

Antibióticos

1. Histórico
2. Mecanismos de ação
3. Mecanismos de Resistência

Antibiotics

What are antibiotics?
Who are the main producers?
Biological functions?
Resistance
New developments

First antimicrobial drugs

Louis Pasteur (1822-1895):

“pasteurization”

Fermentation: wine
contamination

Germ theory: silkworm disease

Vaccine: anthrax, fowl cholera

Rabies

First antimicrobial drugs

Paul Ehrlich (1854-1915):

- Methylene blue: malaria

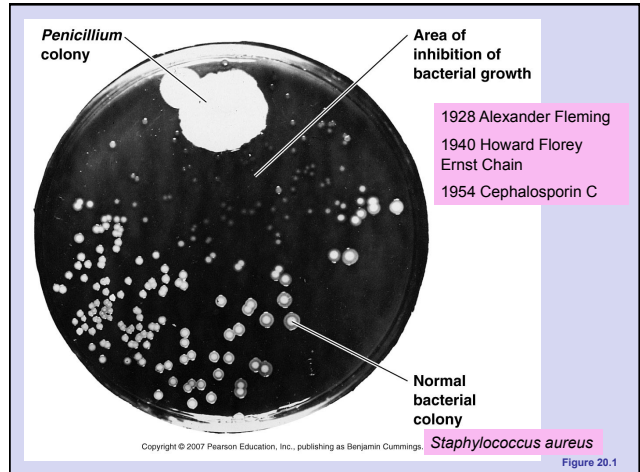
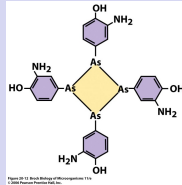
-Toxin and antitoxin

-Salvarsan: magic bullet
against syphilis, *Treponema
pallidum*

First antimicrobial drugs

- Gerhard Domagk (Nobel Prize 1939)

- Sulfa drugs
- Prontosil
- Sulfanilamide, analog of p-aminobenzoic acid (part of folic acid, precursor of nucleic acids)
- Development of antituberculosis compounds thiosemicarbasone and isoniazid

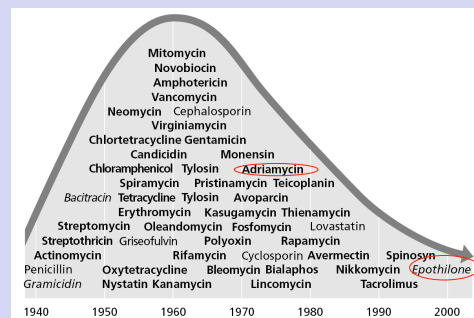


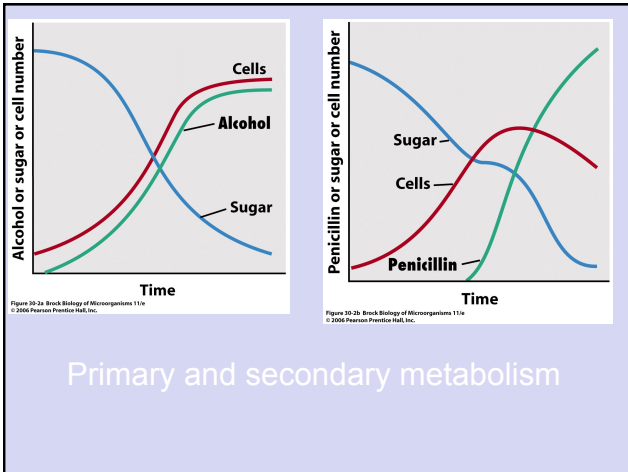
Salman Waksman, Albert Schatz

1943. Actinomycin

Streptomycin

Diminishing returns in finding natural products: Genetics to the rescue?



