 10^4 organisms /cm^2 of skin . Most of them are located superficially in the stratum corneum , but some are found in the hair follicles and act as a reservoir to replenish the superficial flora after hand washing . Anaerobic organisms , such as Propionibacterium and Peptococcus , are situated in the deeper follicles in the dermis , where oxygen tension is low .

Propionibacterium acnes is a common skin anaerobe that is implicated in the pathogenesis of acne .

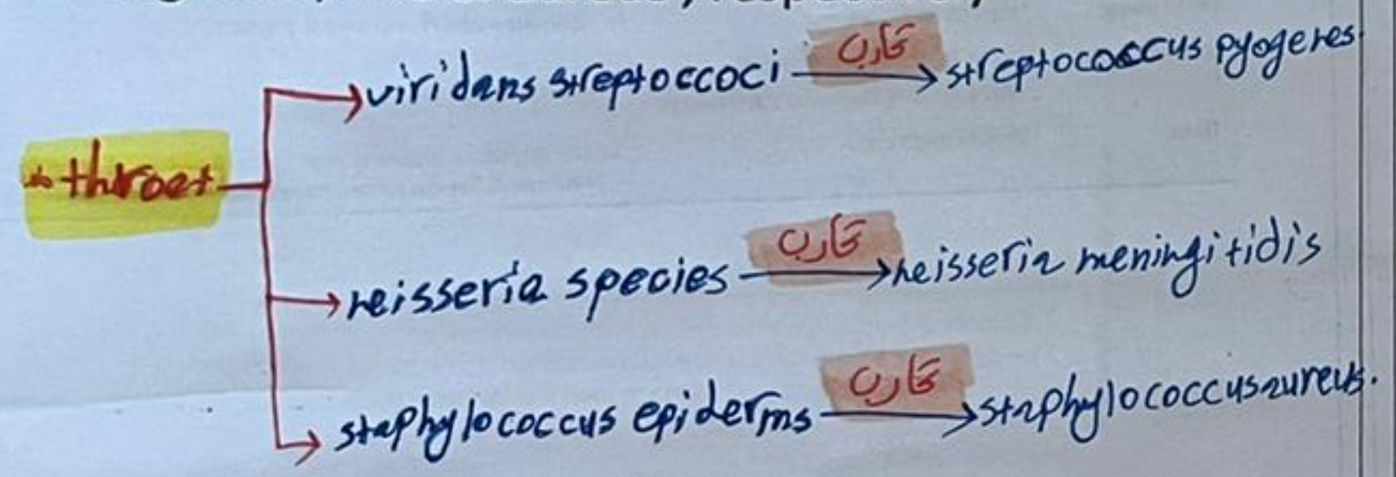
Location	Important Organisms'	Less Important Organisms'
Skin	*Staphylococcus epidermidis*	*Staphylococcus aureus*, *Corynebacterium* (diphtheroids), various streptococci, *Pseudomonas aeruginosa*, anaerobes (e.g., *Propionibacterium*), yeasts (e.g., *Candida albicans*)

The yeast Candida Albicans is also a member of the normal flora of the skin . It can enter a persons bloodstream when needles pierce the skin (e.g., in patients with intravenous catheters or in those who use intravenous drugs) . It is an important cause of systemic infections in patients with reduced cell-mediated immunity .

: Normal flora of the respiratory tract

A wide spectrum of organisms colonize the nose , throat , and mouth , but the lower bronchi and alveoli typically contain few , if any , organisms. The nose is colonized by a variety of streptococcal and staphylococcal species , which the most significant of is the pathogen S. aureus . Occasional outbreaks of disease due to this organism , particularly in the newborn nursey . Can be traced to nasal , skin , or perianal carriage by health care personnel .

The throat contains a mixture of viridans streptococci , Neisseria species , and S. epidermidis . These nonpathogens occupy attachment sites on the pharyngeal mucosa and inhibit the growth of the pathogens Streptococcus pyogenes , Neisseria . meningitidis , and S. aureus , respectively

