

# The Evolution of Antibiotic Resistance

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# Evolution of Modern Medicines

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- Sumerians
- Babylonians
- Ancient Greeks
- Ancient Egyptians
- Incas

# Evolution of Modern Antibiotics

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- Pasteur
- Fleming and Penicillin
- Sulfonamides
- Streptomycin, Tetracycline, Chloramphenicol
- Fluoroquinolones
- Vancomycin

# Major Classes of Antibiotics

- Beta-lactams
  - First class of antibiotics discovered
  - Ex. Penicillins, Cephalosporins
- Macrolides
  - Prescribed for patients allergic to penicillin
  - Ex. Erythromycin
- Quinolones
  - Stronger class of antibiotics used to treat broader ranges of bacteria
  - Ex. Cipro®, Levaquin®

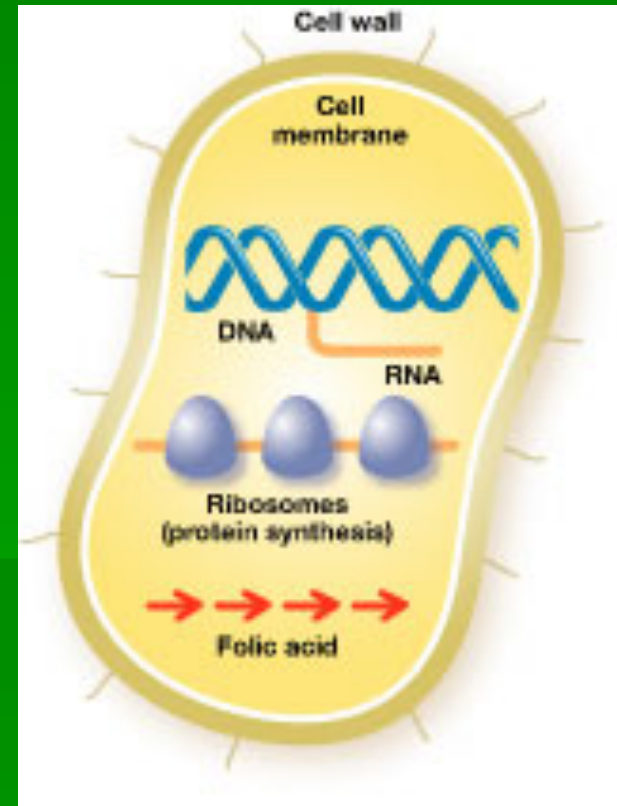


# Most Commonly Prescribed Antibiotics

<u>Antibiotic</u>	<u>Introduction</u>	<u>Resistance</u>
Penicillin	1943	1946
Sulfonamides	1930's	1940's
Cephalosporins	1964	Late 1960's
Tetracycline	1948	1953
Erythromycin	1952	1988
Vancomycin	1956	1988

# How Antibiotics Function

- Inhibit cell growth/  
protein production
- Inhibit DNA  
replication
- Interfere with  
formation of  
bacterial cell walls



[http://www.wellcome.ac.uk/  
doc\\_WTX026109.html](http://www.wellcome.ac.uk/doc_WTX026109.html)

# Bacteria

- Prokaryotes
- One-celled
- Smaller, less complex genomes
- Plasmids
- Reproduce asexually
- Different shapes



[http://fig.cox.miami.edu/~cmallery/150/proceuc/c27x3proc\\_shapes.jpg](http://fig.cox.miami.edu/~cmallery/150/proceuc/c27x3proc_shapes.jpg)

# Bacterial Strains that Demonstrate Antibiotic Resistance

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- *Streptococcus pneumoniae*
  - Meningitis
  - Middle ear infections
  - Pneumonia
  - Sinus infections
- *Escherichia coli*
  - Urinary tract infections
  - Diarrhea
  - Kidney problems