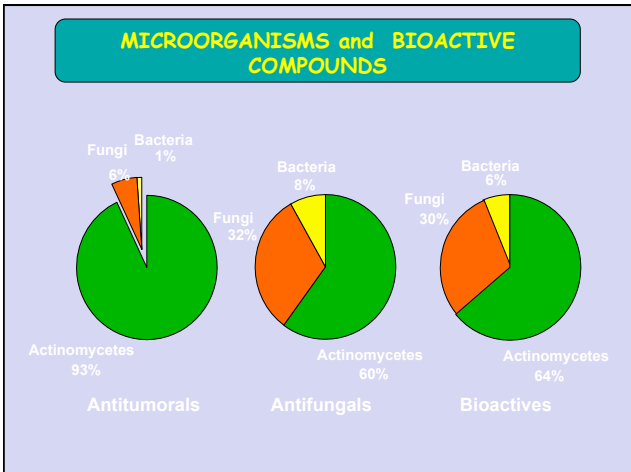


What are antibiotics?

- Secondary metabolites synthesized by some microorganisms
- Any compound able to cause a damaged in a target cell

Who are the main producers

- Bacteria
Gram positive *Streptomyces*
- Fungi
- Other bacteria



BIOACTIVE COMPOUNDS SYNTHESIZED BY ACTINOMYCETES

ANTIBACTERIALS	ANTIFUNGALS	ANTIPARASITICS
Erythromycin Tetracycline Gentamicin	Amphotericin B Nystatin	Avermectins
ANTITUMORALS	IMUNOSUPPRESSANTS	
Doxorubicin Mitramycin Bleomycin	Rapamycin FK506	
INSECTICIDES	HERBICIDES	
Espinosin	Bialaphos	

LIFE CYCLE OF *Streptomyces*

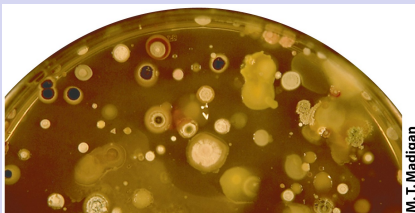
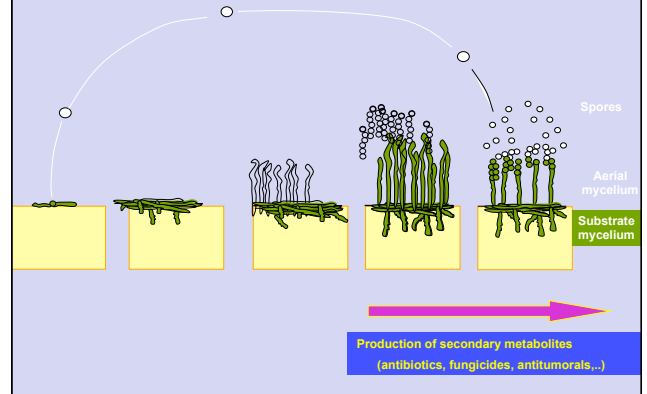


Figure 12-76a. Brock Biology of Microorganisms 11e
© 2008 Pearson Prentice Hall, Inc.

M. T. Macdigan



Figure 12-76b. Brock Biology of Microorganisms 11e
© 2008 Pearson Prentice Hall, Inc.

David A. Hopwood

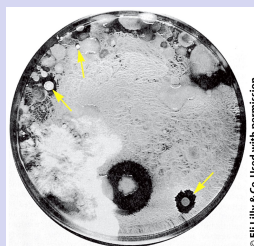


Figure 12-77a. Brock Biology of Microorganisms 11e
© 2008 Pearson Prentice Hall, Inc.

© BIL Lilly & Co. Used with permission.