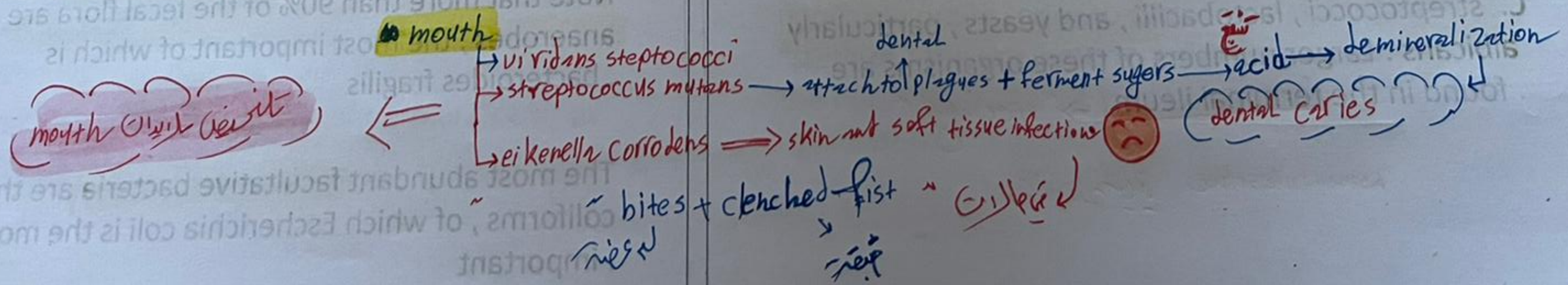


In the mouth , viridans streptococci make up about half of the bacteria . Streptococcus mutans , a member of the viridans group , is of special interest since it is found in large numbers in dental plaque , . the precursor of caries

when reaching blood in dental surgery.

The viridans streptococci are also the leading cause of subacute bacterial (infective) endocarditis . These organisms can enter the bloodstream at the time of . dental surgery and attach to damaged heart valves

The plaque on the enamel surface is composed of gelatinous , high-molecular-weight glucans secreted by the bacteria . The entrapped bacteria produce a large amount of acid , which demineralizes the . enamel and initiates caries



Eikenella corrodens , also part of the normal oral flora , causes skin and soft tissue infections associated with human bites and “clenched-fist” injuries (i.e., injuries to the hand that occur during .fist fights)

Anaerobic bacteria , such as species of Bacteroids , Prevotella , Fusobacterium , Clostridium , and Peptostreptococcus , are found in the gingival crevices , where the oxygen concentration is very low . If aspirated , these organisms can cause lung abscesses , especially in debilitated patients with poor dental hygiene . In addition . The gingival crevices are the natural habitat of Actinomyces israelli – an anaerobic actinomycete that can cause . abscesses of the jaw , lungs , or abdomen

gingival crevices → Anaerobic bacteria ~ clostridium, fusobacterium, Peptostreptococcus ~ ~ ↓O_2 بيئة ~
→ Antinomyces israelli. نادر ⇒ Abscesses of lung, jaw, Abdomen

Nose	*Staphylococcus aureus*[1]	*S. epidermidis*, Corynebacterium (diphtheroids), various streptococci
Mouth	Viridans streptococci	Various streptococci, Eikenella corrodens
Dental plaque	*Streptococcus mutans*	*Prevotella intermedia*, Porphyromonas gingivalis
Gingival crevices	Various anaerobes (e.g., Bacteroides, Fusobacterium, streptococci, *Actinomyces*)	
Throat	Viridans streptococci	Various streptococci (including *Streptococcus pyogenes* and *Streptococcus pneumoniae*), Neisseria species, *Haemophilus influenzae*,[1] *S. epidermidis*

: Normal flora of the intestinal tract

In normal fasting people , the stomach contains few organisms , primarily because of its low pH . The small intestine usually contains small numbers of C. streptococci , lactobacilli , and yeasts , particularly albicans . Larger numbers of these organisms are . found in the terminal ileum ⇒ "specially"

. small intestine في الأمعاء الدقيقة

The colon is the major location of bacteria in the body . Roughly 20% of the feces consists of bacteria, . approximately 10^11 organisms/g

Note that more than 90% of the fecal flora are anaerobes , the most important of which is . bacteroides fragilis ← e.x: bacteroides fragilis.

The most abundant facultative bacteria are the coliforms , of which Escherichia coli is the most . important ← e.x: E. coli

TABLE 6–3 Major Bacteria Found in the Colon

Bacterium[1]	Number/g of Feces	Important Pathogen
Bacteroides, especially *B. fragilis*	10^{10}–10^{11}	Yes
Bifidobacterium	10^{10}	No
Eubacterium	10^{10}	No
Coliforms	10^{7}–10^{8}	Yes
Enterococcus, especially *E. faecalis*	10^{7}–10^{8}	Yes
Lactobacillus	10^{7}	No
Clostridium, especially *C. perfringens*	10^{6}	Yes

[1] *Bacteroides*, *Bifidobacterium*, and *Eubacterium* (which make up more than 90% of the fecal flora) are anaerobes. Coliforms (*Escherichia coli*, *Enterobacter* species, and other gram-negative organisms) are the predominant facultative anaerobes.

The normal flora of the intestinal tract plays a . significant role in extraintestinal disease

For example , E. coli is the leading cause of urinary tract infections and B. fragilis is an important cause of peritonitis associated with perforation of the intestinal wall following trauma , appendicitis , or . diverticulitis

- B fragilis → peritonitis "trauma, appendicitis
  → obligate anerobic
- E. coli ⇒ facultative anerobic

colon.

