
MICROBIOLOGY
SAEF DAWWAS

Antibacterial drugs resistance

Pharmaceutical Microbiology

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* من سلبيات استخدام ال antibacterial انو الها advers effect ومرات انها بتدعم نمو ال infection

* اكثر مشكلة بتواجه انتاج ال antimicrobial هي حدث ال drug resistance

Introduction

تعتبر كارثة عالمية لانو اذا شخص مصاب ببكتيريا معينة وهاي بكتيريا عندها مقاومة للدوا وهاذ الدوا بفشل بأداء عملوا فبتأدي الي مصيبة وموت مرضى كثير

- The global increase in resistance to antimicrobial drugs, including the emergence of bacterial strains that are resistant to all available antibacterial agents, has created a public health problem of potentially crisis proportions.

- Most pathogenic microorganisms have the capability of developing resistance to at least some antimicrobial agents

- It is the emergence of multiple resistance, i.e. resistance to several types of antibiotic agent, that is causing major problems

بتصير مشكلة خطيرة كثير اذا البكتيريا بتقاوم اكثر من دوا

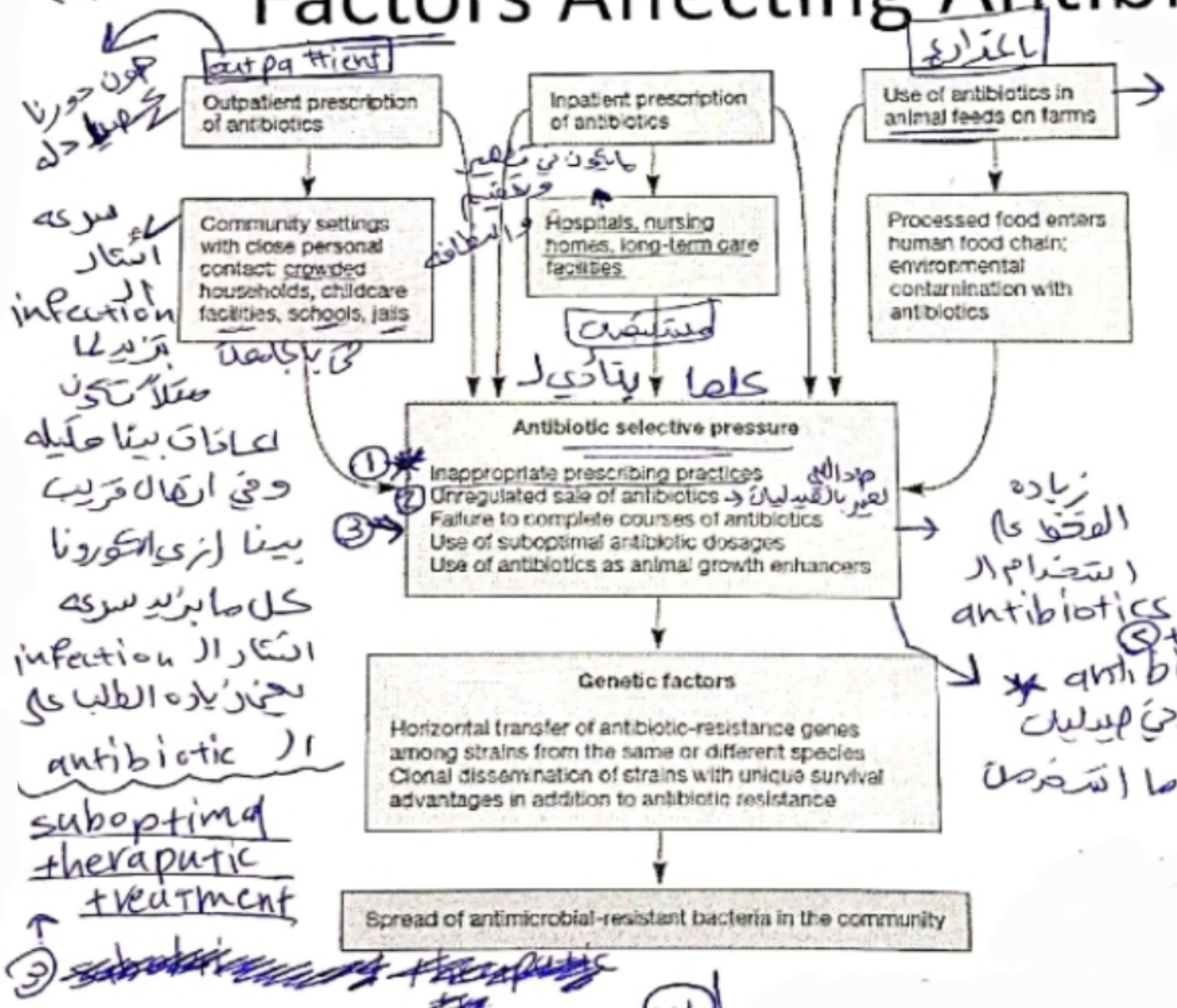
Drug resistance

- Resistance represents a **CHANGE from** susceptible phenotype to a less susceptible phenotype that leads to **THERAPEUTIC FAILURE of that agent.**

كلمة sesceptible انو قدرة الدوا على
انو يعمل inhibition لنمو البكتيريا

بس في حالة ال resistance قدرة الدوا
