

Bacteriophages

Bacteriophages are viruses that infect bacteria. Replicating within the bacterial cell therefore they are obligate intracellular parasites that multiply inside bacteria by making use of some or all of the host biosynthetic machinery. The term is commonly used in its shortened form, phage. Bacteriophages are much smaller than the bacteria they destroy. Infection with bacteriophages is restricted to particular strains within a single bacterial species. Phages are ubiquitous and can be found in all reservoirs populated by bacterial hosts, such as soil or the intestines of animals. One of the densest natural sources for phages and other viruses is sea water. They occur widely in nature and can readily be isolated from feces and sewage. There are at least 12 distinct groups of bacteriophages, which are very diverse structurally and genetically.

Typical phages have hollow heads (**where the phage DNA or RNA is stored**) and tunnel tails, the tips of which have the ability to bind to specific molecules on the surface of their target bacteria. The viral DNA is then injected through the tail into the host cell, where it directs the production of progeny phages often over a hundred in half an hour. These "young" phages burst from the host cell (killing it) and infect more bacteria.

Composition

Depending upon the phage, the nucleic acid can be either **DNA or RNA** but not both. The nucleic acids of phages often contain unusual or modified bases, which protect phage nucleic acid from nucleases that break down host nucleic acids during phage infection. Simple phages may have only 3-5 genes while complex phages may have over 100 genes. The phages majority contain **double strand DNA (dsDNA)**, while there are small phage groups with **ssRNA, dsRNA, or ssDNA**. There are three morphological forms of phages: filamentous phages, isosahedral phages without tails, phages with tails, and

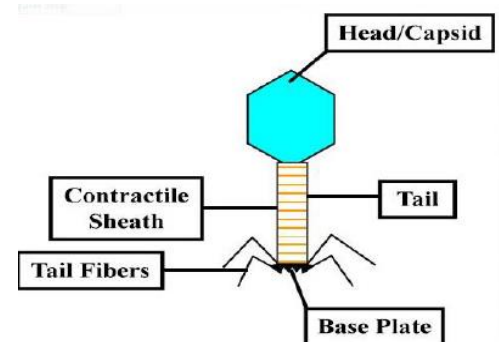
even several phages with a lipid-containing envelope or contain lipids in the particle shell.

Structure of bacteriophages

Size: Most phages range in size from 24-200 nm in length. **T4** is among the largest phages; it is approximately 200 nm long and 80-100 nm wide.

Head or capsid: All phages contain a **head structure**, which can vary in size and shape. Some are icosahedral (20 sides) others are filamentous. The head or capsid is composed of many copies of one or more different proteins. Inside the head is found the nucleic acid. The head acts as the protective covering for the nucleic acid.

Tail: Some phages have tails attached to the phage head. The tail is a hollow tube through which the nucleic acid passes during infection. T4 tail is surrounded by a contractile sheath, which contracts during infection of the bacterium. At the end of the tail, phages like T4 have a base plate and one or more tail fibers attached to it. The base plate and tail fibers are involved in the binding of the phage to the bacterial cell. Not all phages have base plates and tail fibers.



Bacteriophage Replication Cycle

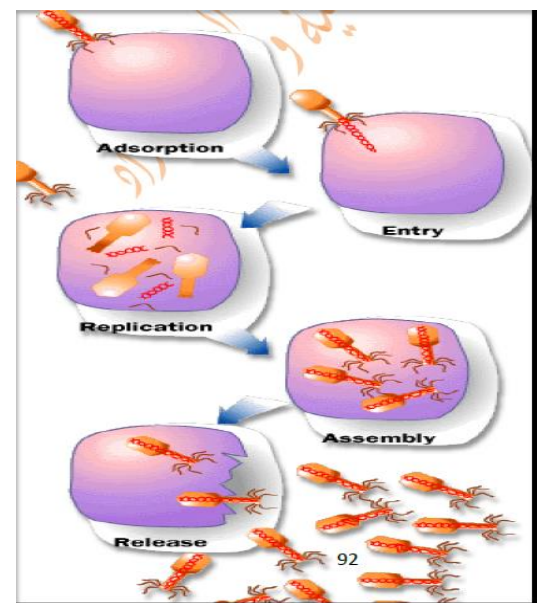
All known bacteriophages can be divided into **two groups** according to the **type of infection**: One group is characterized by a **lytic infection** and the other is represented by a **lysogenic**, or **temperat**.

1- Lytic or virulent phages are phages, which multiply in bacteria and kill the cell by lysis at the end of the life cycle. Soon after the nucleic acid is injected, the phage cycle is said to be in **eclipse period**. During the eclipse phase, no infectious phage particles can be found either inside or outside the bacterial cell. Eclipse phase represents the interval between the entry of phage nucleic acid into bacterial cell and release of mature phage from the infected cell occurs. The phage nucleic acid takes over the host biosynthetic machinery and

phage specified m-RNA's and proteins are made. Nucleic acid is then packaged inside the head and then tail is added to the head. The assembly of phage components into mature infective phage particle is known as maturation. In Lysis and Release Phase the bacteria begin to lyse due to the accumulation of the phage lysis protein (holins and endolysins) and intracellular phage are released into the medium.