Other important anaerobic pathogens include Fusobacterium and Peptostreptococcus , and other important facultative bacteria include Enterococcus facecalis , which causes urinary tract infections , particularly in hospitalized patients with decreased . host defenses

pseudomonas.

P. Aeruginosa is present in 10% of normal stools , as . well as in soil and water

Antibiotic therapy (e.g., with clindamycin) can suppress the predominant normal flora , thereby allowing a rare organism such as the toxin-producing Clostridium difficile to overgrow and cause severe colitis . Administration of certain antibiotics , such as neomycin orally , prior to gastrointestinal surgery to "sterilize " the gut leads to a significant reduction of the normal flora for several days . Followed by a . gradual return to normal levels

Colon	Bacteroides fragilis, Escherichia coli	Bifidobacterium, Eubacterium, Fusobacterium, Lactobacillus, various aerobic gram-negative rods, Enterococcus faecalis and other streptococci, Clostridium

group B streptococci ← تيبي → sepsis + meningitis in newborn during delivery
~ 20-15% حاملين ~
* staphylococci aureus ⇒ toxic shock syndrome in newborn
↳ 5% of pregnants. ⇒ (antibiotic before delivery.)

: Normal flora of the genitourinary tract

The vaginal flora of adult women consists primarily of lactobacillus species . Lactobacilli are responsible for producing the acid that keeps the pH of the adult . woman's vagina low

⇐ عشان needs estrogen.

Before puberty and after menopause , when estrogen levels are low , lactobacilli are rare and the vaginal pH is high . Lactobacilli appear to prevent the growth of potential pathogens , since their suppression by antibiotics can lead to overgrowth by C. albicans . Overgrowth of this yeast can result in Candida vaginitis

The vagina is located close to the anus and can be colonized by members of the fecal flora . For example , women who are prone to recurrent urinary tract infections harbor organisms such as E. coli and Enterobacter in the introitus . About 15% to 20% of women of childbearing age carry group B streptococci in the vagina . This organism is an important cause of sepsis and meningitis in the newborn and is acquired during passage through the birth canal . The vagina is colonized by S. aureus in approximately 5% of women , which predisposes . them to toxic shock syndrome

Urine in the bladder is sterile in the healthy person , but during passage through the outermost portions of the urethra , it often becomes contaminated with S. epidermidis , coliforms , diphtheroids , and nonhemolytic streptococci . The area around the urethra of women and uncircumcised men contains secretions that carry Mycobacterium smegmatis , an acid-fast organism . The skin surrounding the genitourinary tract is the site of Staphylococcus saprophyticus , a cause of urinary tract infections in .women

↓ سبب women UTI

Ch-7 ⇒ pathogenesis

terms

- pathogen ⇒ microorganism that can cause disease.
- opporturnstic pathogen ⇒ Photogen that cause the disease in immuno compromised patient.
  ممرضات انتهازية.

parasite
- → any organism that can cause harm
- → usually for protozoa + helminthes
- → intracellular parasites "rickettsia, chlamydia"
- → There are facultative parasites

infection
- → literally ⇒ an organism has entered the body.
- → in medical context ⇒ an organism has entered the body + caused symptoms "disease"
  ↳ يعني إذا تشكل "normal flora"

virulence
- → The No. of organisms required to cause disease.
- → LD 50 → Lethal dose of 50% of population.
- → ID 50 → infective dose of 50% of population.
  - ↳ e.x ⇒ ID 50 in salmonella is 10^5
  - ↳ ID 50 shegella is 10^2
  - ↳ ID 50 in yersinia 10
- → $ID \propto \frac{1}{virulence}$

notes ⇒ Bacteria may have more than 1 virulence factor.
- ↳ the main equation of phatogenesis is (pathogen vs immune system)
  - pathogen: number, site, virulence
  - immune system: humoral, cellular, disease

virulence factor
- → agent used by pathogen to sneak disease into the body
- ↳ it helps the pathogen for:

① colonization → needs attachment by pili, Glycocalyx
- pili: "N. gonorrhea"
- Glycocalyx: ↳ "strepto. mutans"

② immunoevasion
- → by Genetic variation" — تغيير ال Ags"
- → by Rokect transmission" — ما بلحق جهاز مناعة يشوفها"
  - ↓ "meningitis."

③ Immunosuppression → inhibit the immune response.