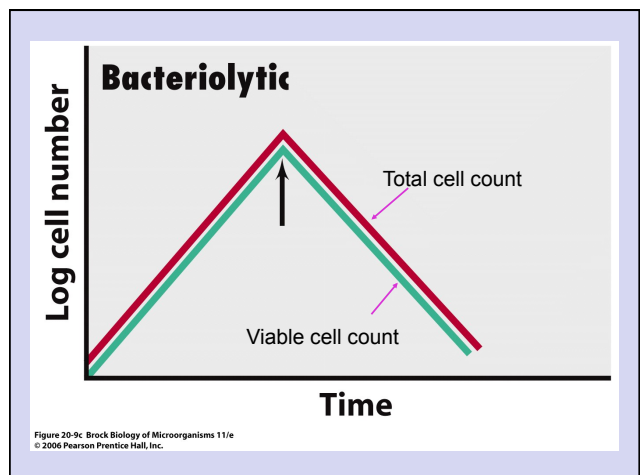
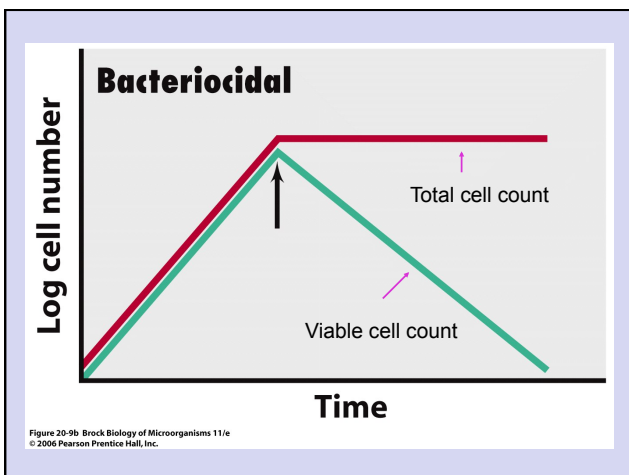
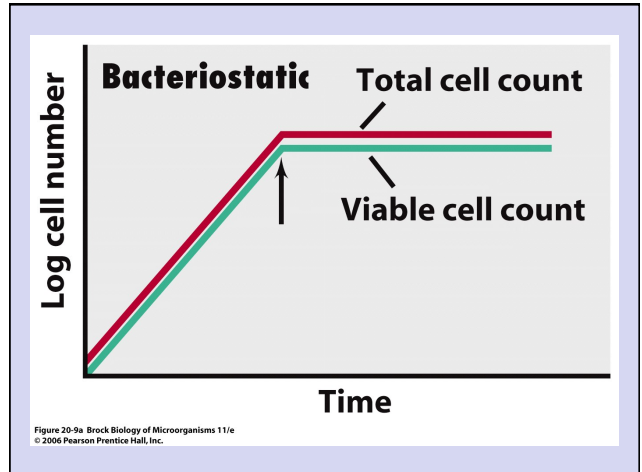