بتقل

Factors Affecting Antibiotic Resistance



Incomplete and indiscriminant use of antibiotics in people and animals leads to increased selective pressure on bacteria. Bacteria capable of resisting antibiotics survive and spread these traits

بأستخدام ال antibiotic في مسؤولية على
الصيدلاني والمريض (كل هاي الأمور بتأثر على مقاومة الدوا)
-> الصيدلاني لازم يشخص المريض صح ويعطيه
العلاج الصح ويعطي المريض ارشادات استخدام الدوا
-> المريض بتحمل مسؤولية انو مثلا حس بتحسن وما
كمل ال course كامل وكمان انو مثلا انو حالتوا
المادية ما بتسمحلوا انو يشتري ال cousre كامل

Usage of antibiotics

هاي الأخطاء في استخدام antimicrobial الي بتأدي لحدوث ال resistance

- Overuse and misuse of antibiotics by patients
- Misdiagnosis of infections and incorrect prescription
- Misuse of antibiotics in animals
- Lack of tools to monitor antibiotic resistance
- Lack of coordination between stakeholders.
- Patients should finish the prescribed course of antibiotics even when they already ‘feel better’
- Antibiotics should only be used when prescribed by a doctor and
- over-the-counter sales of antibiotics need to be closely monitored to prevent misuse
- People should not share antibiotics with others or use leftover prescriptions

كيف نعمل تفادي لحدوث resistance

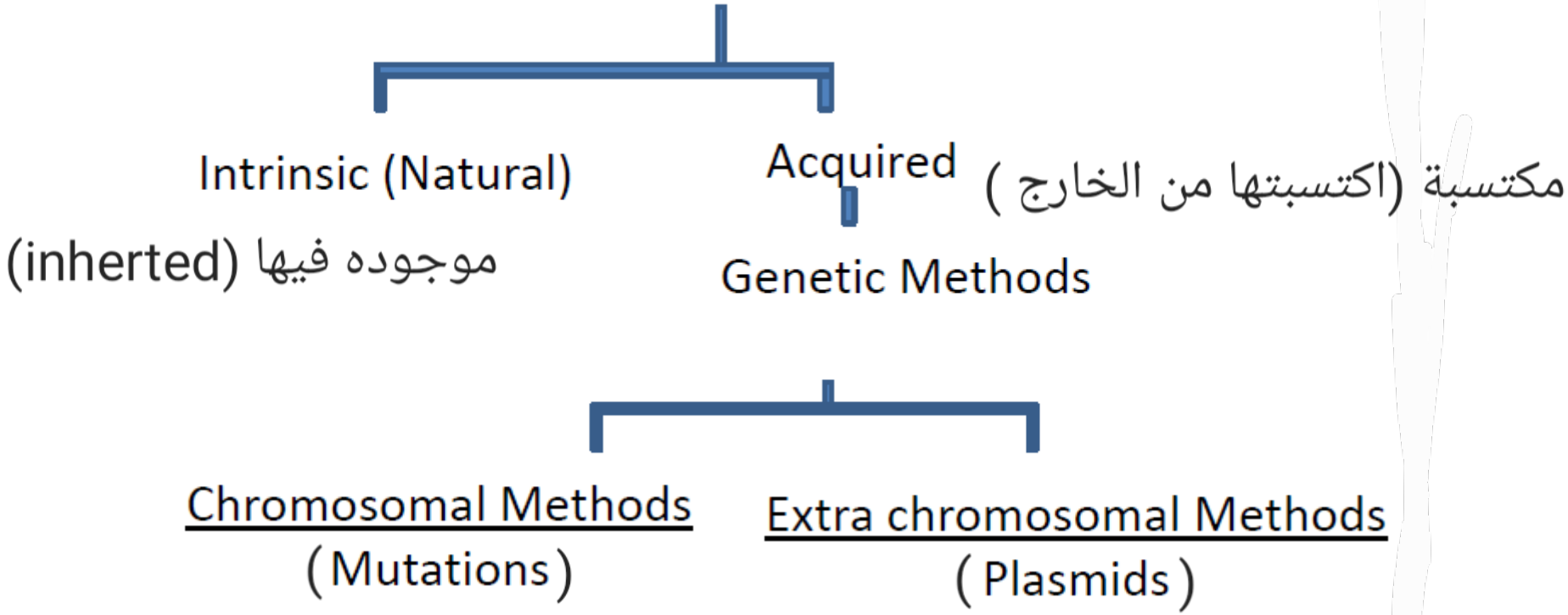
- Prevention includes:

- Reduce incidence of infection through effective hygiene and infection prevention and control .
- Appropriate Use of Antibiotics
- Use drugs combination
- Avoiding close contact with sick people
- better infection control in health care facilities
- immunisation programs استخدام اللقاحات
- tools to track resistance

ال stake holders بكونوا اشخاص
موجودين بأي مؤسسة صحية بعملو
control لأستخدام المضادات الحيوية

Antimicrobial resistance

البكتيريا كيف بتكسب مقومة للدوا



Antimicrobial resistance

- Antimicrobial resistance can be of two

1. Intrinsic or chromosomal (always expressed in the species),

It is the innate ability of a bacterium to resist a class of antibiotics.

بتكون خصائص موجودة اصلا بالبكتيريا بتخليها انها ما تتجاوب مع الدوا

- Having features such as permeability barriers, a lack of susceptibility of the cell wall, or ribosomal targets or enzymes production that make them inherently insusceptible

Antimicrobial resistance

بتكون هاي الخصائص مش موجودة
عندها اخذتها من البيئة المحيطة

2. Acquired resistance

A species may initially be susceptible to an antibiotic, but subsequently develop resistance. Such acquired resistance may be due to a genetic mutation within that organism, or may be derived from another organism by the acquisition of new genes.

- a. **Mutations**

Happened in structural or regulatory genes can confer resistance

بصير تغير بالكروموسوم تاع البكتيريا
بعطيها خاصية انها تقاوم الدوا

Antimicrobial resistance

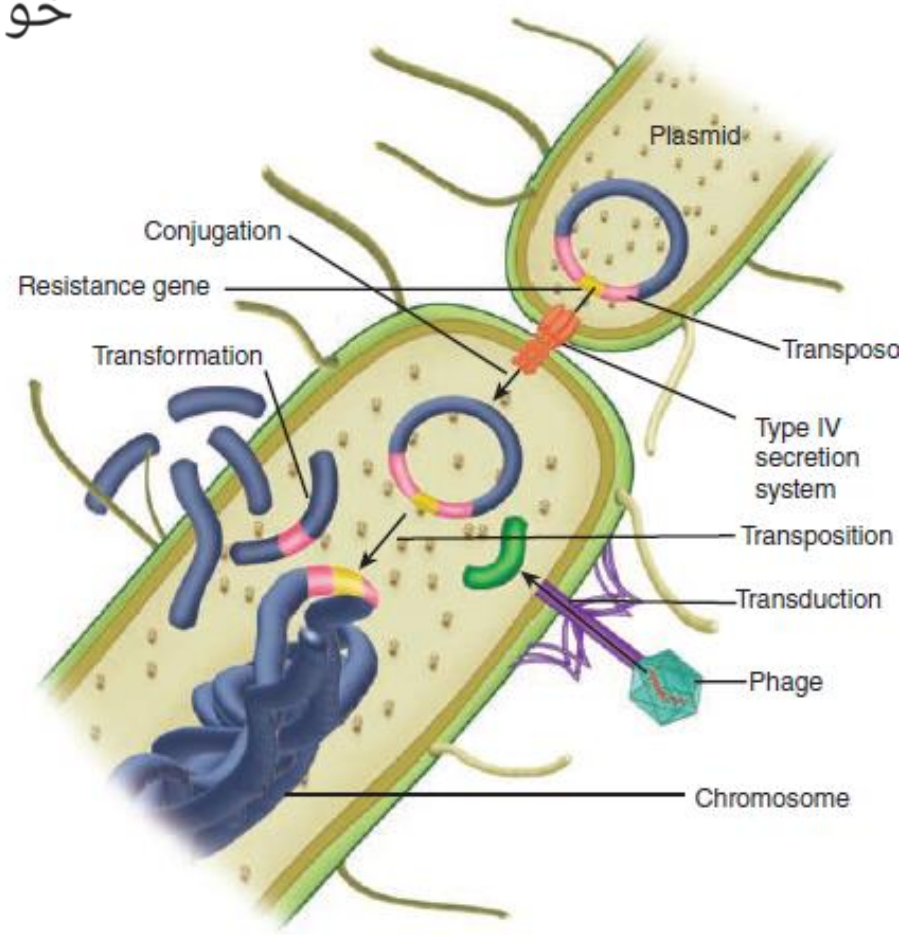
بصير في عنا تبادل لل dna بين البكتيريا بخليها عندها خواص لمقاومة الأدوية

b. Genetic Exchange

- four major mechanisms of genetic exchange among bacteria.

1. **transformation,**
2. **transduction,**