④ entry and exit of cells → like intracellular bacteria

⑤ obtain nutrition from the host

***Types of virulence factor.**

① Adherence component → pili, Glycocalyx

② capsule → for evasion ~ antiphagocytic ~

③ invasion enzymes → hyaluronidase, collagenase, fibrolytic enzyme.
- hyaluronidase, collagenase → degrade collagen
  + hyaluronic acid, important cellulitis by "streptococcus"
- fibrolytic enzyme → "streptokinase"
- coagulase ⇒ staphylococcus aureus + yersinia

④ toxins ⇒ exotoxins → enterotoxin of E. coli.
- endotoxins ⇒ "lipid A, Teichoic Acid
  - G tive ↓
  - G tive ↑

*note ⇒ Bacteria differs in their virulence factors
- strain of E. coli ⇒ extoxins 1 ⇒ watery diarrhea
- other strain of E. coli ⇒ extoxins 2 ⇒ Bloody diarrhea.

Why dose people get infections diseases?

① from organism's perspective ⇒ ① infection & No ② infection & virulence.

② from host's perspective ⇒ weak immunity "innate ↓ > humoral ↓ < cellular ↓"

* why the immune system becomes weak?
① → Genetic immunodefficiecy ⇒ agammaglobulinemia
② → Aquired 〃 〃 ⇒ AIDS, diabetes
③ → drug-induced immunosuppression ⇒
<= organ transplant, auto immune, cancer فمرضى كل الا ضياب بالعدوى.

(note) ⇒ sometimes, the immune system is stronge enough that the disease cannot cause symptoms "Asymptomatic"
↳ كيف نكشفهم ؟؟
→ .serum وجود ال Ag في ال
↳ e.x ⇒ hepatitis B surface Ag
→ وجود ال Ab في ال serum
↳ e.x ⇒ hepatitis C Ab, hepatitis A Ab.

* type of bacterial infections.
① communicable → can be transmitted "TB via air"
معدي جداً ⇐ contagious ⇒ highly communicable.
② non communicable → not transmitted " botulism " مثال

* epidemic ⇒ outbreak of the disease / endemic ⇒ present at low level in specific population.
pandemic ⇒ world wide distribution.

* terms *
① subclinical infection ⇒ there is no or mild symptoms to escape diagnosis
② Asymptomatic ⇒ No symptoms
الجهة ماري ☺
③ chronic carrier ⇒ the organism continues grow with or without symptoms. ⇒ typhoid mary
④ latent state ⇒ there is reactivation of the organism and reactivation of symptomes.

* بس 1 و 2 و 3 ⇐ عامل مشترك في كلهم انه عكس للعدوى / بس ③ و ④ فيهم بينهم
③ → العدوى دائماً
④ → عدوى بيرجع نشاطها reactivation

(* How to detect asymptomatic people ?) colonization, normal flora كيف نميز بين ال

① the name of bacteria + it's anatomical site
↳ ولازم نكون حذرين عند أخذ العينة.

② Ab titer ⇒

stages of bacterial pathogensis:

① transmission ⇒ to the portal of entry. ⇐ مسببات المرض
② evasion ⇒ host defense آليات دفاع العائل
③ Adherence ⇒ لبعض البكتيريا أهداب تساعدها على الالتصاق ⇒ mucous membranes by pili.
④ Colonization ⇒ ↑ No of bacteria ⇒ Adherence التصاق
⑤ disease production ⇒ exotoxin, invasion + inflammation.
⑥ Host response ⇒ 5, 4, 3 تحدث في نفس الوقت ⇒ Adherence ✓, colonization ✓, disease production. ✓
⑦ progression or resolution.

determination of bacterial pathogenesis

① transmission ② Adherence to cell surface ③ invasion + inflammation ④ toxin production ⑤ immunopathogenesis.

① transmission

- modes of transmission

② human to human
- direct contact → Gonorrhoea (sexual / birth canal)
- non-direct contact → dysentery ⇒ hepatitis A
- transplacental → congenital syphilis
- blood → syphilis.

② non human to human
- soil ⇒ tetanus (spores)
- water ⇒ legionnaires disease, pseudomonas
- fomites → staphylococcus skin infections
- Animal source
  - direct → cat scratch fever (pasteurella)
  - insect vector ⇒ lyme disease "Ticks"
  - animal excret → hemolytic-uremic syndrom

* note → disease transmitted through brith canal during delivery is **Not** sexually transmitted.
→ puncture wounds contaminated with anaerobic bacteria should Not be sutured "cat scratch" ↳ "pasteurella"
→ E.coli O157H7 can be transmitted via "fecal-oral" in undercooked meat "burger"

* normal flora (N.F) can cause disease, then infection via airborne droplets "respiratory N.F" or fecal oral ~ GIT ~

* blood borne diseases ⇒ hepatitis B,C / HIV / west nile virus / syphilis / T-cell lymphotropic V

hepatitis B,C /, HIV ~ ← [illegible] / [illegible] screeing [illegible]

* diseases transmitted by ticks ⇒ lyme disease, tularemia, relapsing fever
, rocky mountain spotted fever.

horezontal transmission ~ person to person ~

* vertical transmission ~ mother → offspring ~
① placenta ⇒ syphilis, toxoplasma, cytomegallo virus
② Brith canal ⇒ Gonorrhoea, streptogalaction.
③ milk ⇒ viruses > bacteria ⇐ staphylococcus aureus.