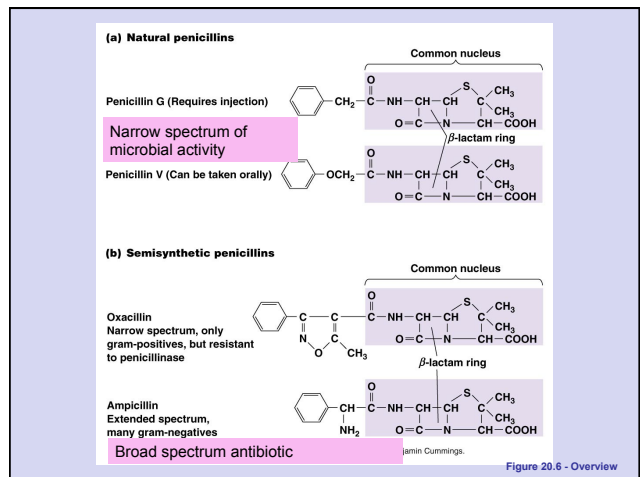
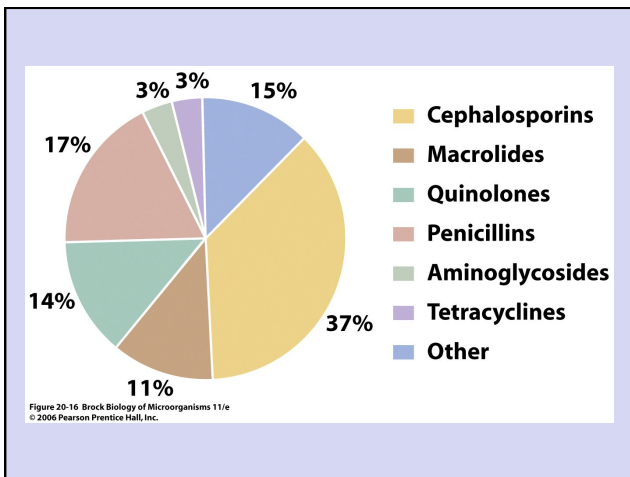
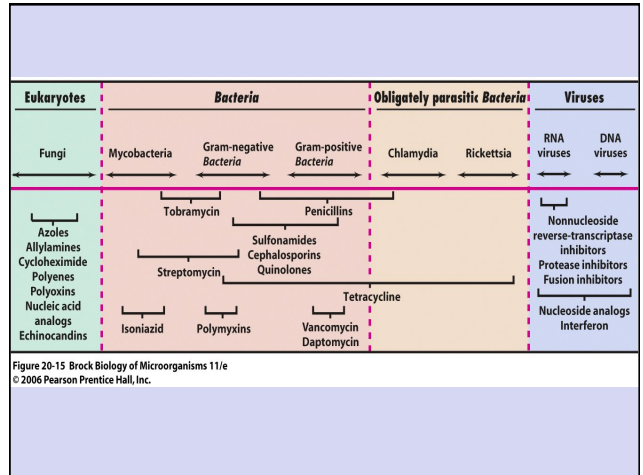
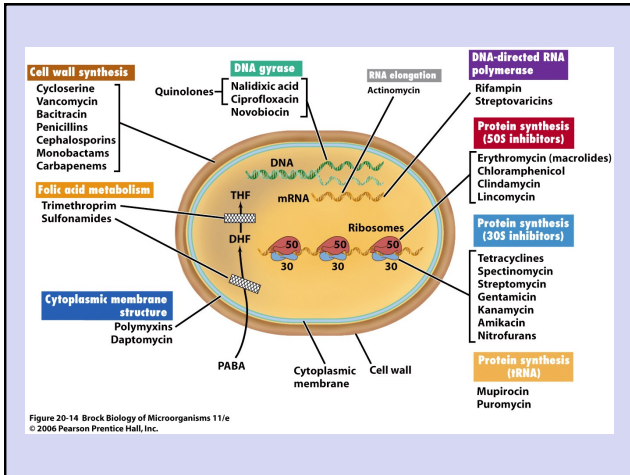
Figure 12-77b. Brock Biology of Microorganisms 11e
© 2008 Pearson Prentice Hall, Inc.

David A. Hopwood

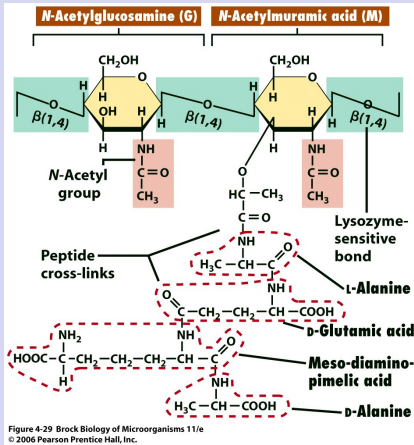
Biological functions of antibiotics?