3. **conjugation,** <-- اكثر اشي بتصير بهاي الطريقة
4. **Transposition.**

- **Conjugation and transposition are the most important clinically and often work in tandem.**



* الرسمه عندي فيها two Bacteria plasmide

Extra chromosom carried circular carrier certain DNA

البلازميد بحتوي على جينات مختلفة في منها R-factor

الي هية مسؤولة عن مقاومة الدوا

فلما يندمجوا البكتيريا هاذ الجين بنتقل للبكتيريا الثانية فلما تتكاثر بتنتج كروموسومات مقاومة بتصير البكتيريا هاي تفرز انزيمات معينة بتعمل تحطيم لل antibiotic

ال transduction بتكون bacteriophage بتنتقل من بكتيريا لثانية وبتحقن الكروموسومات المقاومة جوا البكتيريا

ال transformation

pieces of chromosom

ممكن تكون موجوده بال environmem وممكن تنتقل وتدخل داخل البكتيريا وعاده هاي بتصير من ال Strain

ال transposition

chromosomal segment
بتكون موجودة بال DNa
او بالبلازميد واللي ممكن تكون trans located ممكن تنقل كلها
أو جزء منها بين البلازميد من بكتيريا لبكتيريا

Plasmid-Mediated Resistance

- **Resistance plasmids (resistance factors, R factors) are**

extrachromosomal, circular, double-stranded DNA molecules that carry the genes for a variety of enzymes that can degrade antibiotics and modify membrane transport systems.

- The transfer of plasmids by conjugation was the first discovered mechanism for the acquisition of new resistance genes, and it continues to be the most important.

Transfer of r-genes from one bacterium to another

- **Conjugation : Main mechanism for spread of resistance**

The conjugative plasmids make a connecting tube between the 2 bacteria through which plasmid itself can pass.

- **Transduction : Less common method**

The plasmid DNA enclosed in a **bacteriophage is** transferred to another bacterium of same species.