* portal of entery
① respiratory ② GIT ③ skin ④ Genital tract ~ GUT ~

② Adherence to cell surface (no adherence → no disease)
① pili → neisseria + E.coli
② Glycocalyx → strepto mutans + staphyococcus epidermidis (S.) [illegible]
③ capsule (antiphagocytic + Adherent) → G tive in general.

* notes → the molecules of attachment are called adhesins
→ E.coli, proteus ⇒ have flagella that allow them to move aganist urine flow.

* Biofilms

① structure → polysaccharides + proteins surround microbs.
② function → protection from Antibiotics + cellular immunity
③ predisposing factor → foregin bodies / synthetic valves or joints
④ risk → retared wound healing in diabetics
→ pseudomonas persistence in cystic fibrosis patients
⑤ mech → cell entry → colonization → Quorum sensing
attack ← biofilm + virulence factors ← تحسس الـ density لإنتاج عوامل الضراوة
Adhesins مسؤولة

(notes) ⇒ E. coli + salmonella produce curli protein
binding on endothelium + fibronetic ①
active factor XII → Thrombosis → DIC ②
disseminated intravascular coagulation
الكلمة انتشرة داخل أوعية دموية.

③ invasion + inflammation

* invasion ⇒ entry to host cell "need enz"

* enzymes
① (collagenase + hyaluronidase) → degrade collagen + hyaluronic acid → spreading bacteria
* e.x ⇒ strepto. pyogens * — cellulitis
② coagulase → coagulation "fibrinogen → fibrin" → walling off → protection
* e.x ⇒ S. aureus, yersinia.

③ IgA protease → degrad IgA in mucus → Adherence + colonization.
↳ "immunoglobulin" — site of attachment
* e.x ⇒ H. influenzae, strepto pneumoniae.

④ leukocidin → kill neutrophils + macrophages.

other virulence factor for invasion

Give: Give: Give rods

① Anti phagocytic factors → capsule ~ N. meningitidis, strepto pneumonia, H. influenzae

② cell wall protein of G+ve cocci

M protein ~ group A strepto cocci → anti phagocytic (pyogens)

A protein (S. aureus) → ⊖ complement.

notes:
- some capsules can be used in vaccination
- no capsule → non pathogenic
- anti capsule Ab enhance phagocytosis.

opsonization → enhancing pathogen phagocytosis by labeling it with opsonins IgG, C3b

inflammation:
- host defense mechanism, against pathogens
- signs: redness, pain, loss of function, swelling, hotness
- mediators → histamine, LTs, PGs → prostaglandins
  - Leukotrienes
- by ↑ VD, ↑ permeability
- types:
  - pyogenic → neutrophils are predominant cells.
  - granulomatous → lymphocytes & macrophages.

intracellular survival:
- Def: the ability of pathogens to grow within cells.
- These pathogens are Not obligate intracellular
- They can be grow on media
- e.x: bacteria: TB, legionella, listeria.
  - fungi: histoplasma

benefits: protection from Ab + neutrophils.

mechanism:
1. inhibition of fusion of phagosome with lysosome → avoid degradation
2. inhibition of acidification of phagosome → ↓ lysosomal enzyme activity.
3. escape from phagosome into cytoplasm

TB + legionella ← 1, 2
e.x: listeria ← 3

* invesins ⇒ bacterial surface proteins interact with cellular receptor to allows invasion

phagosome ←] ← بعد يدخل ميكروب ع سيتر
cytoplasma ←

⟸ listeria ← cytoplasma

move from one cell to another by Actin rokets to evade the immune system

* Yops ⇒ Yersinia outter-membrane proteins
- → inhibit phagocytosis by neutrophils
- → inhibit cytokine production by macrophages ⟹ inhibit immune system

(notes)
- → yersinia also use to coagulase to inhibit phagocytosis
- → yop J ⇒ cleaves the proteins in the cascade for TNF induction (tumor necrosis factor)
- → type of yersinia ⇒ GIT, pneumonic

* pathogenicity islands *

* cluster of genes that encode many virulence factor
- → invasins
- → exotoxin
- → Adhesins.

* tranfer together via ⇒ conjugation / transduction.