- In the producer:
Activators of morphological differentiation, UV protector, communication
- In the target microorganism:
Toxicity

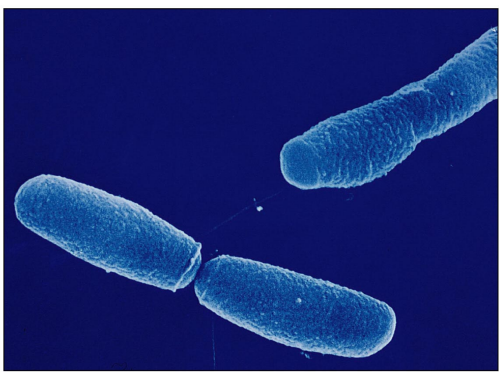
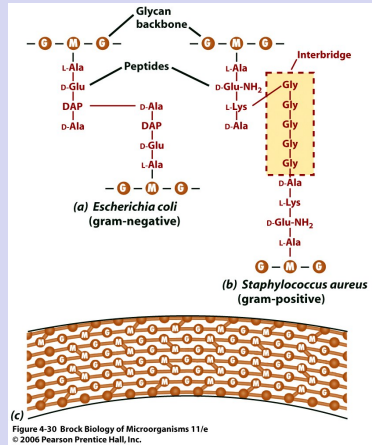




Structure of peptidoglycan glycan tetrapeptide



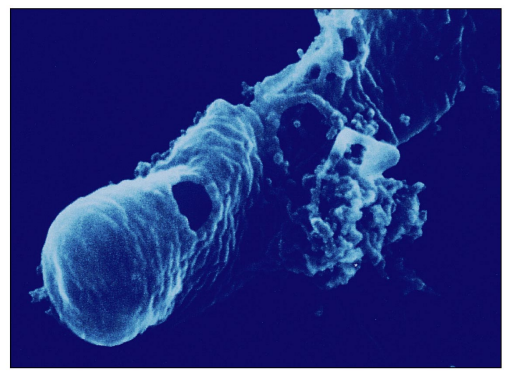
Peptidoglycan sheet in Escherichia coli and Staphylococcus aureus



(a) Rod-shaped bacterium before penicillin. SEM 1 μ m

Copyright © 2007 Pearson Education, Inc., publishing as Benjamin Cummings.

Figure 20.3a



(b) The bacterial cell is lysing as penicillin weakens the cell wall. SEM 1 μ m

Copyright © 2007 Pearson Education, Inc., publishing as Benjamin Cummings.