- **Transformation : least clinical problem.**
- Free DNA is picked up from the environment (i.e.. From a cell belonging to closely related or same strain

Transposons and Transposition

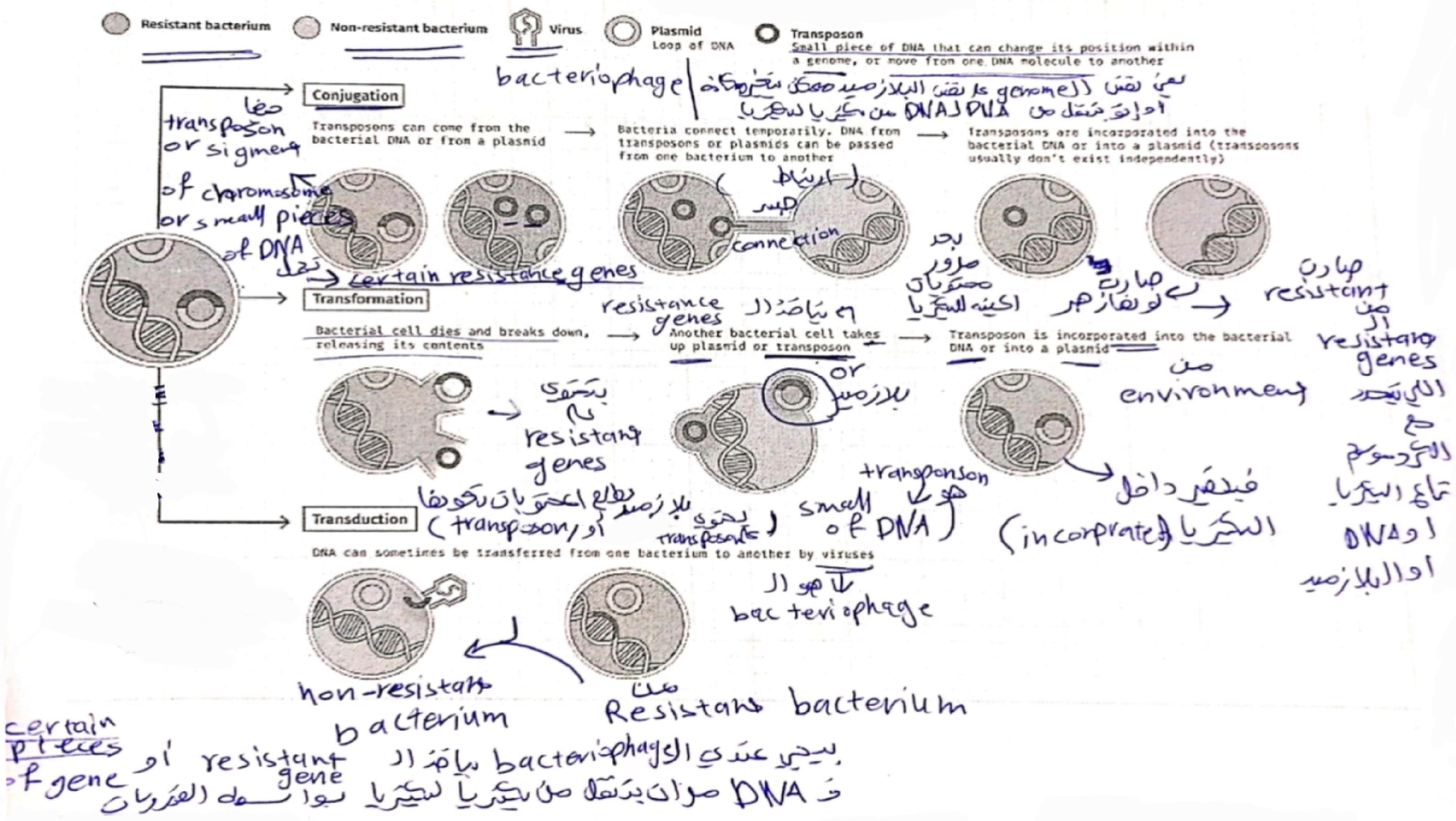
- Transposons containing resistance genes can move from plasmid to plasmid or between plasmid and chromosome.

- Most of the resistance genes carried on plasmids are transposon insertions that can be carried along with the rest of the plasmid genome to another strain by conjugation .
- Transposons are sequences of DNA that can move around different positions within the genome of single cell.

- The donor plasmid containing the Transposons, co-integrate with acceptor plasmid. They can replicate during co-integration

How antibiotic resistance spreads ?

EMBL



Plasmid-Mediated Resistance

Plasmid-mediated resistance is very important from a clinical point of view for three reasons:

(1) It occurs in many different species, especially gram negative rods.