2- Lysogenic or temperate phages

Temperate phage has the ability to enter a lysogenic cycle and become a dormant state in the cell, in which the phage DNA is integrated into the host genome. The DNA is replicated along with the host genome. This integrated state of phage DNA is termed **prophage**. This process is known as lysogeny and the bacteria harboring prophage are called **lysogenic bacteria**. Since the prophage contains genes, it can confer new properties to the bacteria. 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.

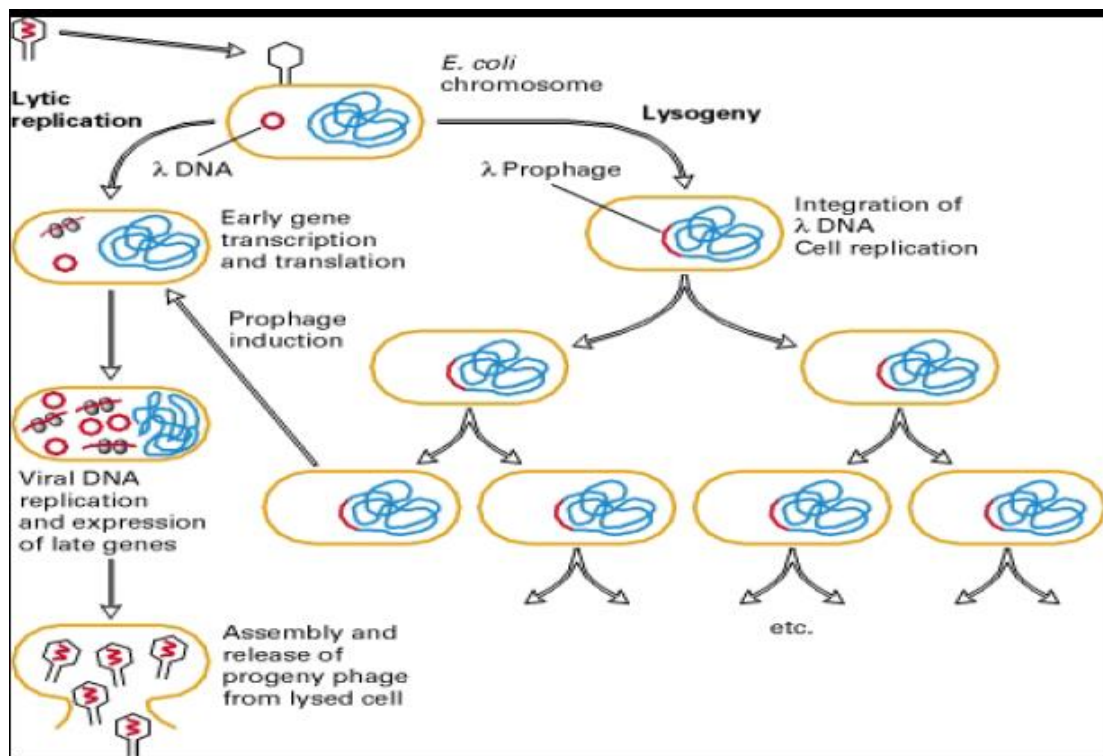


Anytime a lysogenic bacterium is exposed to adverse conditions, the lysogenic state can be terminated. This process is called **induction**. Conditions which favor the termination of the lysogenic state include: desiccation, exposure to UV or ionizing radiation, exposure to mutagenic chemicals.

Significance of lysogenic conversion includes:

- Lysogenic phages have been shown to carry genes that can modify the Salmonella O antigen, which is one of the major antigens to which the immune response is directed.

- Toxin production by *Corynebacterium diphtheriae* is mediated by a gene carried by a beta phage. Only those strains that have been converted by lysogeny are pathogenic.
- *Clostridium botulinum*, a causative agent of food poisoning, makes several different toxins, 2 of which are actually encoded by prophage genomes.
- Lysogenised bacteria are resistant to superinfection by same or related phages. This is known as super infection immunity.



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.

Phages are highly effective in killing their targeted bacteria (their action is bactericidal). Phages may be considered as good alternative for patients allergic to antibiotics.

Phage therapy benefits

- Phages work against both treatable and antibiotic-resistant bacteria.

- They may be used alone or with antibiotics and other drugs.
- Phages multiply and increase in number by themselves during treatment (only one dose may be needed).
- They only slightly disturb normal “good” bacteria in the body.
- Phages are natural and easy to find
- They are not harmful (toxic) to the body.
- They are not toxic to animals, plants, and the environment.

Phage therapy disadvantages

- Phages are currently difficult to prepare for use in people and animals.
- It's not known what dose or amount of phages should be used.
- It's not known how long phage therapy may take to work.
- It may be difficult to find the exact phage needed to treat an infection.
- Phages may trigger the immune system to overreact or cause an imbalance.
- Some types of phages don't work as well as other kinds to treat bacterial infections.
- There may not be enough kinds of phages to treat all bacterial infections.
- Some phages may cause bacteria to become resistant.