(* note) cannot replicate independantly

e.x ⇒
- → G-tive bacilli ⇒ E.coli, salmonella, pseudomonas.
- → G+tive cocci ⇒ strepto.pneumonia

(* note) بعما تحركة بكتيريا تتكاثر وتشغل عالجسم لما تستطع بعطولات target الاسمها receptor

* pseudomembranes ⇒ Thick adherent exudate on mucosal surface

e.x ⇒
- → Diphteria ⇒ cornyebacterium diphteria
- → pseudomembranes colitis ⇒ clostridium.

④ toxin production.

properities of exotoxin	(endotoxin in the opposite)
① excereted by living cell	• intergral part, after cell death.
② G tive, G tive	G tive only
③ polypeptide	lipopolysaccharide
④ highly antigenic	weak
⑤ toxoid can be made	cannt
⑥ highly toxic	moderately
⑦ heat labile	stable
⑧ bind to specific receptor.	don't
⑨ not-pyrogenic	pyrogenic ⇒ interleukin 1
⑩ No enzymetic activity.	Yes
⑪ extra chromosmal gene.	chromosomal

examples

S. aureus (food poisoning)	E. coli, salmonella
Bacillus cereus ( )	shigella, cholera " cholera gene "
Bacillys anthrcis (α-toxin)	
strepto coccus pyogenes.	

Disease

tetanus, diphteria, botulism	G tive bacilli. ↑ meningio coccemia, sepsis

• notes
- toxoid ⇒ toxin + formalin processing or heat processing.
- specific receptors " Ach receptors"
- exotoxin found in plasmid ⇒ can be passed to other balteria.
- toxiodis used to induce antitoxins → treatment / prevention
  - antitoxin ← botulism / tetanus
  - toxoid ←

A-B subunit structure.

- exotoxin has
  - → A subunite ⇒ toxic activity.
  - → B subunit ⇒ Binding to receptors

e.x ⇒ toxins of (diphteria, tetanus, botulism, cholera, E.coli]

Activity of A-subunit.

① ADP-Ribosylation of Gs (← protein) (stimulatory) → ⊕ G_s protein → ⊕ Adenylyl cyclase → ↑ cAMP → electrolyte inbalance → watery diarrhea

→ e.x ⇒ cholera, E.coli toxins.

② ADP-R of Ef-2 (elongation factor)
- → hyperactivate target protein → symptoms
- → e.x ⇒ pseudomonas exotoxin → ⊖ Ef-2 → ⊖ ↓ protein synthesis.

③ ADP-R of Gi (inhibitory) → ⊖ Gi → ⊕ Adenylyl cyclase → ↑ cAMP → whooping cough.

way of secretion ⇒ by secretion system → secret to toxin. → to ⇒ extracellular
⇒ cell directly

. Ab [illegible] "more effective"

(injectosome.) : Type 3 secretion system ⇐ secretion system ما آخر نوع ال
→ in pseudomonas, shagella, salmonella, E.coil

. toxin [illegible] transport pump [illegible] molecular projunction [illegible]

* exotoxin of Gtive bacteria (mechanism + examples)

① ADP-R ⇒ ex~ corynebacterium diphterie

Diphteria toxin ⇒ ADP-R of EF-2 → ↓ protein synthesis → cell death → pseudomembrane
→ myocarditis

tox gene expression ⇒ exotoxin production.
- required by lysogenic bacteriophage
- regulated by Iron (↑iron → ↓ expression)

-2+3 neurotoxin.

② Blocking inhibitory neurotransmitters (glycine

*clostridium tetani → tetanus toxin → ⊖ glycin → ⊕ excitatory → neurons
~ spinal arch lock jow ~ ← spastic paralysis
(شلل تشنجي)

*tetanus toxin is composed of
- heavy chain (B-subtype) ⇒ binds ganglosids of neural membrane
- light chain (A-subtype) ⇒ protease degrades proteins needed for release of inhibitory neurotransmitter.

ⓑ Blocking stimulatory NT

*clostridium. botulinum → botulinum toxin → ⊖ Ach → flaccid paralysis.

2 subunits → 1 for binding
→ 1 protease → degrade proteins for Ach release.

*there are 6 subtypes
- type → encoded on plasmid
- type → // ~ chromosomal DNA
- type → ~ ~ temperate bacteriophage.

④ enterotoxin + cytotoxins

* clostridium difficile → exotoxin A → enterotoxin → watery diarrhea
→ exotoxin B → cytotoxins → damage to colonic mucosa.

A+B → pseudomembranous colitis
→ mech ⇒ Glycosyltransferase → Glucosylation of inhibition Rho GTPases. → inhibition → ⊖ single transduction.
→ disaggregation of Actine filaments → apoptosis.