(2) Plasmids frequently mediate resistance to multiple drugs.

(3) Plasmids have a high rate of transfer from one cell to another, usually by conjugation.

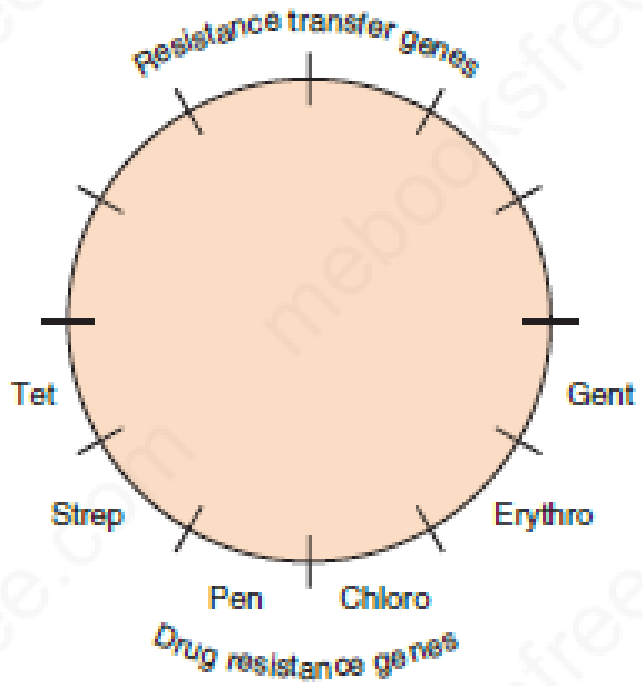


FIGURE 11–1 Resistance plasmid (R plasmid, R factor). Most resistance plasmids have two sets of genes: (1) resistance transfer genes that encode the sex pilus and other proteins that mediate transfer of the plasmid DNA during conjugation, and (2) drug resistance genes that encode the proteins that mediate drug resistance. The bottom half of the figure depicts (from left to right) the genes that encode resistance to tetracycline, streptomycin, penicillin (β-lactamase), chloramphenicol, erythromycin, and gentamicin.

https://www.youtube.com/watch?v=n7Z5-mRB_gI

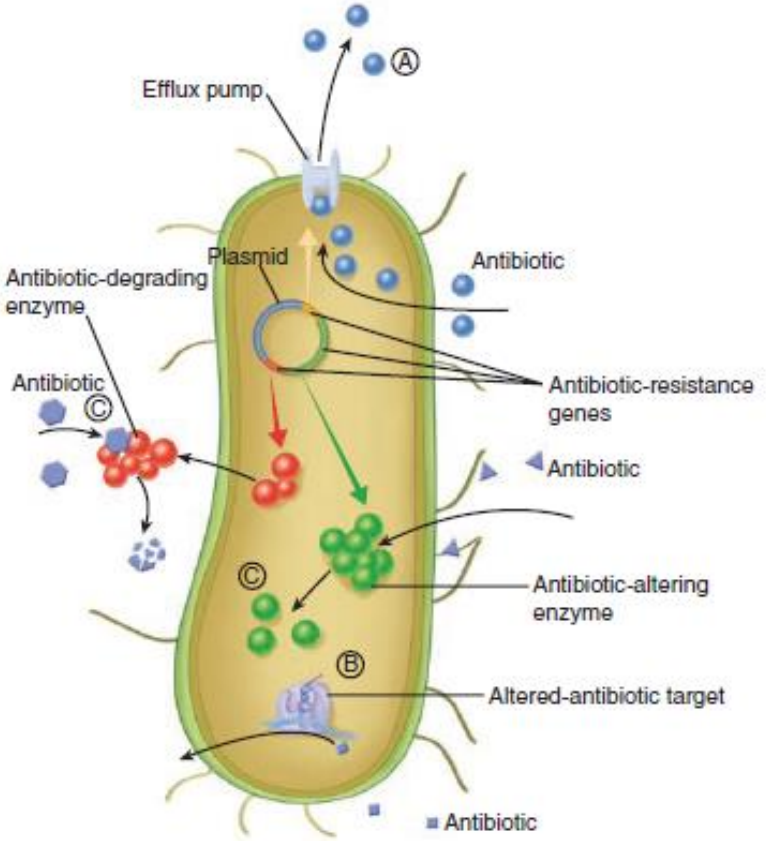
Mechanisms of resistance

البكتيريا بعد اكتسابها للجين كيف بتبلش تقاوم الدوا

- Resistance to antimicrobial agents typically occurs by one or more of the following mechanisms:

1. Inactivation of the drug — انو بعمل تغيير بالمكان الي لازم يتواجد الدوا فيع فبمنع ارتباط الدوا <<< ----------
2. Alteration of the target
3. Reduced cellular uptake <--- من خلال porin protien
4. Increased efflux < --- من خلال اخراج الدوا خارج الخلية (بمنع تواجدوا داخلها)

Mechanisms of resistance



Antimicrobial resistance mechanisms. هاذ الي بطلع الدوا

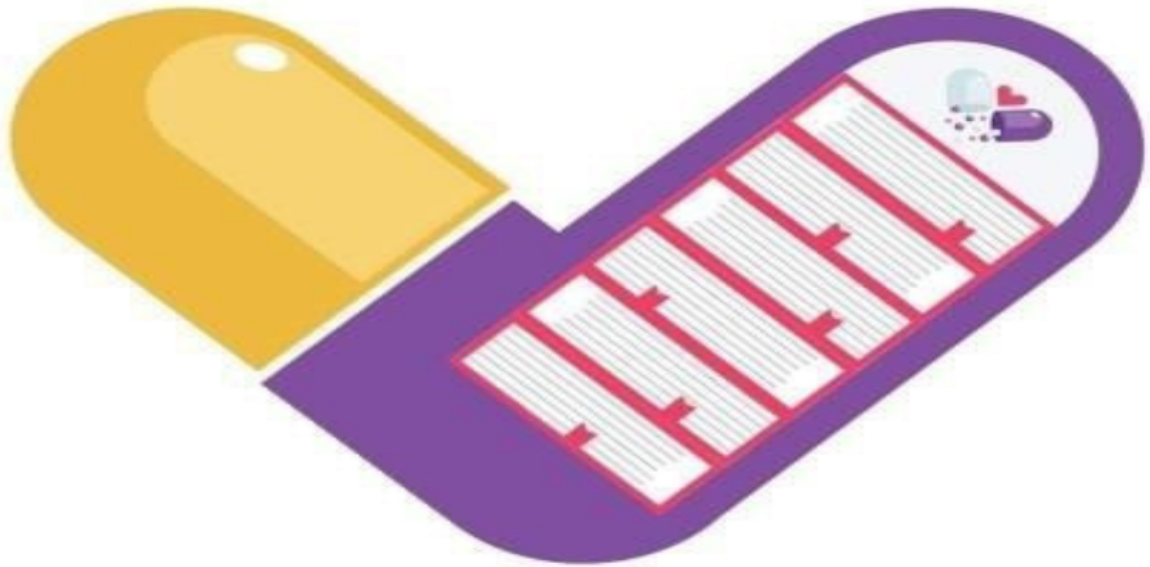
A. Exclusion barrier. <– برا الخلية
B. Altered target.
C. Enzymatic inactivation.
افراز انزيمات معينة بتحطم الدوا

Mechanisms and examples of Drug Resistance

Mechanism	Important Example	Drugs Commonly Affected
Inactivate drug	Cleavage by β-lactamase	β-Lactam drugs such as penicillins, cephalosporins
Modify drug target in bacteria	1. Mutation in penicillin-binding proteins	Penicillins
	2. Mutation in protein in 30S ribosomal subunit	Aminoglycosides, such as streptomycin
	3. Replace alanine with lactate in peptidoglycan	Vancomycin
	4. Mutation in DNA gyrase	Quinolones
	5. Mutation in RNA polymerase	Rifampin
	6. Mutation in catalase-peroxidase	Isoniazid
Reduce permeability of drug	Mutation in porin proteins	Penicillins, aminoglycosides, and others
Export of drug from bacteria	Multidrug-resistance pump	Tetracyclines, sulfonamides, quinolones

آخر سلايد بالمحاضرة

بالتوفيق



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