Figure 20.3b

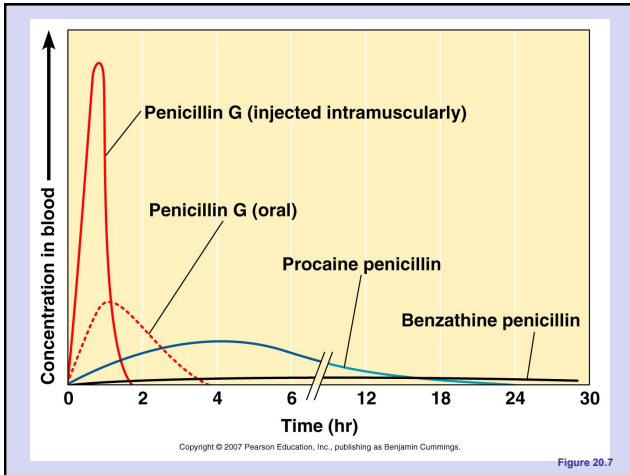


Figure 20.7

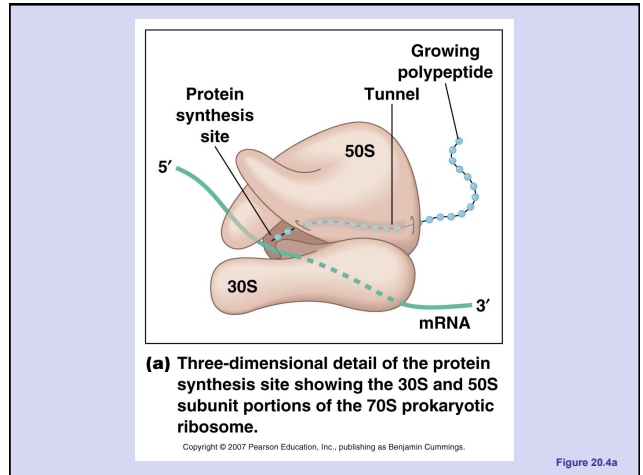


Figure 20.4a

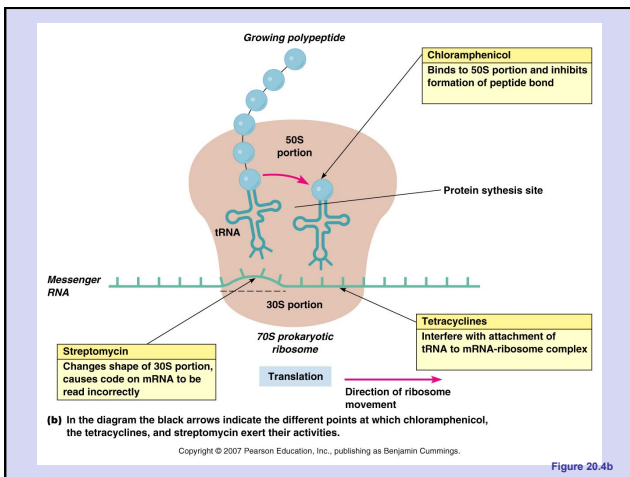


Figure 20.4b