⑤ multiple toxins

* clostridia have → 7 lethal factor → necrosis + hemolysis
→ 5 enzymes → collagenase, protease, DNase, hyaluronidase, α-toxin.
~ deoxyribonuclease. ~ ↓ ↳ lecithinase

* note → hydrolize Lecithinase ⇒ destruction of membrane → death
→ No single clostridum species has the 12 factors
→ clostridum perfringens → food poisoning
→ watery diarrhea (enterotoxin)
· sta. aureus ⇒ superantigens ↓

⑥ exfoliation.
[redacted].
* S. aureus → exfoliation ~ epidermolytic toxin ~ → cleavage of demoglin of desmasomes
~ scalded skin syndrome ~ ⇐ detatchment of epidermis ↓

⑦ cooperative exotoxins.

* Bacillus anthracis → edema factor → ⊕ Adenylyl cyclase → edema.
→ Lethal factor → a protease → ⊖ cell growth → cell death.
→ protective Ag → bind to receptor → pors to allow entry of edema ⊕ Lethal fac

* note ⇒ Ab against protective Ag prevent the activity of 3 factor

⑧ superantigen

* S. aureus ⇒ TSST "toxic shock syndrom toxin" → ① binds major histocompetibility II "MHC II" on macrophages without processing → ⊕ TH cells (helper T cells) → IL-1

② T cell multiplication → cytokine overproduction

TSST ⇒ ① in it acts as superantigen → ② in it acts as T-cell mitogen.

⑨ other superantigen.

* S. aureus ⇒ locally acting superantigen "enterotoxin" → vomiting + watery diarrhea "food poisoning"

(note) ⇒ toxin → ⊕ macrophages → cytokines → ⊕ enteric nervous → ⊕ vomiting center → vomiting.

⑩ pore-forming

* methicillin resistance S. aureus "MRSA" → panton-valentin leukocidin (PV) ⇒ exotoxin → destruction of WBCs ⇒ skin ⇒ subcutaneous tissue.

(note) ⇒ VRSA ⇒ vancomycin resistance S. aureus.

⑪ superantigen causing rash. (strawberry tongue)

* strepto. pyogens → erythrogenic toxin → scarlet fever

* The DNA for the toxin is acquired by temperate bacteriophage.

* Non-lysogenized → pharyngitis without scarlet fever.

② G ve bacteria → mechanisms & exampels.

① heat labile + heat stable enterotoxins.

heat labile → inactivated by 65C for 30 min.
- A+B subunits ~ activate G_s
- ex → E.coli → Cholera → watery diarrhea

heat stable → not inactivated by boiling for 30 min.
- Acts on Guanylyl cyclase → ↑cGMP → ⊖ Na^+ reabsorption → diarrhea.
- ex → E.coli

(note) → Genes for heat labile + stable are on plasmid.

② shiga toxin.

E.coli O157:H7 → verotoxin → remove adenine from 28S rRNA → ⊖ protein synthesis → cell death → bloody diarrhea

(notes)
- acts like the toxin of shigella dysentry
- found in under cooked meat of hamburger
- encoded by temperat bacteriophage.

- cell death in kidney → renal failure
- endothelial cell death → microangiopathic hemolytic anemia.
- hemolytic-uremic syndrome → "HUS"

- ciprofloxacin → shiga toxin → predisposes HUS

③ enterotoxin of vibrio cholera, Bacillus cereus ≡ heat-Labile toxin of E.coli → watery dirrhea.

④ pertussis toxin

* Bor. pertussis → pertussis toxin → ADP-R of Gi → Gi inhibition → ⊕ Adenylyle cyclase → ↑cAMP → edema + changes in respiratory tract "whooping cough"
→ chemokine receptor transduction → lymphocytosis ⇐ not true ، لو جينا في الـ lymphocytes اللي تهيجت مستقرة في ال lymph tissue ال spleen, node

ختبقى في الدم . 😊

endotoxin

Lipopolysaccharides "LPS"
→ core polysaccharide
→ somatic "O" antigen: (3 or 4 or 5) repeated 25 times → antigenic variation
(salmonella have > 1500 antigenic type.
→ lipid A → toxic protein.

(note) → All endotoxins have the same symptoms "fever, shock", but differ in their severity.
→ endotoxin is less toxic than exotoxin.

how the LPS produce the symptoms of septic shock:

LPS
→ ⊕ macrophage → IL-1, TNf ⇒ "fever, hypotesion
  ↳ tumor necrosis factor
→ ⊕ complement
  → C_3a → hypotesion + edema
  → C_5a → nutrophil recruitment ⇒ (تجمع)
→ ⊕ tissue factor → ⊕ coagulation cascade → DIC

(notes) → other featurs of septic shock Tachycardia, Tachypnea, leukocytosis death of (30% → 50%) in IUC) → intensive care units.
→ septic shock can be caused by G tive⁺ via Teichoic acid

* culture in → toxic shock → -ve result
                → septic shock → +ve result

* 2 forms of septic shock are interesting.