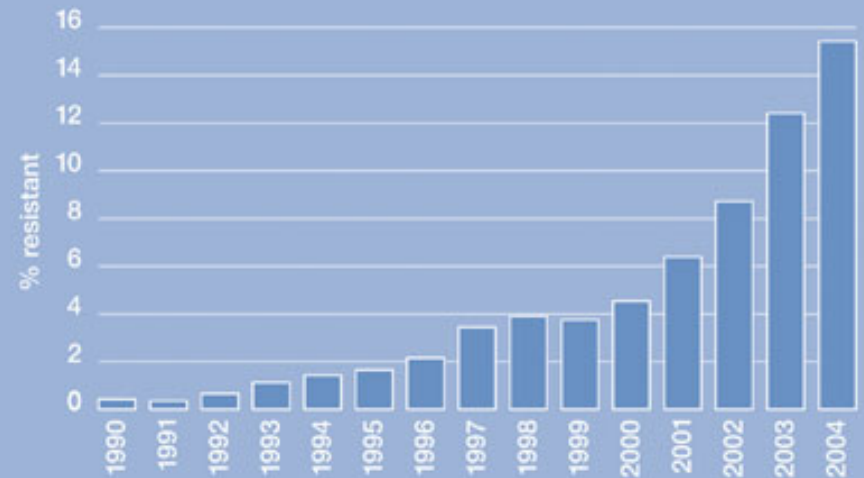
- *Salmonella typhimurium*
  - Food poisoning
- *Mycobacterium tuberculosis*
  - Tuberculosis
- *Haemophilus influenzae*
  - Blood poisoning
- *Staphylococcus aureus*
  - Pneumonia
  - Ear infections
  - Meningitis

# Antibiotic Resistance

- Early Penicillin resistance
- Increasingly widespread resistance having disastrous effects
- Recent increase in infectious disease deaths
- Antibiotic resistance major problem for hospitals
- VRE and other superbugs

## Ciprofloxacin resistance in *E. coli*

*E. coli* infections of the blood and cerebrospinal fluid have become increasingly resistant to the quinolone ciprofloxacin.



[http://www.wellcome.ac.uk/doc\\_WTX026098.html](http://www.wellcome.ac.uk/doc_WTX026098.html)

# Causes of Antibiotic Resistance

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- Over use/wrongly prescribed
- Improper use
- Agricultural/animal use
- Widespread use of antimicrobial agents

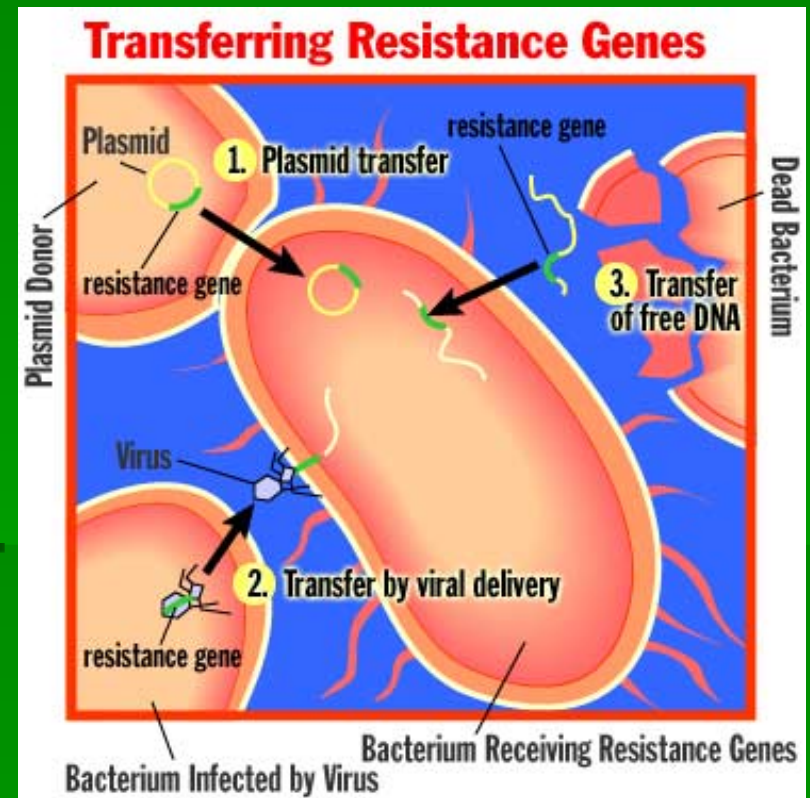
# Genetic Basis for Resistance

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- Resistance genes
  - Normal features of bacterial genome
  - Occurred before discovery of antibiotics
- Adaptations
  - Natural Selection
  - Fast reproduction rates
- Spontaneous mutations
  - Point mutations
  - Very rare
- Transposons
  - Mobile elements of the chromosome
  - Basis for rapid bacterial evolution