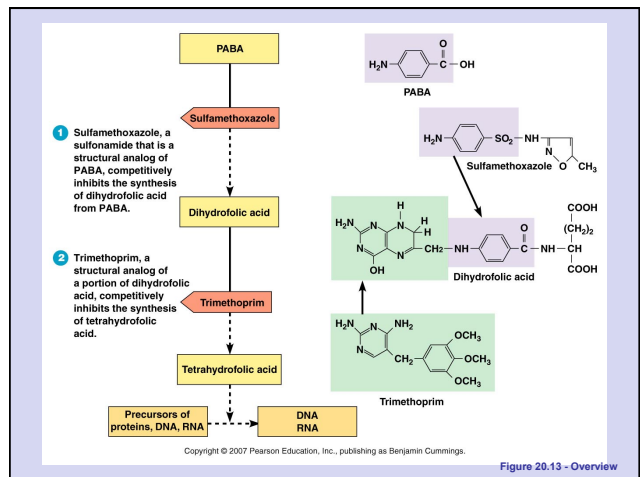
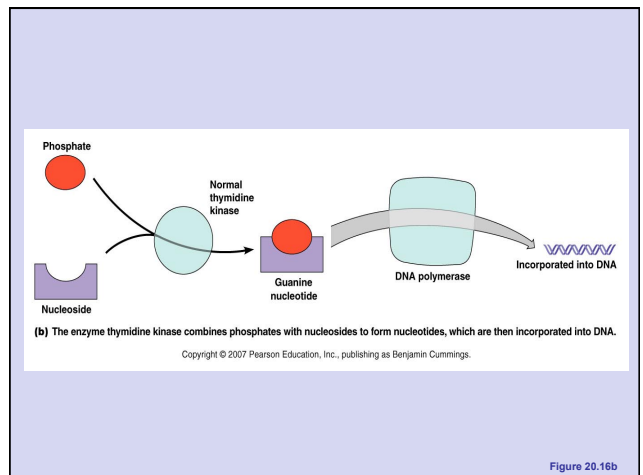
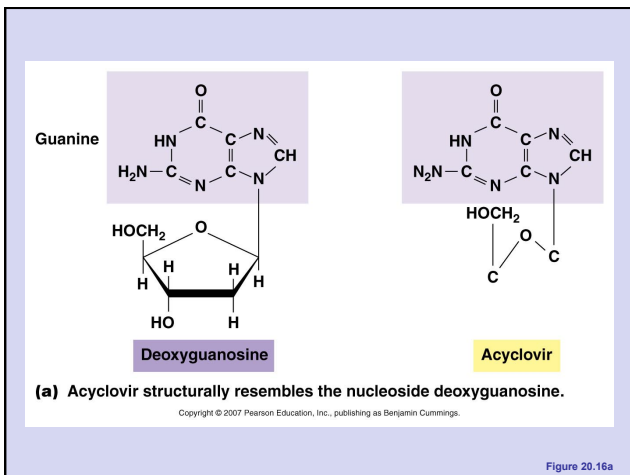
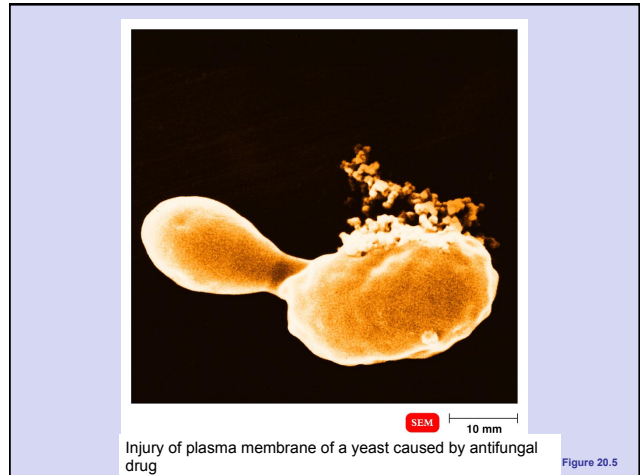
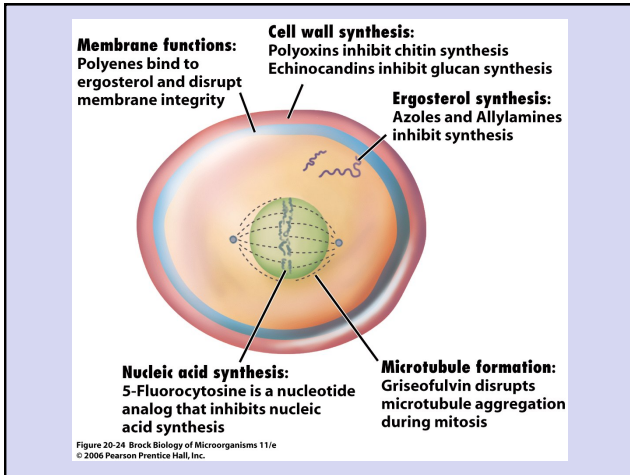


