Plasmids:

These are extrachromosomal DNA molecules. They are capable of autonomous replication and carrying genetic information for several characters e.g. resistance to drugs, toxin, production, and enzyme synthesis….etc. They are transmissible to other bacterial cells.

**Bacterial physiology, Metabolism and Nutrition**

The energy required to carry out the many metabolic activities may be supplied to the cell in basically two different forms:

1- **Phototrophs**:  
Take energy in the form of radiation from the sun and converts it to chemical energy. All phototrophic bacteria is of no medical importance.

2- **Chemotrophs**:
Take energy from chemical compounds (organic & inorganic molecules). All bacteria of medical importance are chemotrophs. Microorganisms can be separated into two types based on their main source of carbon:-
a- Autotrophs:
If the carbon source is simple inorganic substances (e.g. CO2). They are free living – non parasitic of no direct medical importance. The energy needed for their metabolism is obtained from light.

b- Heterotrophs:
If the carbon source is obtained from more complex organic forms. They live in or on animal body and are called parasitic bacteria (most bacteria of medical importance). They obtain food from plant or animal sources.

Gaseous Requirements:

Oxygen & carbon dioxide influence growth of the organism. As regard O2, bacteria may be classified into four types:

a) **Obligate aerobes**: These organisms grow only in presence of free O2. e.g. T.B.

b) **Obligate anaerobes**: These organisms cannot grow in presence of oxygen e.g. Clostridium group.

c) **Facultative anaerobes**: These organisms can grow either in presence or in absence of oxygen e.g. Staphylococci, E. coli, etc.

d) **Microaerophiles**: These organisms can grow in low oxygen concentration killed by higher concentrations e.g. Vibrio.

AS regards CO2:

It is necessary in small amounts, i.e. the amount normally present in air is quite sufficient. However in a few cases, more CO2 is required, e.g. Brucella abortus needs 20% CO2 and N. gonorrhoae needs 5% CO2.
Physical Requirements Of Bacteria:

a-Temperature:

Multiplication of most bacterial pathogens takes place within a given temperature range (18 – 42C), outside of which no growth occurs. Optimum temperature is that at which growth of the organism is most rapid (maximum activity) & and usually 37C. Low temperature is less destructive than higher ones.

b-Hydrogen ion concentration (pH):

The optimum pH for most pathogenic bacteria is around 7.4 – 7.6. A few types of bacteria such as Lactobacilli can grow well at acid pH (3 – 4) While others such as Vibrio cholera can grow well at high alkaline pH (8.5 – 9).

Bacterial Growth Curve

When Bacteria are inoculated (cultured) into a liquid medium, samples of the culture are taken at regular intervals (starting from the time of initial inoculation), and the number of viable bacterial cells in these samples are blotted against time, typical growth curve will be obtained. The curve may be discussed in terms of 4 phases.

1. Lag Phase:

• It is the stage of preparation for multiplication of the bacterial inoculum, during which the organism adapt itself by synthesis of new enzymes specific for the new medium.

• There is no increase in number of bacteria but slight decrease due to death of some inoculated bacteria.
• The length of this phase depends upon the nature of the organism, i.e. E.coli has a short lag phase, while T.B. has a long lag phase.

• Clinically corresponds to incubation period of the disease.

2. Logarithmic Phase:
• Rapid cell division (the most active phase).
• The numbers of bacterial cells increase steadily by time.
• Clinically corresponds to signs & symptoms of the disease.

3. Stationary Phase:
• Total bacterial count (dead & living) rises slowly.
• Any bacterial multiplication is balanced by an increased death rate and the number of living organisms (viable) remains constant.
• Clinically corresponds to signs & symptoms of the disease.

4. Decline Phase:
• The number of living organisms decreases until all are dead and the culture becomes sterile.
• Clinically corresponds to recovery & convalescence stage of the disease.
Bacterial Growth Curve
**BACTERIAL VIRUSES**

(BACTERIOPHAGE)

Bacteriophage (or phage) is a virus that parasitizes bacteria, i.e., the bacterial cell serves as a host for the virus.

**MORPHOLOGY OF BACTERIOPHAGE**

*In most cases, the bacteriophage consists of:*

1. A head: containing the nucleic acid core (usually DNA, rarely RNA) surrounded by a protein coat (capsid).

2. A tail: consists of a hollow core surrounded by a contractile sheath which ends in a base plate to which are attached tail fibers.

**REPLICATION OF BACTERIOPHAGE:**

*Two cycles for phage replication are known:*

(A) Lytic (vegetative) Cycle

1. **Adsorption:**

   The phage attaches by its tail to specific receptors on the bacterial cell.
2- **Penetration:**
   The tail sheath contracts and the nucleic acid is injected into the cell.

3- **Eclipse phase:**
   In which the viral nucleic acid direct the host cell metabolism to synthesize new enzymes and proteins required to the phage synthesis.

4- **Intracellular synthesis:** of phage nucleic acids, capsids and tails.

5- **Assembly:** The phage components aggregate to form complete phage particle which mature into a typical infectious phage.

6- **Release:** The bacterial cell bursts liberating a large number of phage particles to infect new cells.
Bacteriophage Replication
(B) Temperate (Lysogenic) Cycle:

In this cycle the phage (temperate phage) does not replicate and lyses the bacteria but the phage DNA is integrated with the bacterial chromosome and divide with it to pass into daughter cells. The integrated phage is called prophage and the bacteria carrying it are called lysogenic bacteria.

THE PRESENCE OF PROPHAGE IN LYSOGENIC BACTERIUM MAKES IT:

1- Immune to infection by another phage.