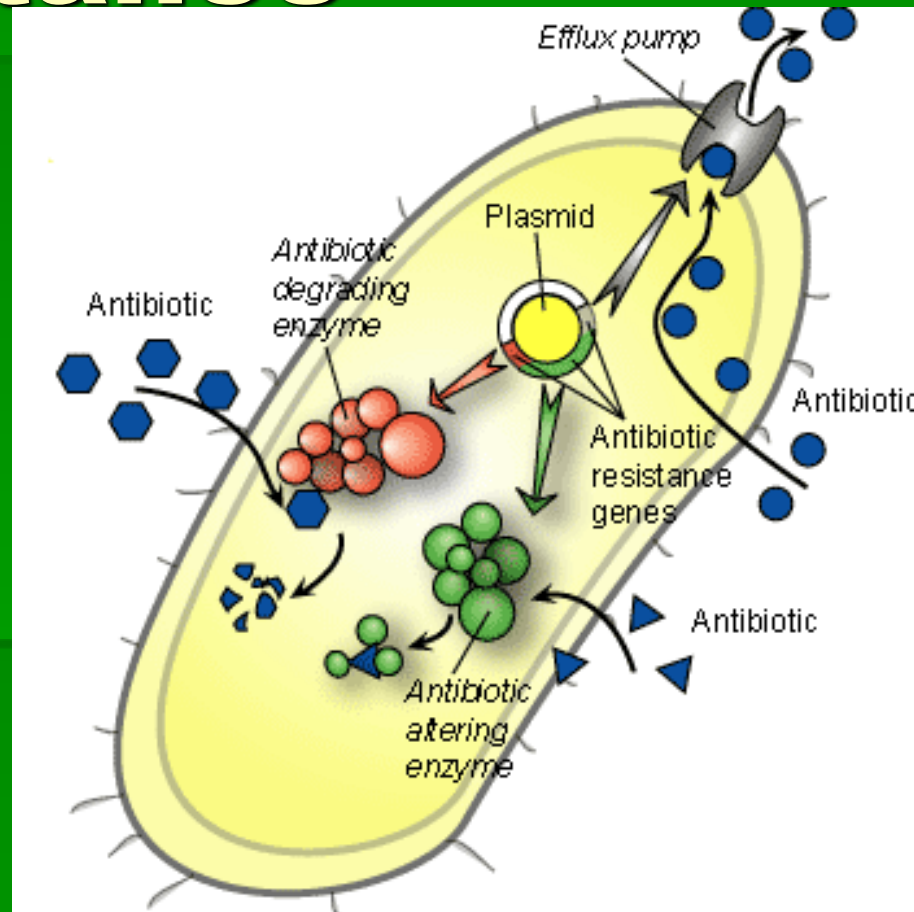
# Bacterial Gene Transfer

- Plasmid Transfer
- Incorporation of fragments from dead bacteria cells
- Viral Transfer



[http://whyfiles.org/shorties/090antibio\\_resist/](http://whyfiles.org/shorties/090antibio_resist/)

# Mechanisms of Resistance



[http://www.bioteach.ubc.ca/  
Biodiversity/  
AttackOfTheSuperbugs/](http://www.bioteach.ubc.ca/Biodiversity/AttackOfTheSuperbugs/)

# Decreased Transport of Antibiotic into Cell Wall

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- First antibiotics designed to interfere with cell wall production
  - Bacteria quickly developed resistance mechanisms
  - Newer antibiotics developed that have targets within the cell
- Eliminate entry ports in cell membrane
  - Changing composition of cell wall
  - Thickening of cell wall

# Antibiotic Destroying Enzymes

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- Bind directly to antibiotics in the cells
- Destroy most functionally active parts of antibiotics
  - Hydrolysis of active portion
  - Binds irreversibly to antibiotic active site
- Ex. lactamase enzyme
  - Attacks and breaks open ring structure of penicillin

# Antibiotics Pumps

- Some antibiotics must accumulate in cell to be effective
- Pump expels drug before it reaches its target
- Antibiotic is expelled faster than it can diffuse into the cell

# Modification of Antibiotic Binding Site

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- Antibiotic becomes useless because it has no site for attack
- Change target
  - Ribosomal protection proteins
- Prevent binding
- Continued function even after binding of antibiotic
  - Ex. Ribosomal mutations

# Alternate Molecules

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- Used against antibiotics that function by disrupting the production of cell products
  - Produce alternate molecules as replacement
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# What Can be Done?

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- Prescribe only when necessary
  - Use common antibiotics first
  - Use most specific antibiotics for a particular infection
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- Isolate patients with contagious superbugs
  - Careful following of instructions and warnings

- Infection control
- Vaccinations
- Limit agricultural usage
- Removal of common antimicrobial agents from household cleaners
- New antibiotics with different bacteria-killing mechanisms