Bacteriophages (Bacterial viruses):

Bacteriophages are viruses that infect bacteria. Replicating within the bacterial cell therefore they are **obligate parasites**. Infection with bacteriophages is restricted to particular strains within a single bacterial species.

Phage exist in many forms and infect all living systems such as animals ،plants, insects and bacteria therefore phages are ubiquitous in nature and they have been showed to be found in soil and sediment.

The death of the host cell result from the release of the progeny and replication of viral particles. About 20-40% of marine bacteria every day have been killed by bacteriophages. Therefore, they play important role in bacterial evolution and ecological systems, and have a considerable role in biogeochemical cycles (carbon, nitrogen, sulfur and phosphorous cycles).

Phages advantages over antibiotics and other antimicrobial agents:

-Host specificity.

- No side effects.

-Easy to isolate and propagate.

- Can overcome resistance.

- Inhibits Gram-positive and Gram-negative organisms.

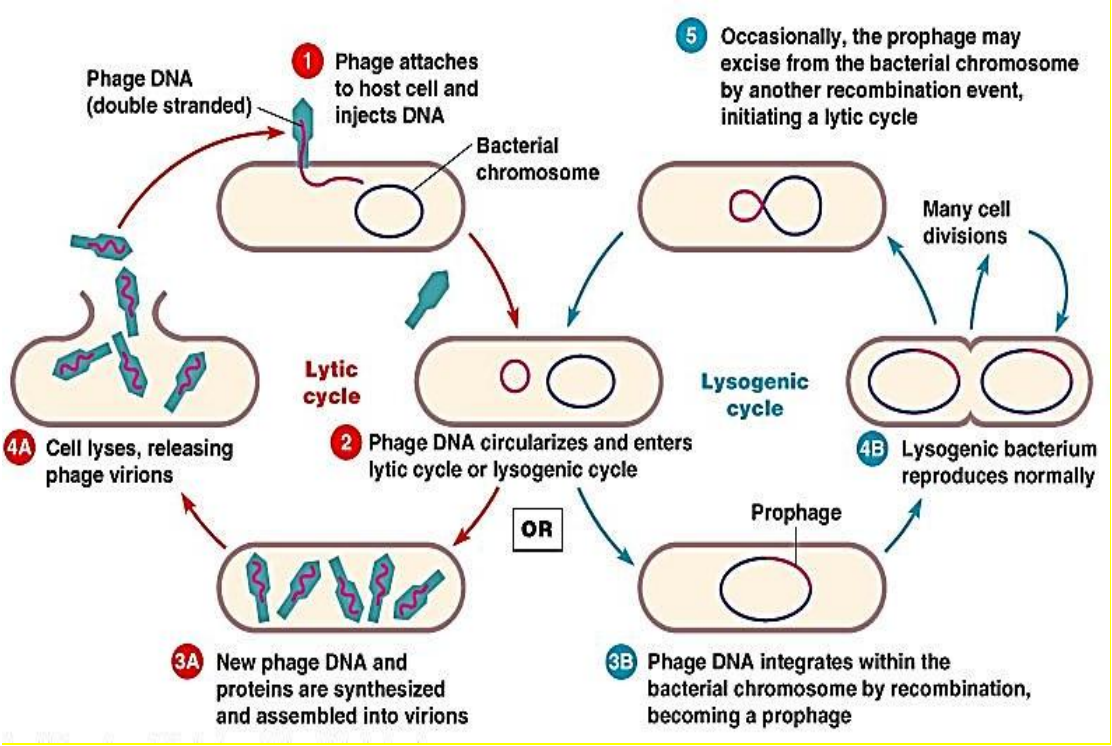
- Potential for use in numerous environments human, animal, food, biofilm, etc, and multiplication in the presence of their hosts.

Bacteriophage Replication Cycle and Classification of Bacteriophages:

The phage infection cycle is important when choosing a phage for antibacterial application. All known bacteriophages can be divided into two groups according to **the type of infection**. One group is characterized by a **lytic infection** and the other is represented by **a lysogenic**, or **temperate**.