① Blood culture of septic shock is +ve (bacteria in blood)
" " " toxic " " -ve (toxin only)

② in septic shock, bacteria killing by Antibiotics Leads to patient death.

* Biologic effects of endotoxin.

① fever [by IL-1, IL-6, TNF on temp-regulating center in hypothalamus)

② hypotension + shock due to nitric oxide, TNF, Bradykinin → ↑ vascular permeability.
↓ vasodilation

③ DIC due to ⊕ coagulation cascade → thrombosis, tissue ischemia ~ failure of vital organs
↳ ~ disseminated-intravascular coagulation ~ , petechial or purpuric rash

note ⇒ coagulation is activated by tissue factor

④ activation of complement alternative pathway → C_3a + C_5a → tissue damage + inflammation.

⑤ Activation of → macrophages → ↑ phagocytic ability
                → B-lymphocyte → ↑ Ab production.

1→5 ⇒ systemic inflammatory response syndrome ~ SIRS ~

fever, hypotension, Tachycardia, Tachypnea, leukocytosis.

* Damage to endothelium → leakage of plasma + RBCs → hypotension
                → site for platlet aggregation → DIC

(b) The evidence that the endotoxin caused the effects.

① purified LPS elicited the same effects

② antiserum against endotoxin blocked the effect.

(c) How to detect DIC ⇒ by assessing D-dimer (of fibrin)
. lab-based, bed site

* endotoxin causes the effect indirectly via IL-1, TNF

* TNF → small amount ⇒ beneficial
→ large amount ⇒ harmful ⇒ DIC, tumor necrosis

* IV fluid sterilization

▲ Autoclaving ⇒ kills all organisms but release endotoxin

* filtration → physical removal of bacteria without releasing endotoxin
→ used in urine agar filtration
→ for examination of H_2O

* G've bacteria (S. aureus, strepto. pyogenes) causes of some effects of endotoxin via lipoteichoic acid.

* septic shock treatment

① Antibodies against LPS, TNF release all sings of septic shock → [DIC]
② protein C / proteins → reversed DIC, but causes bleeding

* immunopathogenesis

- The immune system is the cause of disease not the organism
- e.x ⇒ rheumatic fever (Ab against M protein of strepto. pyogens that cross-reacts with
Joint, heart, Brain
↳ arthritis ↳ cardiitis ↳ chorea

Bacterial infections associated with cancers.

→ H. pylori
- helicobater pylori associated with gastric carcinoma + gastric mucosal-associated lymphoid tissue "MALT" lymphoma

* campylobacter jejuni associated with istestinal "MALT" lymphoid.

* how [redacted] to prove it? Antibiotics in early stages causes of the cancer to regress.

(notes) → h. pylori urease "urea → NH_3" causes ↑ PH to protect it form gastric acid.
↳ how to detect h. pylori → ① IgG ② IgM ③ stool Ag
④ urea breath test ⇒ نعطي radioactive urea لو في بكتيريا بتحللها لـ أمونيا بتطلع
اذا تنفس في container بنجمع الأمونيا وبتعطي radiation.

[redacted]

* viruses that cause cancers ⇒ epstein barr virus, human papilloma virus (HPV), HIV

* different strains of bacteria produce different disease. why? → They have differ virulence factors.

e.x ⇒ s. aureus → pyogenic disease (endocarditis, septic arthritis, osteomyelitis)
↳ non-pyogenic (scalded skin syndrome, toxic shock syndrome, food poisoning)

(notes) ⇒ The virulence factors are encoded on plasmids, transposons, pathogenicity island, lysogenic phages.
↳ different genes + transmission ⇒ different virulence factor → different diseases.

* typical stages of infection disease
① incubation period ⇒ from requisition of agent to symptoms.
② prodrome period ⇒ Non-spesific symptomes.
③ specific-illnes period ⇒ there is characteristic sings + symptoms of the disease occure.
④ recovery period ⇒ the paitents return ~~[illegible]~~ healthy.
- ↳ completely healthy
- ↳ chronic carrier → transmit the disease to others.
- ↳ latent infection → reactivation of organism (new signs)

* koch's postulates:

① The microorganism found in organism suffering from disease but not in healthy

② The microorganism must be isolate + grown in pure culture.
↳ not all organisms can be isolated.

③ The cultured microorganism should cause disease when introduced into the healthy organism
↳ depends to ID50 / immunity

④ The microorganism must be reisolated and be identical to the original causative agent