2- Acquire new properties, e.g. Diphtheria bacilli can produce toxin only when lysogenized.

PRACTICAL USES OF BACTERIOPHAGES:

A) Bacteriophages used as cloning vectors in recombinant DNA technology. A fragment of DNA (foreign gene) is carried on the phage DNA (transduction), as the phage infects a bacterial cell e.g. E.coli, its DNA carrying the foreign gene is incorporated into the bacterial chromosome and the gene is replicated in each cell division.

B) Phage typing: as the phages are used to identify and type bacteria according to the pattern of lysis. In epidemiologic tracing of outbreaks of infection e.g. wound infection or food poisoning.
"Antimicrobial agents"

The substances that can kill or inhibit the growth and multiplication of microorganisms and suitable for systemic use.

Chemotherapeutic agents:

These substances, chemically synthesized and they are used in treatment of infectious diseases.

Antibiotics are antimicrobial substances produced by a living microorganism and are effective against other microorganisms, used in treatment of infectious diseases.

Characteristics of antibiotics:-

- **Bactericidal**: It is a chemotherapeutic that affects bacteria by killing them.

- **Bacteriostatic**: It is a chemotherapeutic that affects bacteria by inhibiting their growth and multiplication.

Spectrum of action:-

**Broad spectrum**: It is the chemotherapeutic that affect wide range of bacteria (both Gram-positive and negative organisms).

**Narrow spectrum**: Effective mainly against only Gram positive or Gram negative organisms.

**Limited spectrum**: Effective only against single organism or disease.
For an antimicrobial drug to be suitable for systemic use, it should have **selective toxicity** i.e. harmful to the microorganism at the therapeutic doses but harmless to the host.

**MECHANISM OF ACTION OF ANTIMICROBIAL AGENTS**

1- **Inhibition of cell wall synthesis:**

E.g. penicillin, cephalosporins, cycloserine and vancomycin. These drugs inhibit the synthesis of peptidoglycan and internal osmotic pressure will be high so the bacteria burst.

2- **Inhibition of cell membrane function:**

E.g. amphotericin B, colistin and polymyxins, these drugs disrupt the functional integrity of the membrane as a result ions escape from the bacteria and it will damage.

3- **Inhibition of protein synthesis:**

E.g. chloramphenicol, erythromycin, tetracyclins and aminoglycosides (streptomycin, gentamycin…etc) leads to inhibition of cell growth.

4- **Inhibition of nucleic acid synthesis:**

E.g. Quinolones inhibit DNA synthesis.

Rifampicin inhibits RNA synthesis.

5- **Competitive Antagonism:**

E.g. Sulphonamides compete with P-aminobenzoic acid (the essential metabolite of folic acid) which is the precursor to the synthesis of nucleic acids. Sulphonamides are structural analogues to PABA. They enter into the reaction in place of PABA and compete for the active center of the enzyme. Nonfunctional analogue of folic acid is formed so nucleic acid synthesis is inhibited.
RESISTANCE TO ANTIMICROBIAL DRUGS

*Its mechanisms are due to:*

1- Microorganisms produce enzymes that destroy the active drug, e.g. penicillin; cephalosporins are destroyed by β-lactamase produced by Staphylococci.

2- Microorganisms develop an alternative pathway to bypass the reaction inhibited by the drug, e.g. bacteria resistant to sulphonamides capable of using preformed folic acid and do not require PABA.

CROSS RESISTANCE
Microorganisms resistant to a certain drug may develop resistance to another drug that is closely related chemically.

COMPLICATION OF CHEMOTHERAPY

(1) **Toxicity:**
Tetracycline, if given to pregnant women or to an infant, cause permanent staining of the teeth. Streptomycin is toxic to eighth cranial nerve causing deafness.

(2) **Allergy:**
Penicillin can cause allergic reaction which varies from simple urticaria to anaphylactic shock.

(3) **Drug resistance:**
Due to abuse of antibiotics, it is recommended to do in vitro sensitivity tests before giving antimicrobials.
(4) **Superinfection:**
Due to elimination of normal flora and flourishing of drug resistant organisms e.g. Staphylococci, leading to staph enterocolitis. Candida leading to oral thrush or vulvovaginitis.

**ANTIBIOTIC COMBINATION**

*Indications:*
- Severely ill patients suspected to have serious microbial disease e.g. staphylococcal and gram negative sepsis in immunocompromized patients.
- To delay the emergence of drug resistance mutants e.g. T.B.
- Mixed infections.

**ANTIMICROBIAL CHEMOPROPHYLAXIS**

*CHEMOPROPHYLAXIS:* Is the administration of antimicrobial drugs to *prevent occurrence of infection by particular organism, e.g.:

1- Use of penicillin or erythromycin before dental procedures to prevent bacterial endocarditis.

2- Use of long-acting penicillin to prevent recurrent throat infections with Strept.pyogens in rheumatic patients.

3- Use of Rifampicin to contacts of a case of epidemic cerebrospinal meningitis.

4- In surgery: In clean operations there is no need for chemoprophylaxis but in large bowel surgery, war wounds and major cardiac surgery, the use of pre- or post-operative antibiotics is recommended.
**Good practice with antibiotics:**

- Be sure that the patient actually requires an antibiotic.
- Avoid treating colonized not actually infected patients.
- Don’t change the antibiotic if the condition improving.
- If no response within 72 hours, so, the diagnosis, antibiotic therapy and secondary infection should be reconsidered.
- Give the antibiotic for the minimal length of time being effective. Review the duration therapy after 5 days.
- For surgical prophylaxis start with induction of anesthesia & continue for maximum 24 hours.