In the first form of infection (lytic cycle) occurs once when a host cell infected by virulent phage immediately begins to exploit the metabolic machinery of the cell and directs it towards replication of new virion particles in which the new phage DNA has been packaged and the protein capsid is fully formed phage-encoded proteins. holins and endolysins work together to cause lysis of the cell causing death of the host bacterial cell and the progeny are released. As aresult, new phages are released into the extracellular space.

The other mode of infection, a temperate phage has the ability to enter a lysogenic cycle, in which the phage DNA is integrated into the host genome. The DNA is replicated along with the host genome. Such transition of viral DNA could take place through several generations of bacterium without major metabolic consequences for it. Eventually the phage genes, at certain conditions impeding the bacterium state, will revert to the lytic cycle, leading to release of fully assembled phages.



Types of viral life cycles

The bacteriophages classification **is depended on several factors** such as their **host preference, viral morphology, genome type, and auxiliary structures such as tails or envelopes**. The bacteriophages.The phage **morphology and nucleic acid** properties are key classification factors. The phages majority contain double strand DNA (dsDNA), while there are small phage groups with ssRNA, dsRNA, or ssDNA (ss stands for single strand).

There are a few morphological groups of phages: filamentous phages, isosahedral phages without tails, phages with tails, and even several phages with a lipid-containing envelope or contain lipids in the particle shell. This makes bacteriophages the largest viral group in nature. More than 5500 bacterial viruses have been examined in the electron microscope.

Phage Therapy:

Phage therapy involves clinical treatment of bacterial infections with phages (bacteriophages). The method, which has gained a renewed interest because of increasing frequency of infections by multidrug-resistant bacteria, has potential benefits.

Comparison of phages and antibiotics regarding their prophylactic and therapeutic use

Bacteriophages	Antibiotics
Phages are highly effective in killing their targeted bacteria (their action is bactericidal).	Some antibiotics are bacteriostatic (they inhibit the growth of bacteria, rather than killing them e.x., chloramphenicol).
Production is simple and cheap.	Production is complex and expensive.
Phages are an 'intelligent' drug. They multiply at the site of the infection until there are no more bacteria. Then they are excreted.	They are metabolized and eliminated from the body and do not necessarily concentrate at the site of infection.
The high selectivity/specificity of bacteriophages permits the targeting of specific pathogens, without affecting desirable bacterial flora which means that phages are unlikely to affect the "colonization pressure"	Antibiotics demonstrate bactericidal or bacteriostatic effects not only on the cause of bacterial disease, but on all microorganisms present in the body including the host normal microflora. Thus their

of the patients.	non-selective action affects the patient's microbial balance, which may lead to various side effects.
Because of phages specificity, their use is not likely to select for phage resistance in other (non-target) bacterial species.	The broad spectrum activity of antibiotics may select for resistant mutants of many pathogenic bacterial species.
Humans are exposed to phages throughout life, and well tolerate them. No serious side effects have been described.	Multiple side effects, including intestinal disorders, allergies, and secondary infections (ex., yeast infections) have been reported.
Phage-resistant bacteria remain susceptible to other phages having a similar host range.	Resistance to antibiotics is not limited to targeted bacteria.
Phages are found throughout nature. This means that it is easy to find new phages when bacteria become resistant to them. Selecting a new phage (ex., against phage resistant bacteria) is a rapid process and frequently can be accomplished in days.	Developing a new antibiotic (against antibiotic resistant bacteria) is a time consuming process and may take several years to accomplish.
Phages may be considered as good alternative for patients allergic to antibiotics.	If patient is allergic to antibiotic, treatment is very difficult.

Disadvantages with the phage therapy:

1. The problem which requires attention is the rapid clearance of phage by the spleen, liver and other filtering organs of reticuloendothelial system
2. This therapy cannot be used for intracellular bacteria as the host is not available for interaction.
3. Theoretically development of neutralizing antibodies against phages could be an obstacle to the use phage therapy in recurrent infections. This needs to be confirmed experimentally. However, in the immunocompromised host where the immune system is depressed such as chronic infections, the phage therapy may work in this situation.
4. Phages are more difficult to administer than antibiotics. A physician needs special training in order to correctly prescribe and use phages.