Figure 20.13 - Overview



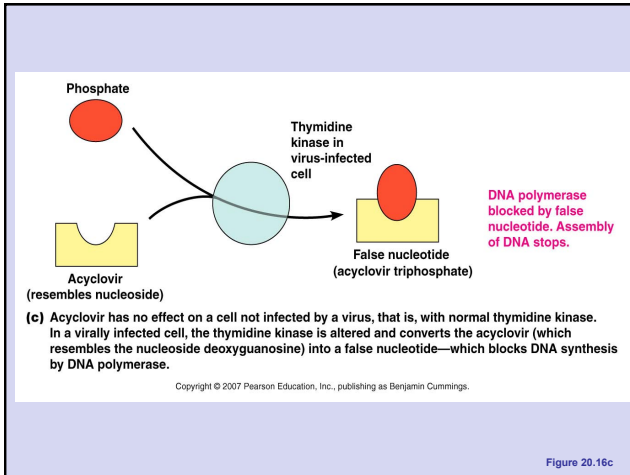


Figure 20.16c

DEFINICIÓN

Prueba in vitro que determina la sensibilidad de un microorganismo frente a diferentes antibióticos.

SENSIBLE RESISTENTE

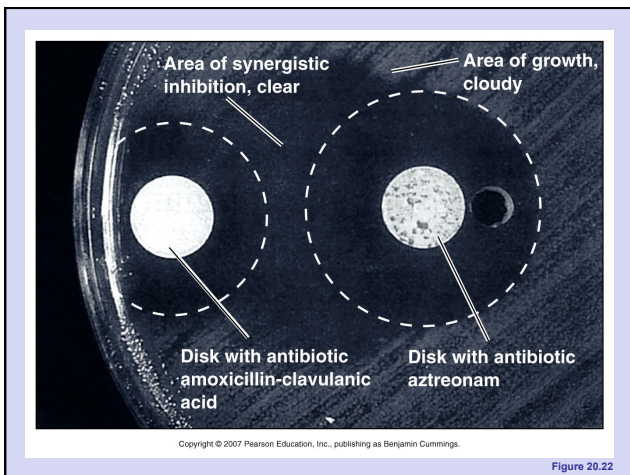
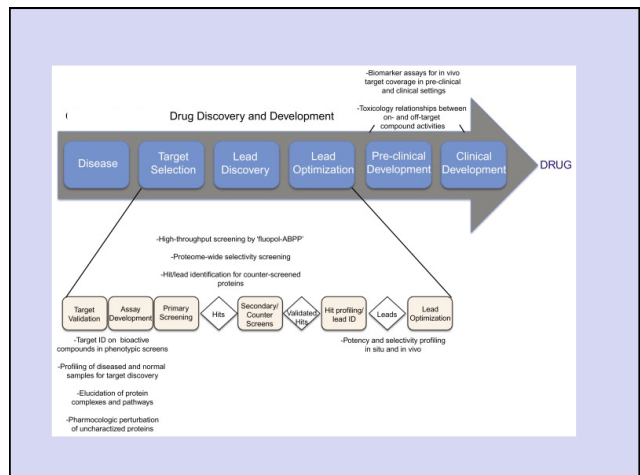


Figure 20.22



Antibiotic classification	Subclassification	Example	Representative structure
I. Carbohydrate-containing compounds	Pure sugars Aminoglycosides Orthosomycins N-Glycosides C-Glycosides Glycolipids	Nojirimycin Streptomycin Evernimycin Streptothricin Vancomycin Moenomycin	
II. Macrocyclic lactones	Macrolide antibiotics Polyene antibiotics Ansamycins Macrotetrolides	Erythromycin Candicidin Rifampin Tetranactin	
III. Quinones and related compounds	Tetracyclines Anthracyclines Naphthoquinones Benzoquinones	Tetracycline Adriamycin Actinorhodin Mitomycin	

Figure 20-13 part 1 Brock Biology of Microorganisms 11/e
© 2006 Pearson Prentice Hall, Inc.

Antibiotic classification	Subclassification	Example	Representative structure
IV. Amino acid and peptide analogs	Amino acid derivatives β-Lactam antibiotics Peptide antibiotics Chromopeptides Depsideptides Chelate-forming peptides	Cycloserine Penicillin, ceftriaxone Bacitracin Actinomycin Valinomycin Bleomycin	
V. Heterocyclic compounds containing nitrogen	Nucleoside antibiotics	Polyoxins	
VI. Heterocyclic compounds containing oxygen	Polyether antibiotics	Monensin	

Figure 20-13 part 2 Brock Biology of Microorganisms 11/e
© 2006 Pearson Prentice Hall, Inc.

Antibiotic classification	Subclassification	Example	Representative structure
VII. Alicyclic derivatives	Cycloalkane derivatives Steroid antibiotics	Cycloheximide Fusidic acid	
VIII. Aromatic compounds	Benzene derivatives Condensed aromatics Aromatic ether	Chloramphenicol Griseofulvin Novobiocin	
IX. Aliphatic compounds	Compounds containing phosphorus	Fosfomicin	

Figure 20-13 part 3 Brock Biology of Microorganisms 11/e
© 2006 Pearson Prentice Hall, Inc.

Antibiotic classification	Subclassification	Example	Representative structure
X. Quinolone compounds	4-Quinolone Fluoro-4-quinolones	Nalidixic acid Ciprofloxacin	
XI. Oxazolidinone	Cyclic lactone	2-Oxazolidinone	

Figure 20-13 part 4 Brock Biology of Microorganisms 11/e
© 2006 Pearson Prentice Hall, Inc.