Viral inactivation

1. Solvent/detergent (S/D) inactivation

This process is only effective for viruses enveloped in a lipid coat, however. The detergents used in this method interrupt the interactions between the molecules in the virus's lipid coating. Most enveloped viruses cannot exist without their lipid coating so are destroyed when exposed to these detergents. Other viruses may not be destroyed but they are unable to reproduce rendering them non-infective. The solvent creates an environment in which the aggregation reaction between the lipid coat and the detergent happen more rapidly. The detergent typically used is Triton-X 100.

2. Pasteurization

Some of the more prominent advantages of these types of processes are that they require simple equipment and they are effective for both enveloped *and* non-enveloped viruses. Because pasteurization involves increasing the temperature of solution to a value that will sufficiently denature the virus, it does not matter whether the virus has an envelope or not because the envelope alone cannot protect the virus from such high temperatures. However, there are some proteins which have been found to act as thermal stabilizers for viruses. Of course, if the target protein is not heat-resistant, using this technique could denature that target protein as well as the viral impurity. Typical incubation lasts for 10 hours and is performed at 60°C.

3. Acidic pH inactivation

This technique is effective against enveloped viruses, and the equipment typically used is simple and easy to operate. This type of inactivation method is not as effective for non-enveloped viruses however, and also requires elevated temperatures. So in order to use this method, the target protein must be resistant to low pHs and high temperatures which is unfortunately not the case for many biological proteins. Incubation for this process typically occurs at a pH of 4 and lasts anywhere between 6 hours and 21 days.

4. Ultraviolet (UV) inactivation

UV rays can damage the DNA of living organisms by creating nucleic acid dimers. However, the damages are usually not important due to low penetration of UVs through living tissues. UV rays can be used, however, to inactivate viruses since virus particules are small and the UV rays can reach the genetic material, inducing the dimerisation of nucleic acids. Once the DNA dimerised, the virus particules cannot replicate their genetic material which prevent them from spreading.

Atypical virus like agents

Because of their simplified structures both prions and viroids are sometimes called subviral particles. Viroids mainly cause plant diseases but have recently been reported to cause a human disease.

Prions

Prion diseases or transmissible spongiform encephalopathies (TSEs) are a family of rare progressive neurodegenerative disorders that affect both humans and animals. They are distinguished by long incubation periods, characteristic spongiform changes associated with neuronal loss, and a failure to induce inflammatory response.

The causative agents of TSEs are believed to be prions. The term "prions" refers to abnormal, pathogenic agents that are transmissible and are able to induce abnormal folding of specific normal cellular proteins called prion proteins that are found most abundantly in the brain. The functions of these normal prion proteins are still not completely understood. The abnormal folding of the prion proteins leads to brain damage and the characteristic signs and symptoms of the disease. Prion diseases are usually rapidly progressive and always fatal.

EX.

Variant Creutzfeldt-Jakob Disease (vCJD) ,Gerstmann-Straussler-Scheinker Syndrom ,Fatal Familial Insomnia ,Kuru

https://www.cdc.gov/prions/index.html

Viroids

Viroids are small, circular RNA molecules that do not encode any protein and that are infectious as naked RNA molecules. Sequenced viroids range from 246 to 375 nucleotides and possess extensive internal base pairing that results in the RNA being rodlike and about 15nm long.

,The only human disease known to be caused by a viroid is hepatitis D(hepatitis δ). This disease was previously ascribed to a defective virus called the **delta agent**. However, it now is known that the delta agent is a viroid enclosed in a hepatitis B virus capsid. For hepatitis D to occur there must be simultaneous infection of a cell with both the hepatitis B virus and the hepatitis D viroid. There is extensive sequence complementarity between the hepatitis D viroid RNA and human liver cell 7S RNA, a small cytoplasmic RNA that is a component of the signal recognition particle, the structure involved in the translocation of secretory and membrane-associated particles. The hepatitis D viroid causes liver cell death via sequestering this 7S RNA and/or cleaving it.

Pseudovirions

are synthetic viruses used to inject genetic material, including DNA and RNA, with specific and desired traits into bacterial and eukaryotic cells. Pseudoviruses are closely related to viruses in structure and behavior but lack many characterists exhibited by true viruses, including the capability to replicate

Defective Viruses

Viruses which lack a complete genome so that they cannot completely replicate or cannot form a protein coat. Some are host-dependent defectives, meaning they can replicate only in cell systems which provide the particular genetic function which they lack. Others, called SATELLITE VIRUSES, are able to replicate only when their genetic defect is complemented by a helper virus.

Viral replication Within the Host Cell

Viral replication is the term used indicate the formation of biological viruses during the infection process in the target host cells. Viruses must first penetrate and enter the cell before viral replication can occur. From the perspective of the virus, the purpose of viral replication is to allow reproduction and survival of its kind. By generating abundant copies of its genome and packaging these copies into viruses, the virus is able to continue infecting new hosts.

Replication between viruses is varied and depends on the type of genes involved. Most DNA viruses assemble in the nucleus; most RNA viruses develop solely in cytoplasm. Viral populations do not grow through cell division, because they are a cellular. Instead, they hijack the machinery and metabolism of a host cell to produce multiple copies of themselves, and they assemble inside the cell.

The life cycle of viruses differs greatly between species but there are **six common basic stages:**

1. Attachment

Attachment is a specific binding between viral capsid proteins and specific receptors on the host cellular surface. This specificity determines the host range of a virus. For example, HIV can infect only a limited range of human leukocytes. Its surface protein, gp120, specifically interacts only with the CD4 molecule – a chemokine receptor – which is most commonly found on the surface of CD4+ T-Cells. This mechanism has evolved to favor those viruses that infect only cells

within which they are capable of replication. Attachment to the receptor can fore the viral envelope protein to undergo either changes that result in the fusion of viral and cellular membranes, or changes of non-enveloped virus surface proteins that allow the virus to enter.

2. Penetration

Penetration follows attachment. Virions enter the host cell through receptor-mediated endocytosis or membrane fusion. This is often called *viral entry*. The infection of plant and fungal cells is different from that of animal cells. Plants have a rigid cell wall made of cellulose, and fungi one of chitin, so most viruses can get inside these cells only after trauma to the cell wall. However, nearly all plant viruses (such as tobacco mosaic virus) can also move directly from cell to cell, in the form of single-stranded nucleoprotein complexes, through pores called plasmodesmata. Bacteria, like plants, have strong cell walls that a virus must breach to infect the cell. However, since bacterial cell walls are much less thick than plant cell walls due to their much smaller size, some viruses have evolved mechanisms that inject their genome into the bacterial cell across the cell wall, while the viral capsid remains outside.

3. Uncoating

Uncoating is a process in which the viral capsid is removed: This may be by degradation by viral or host enzymes or by simple dissociation. In either case the end-result is the release of the viral genomic nucleic acid.

4. Replication

Replication of viruses depends on the multiplication of the genome. This is accomplished through synthesis of viral messenger RNA (mRNA) from “early” genes (with exceptions for positive sense RNA viruses), viral protein synthesis, possible assembly of viral proteins, then viral genome replication mediated by early or regulatory protein expression. This may be followed, for complex viruses with larger genomes, by one or more further rounds of mRNA synthesis: “late” gene expression is, in general, of structural or virion proteins.

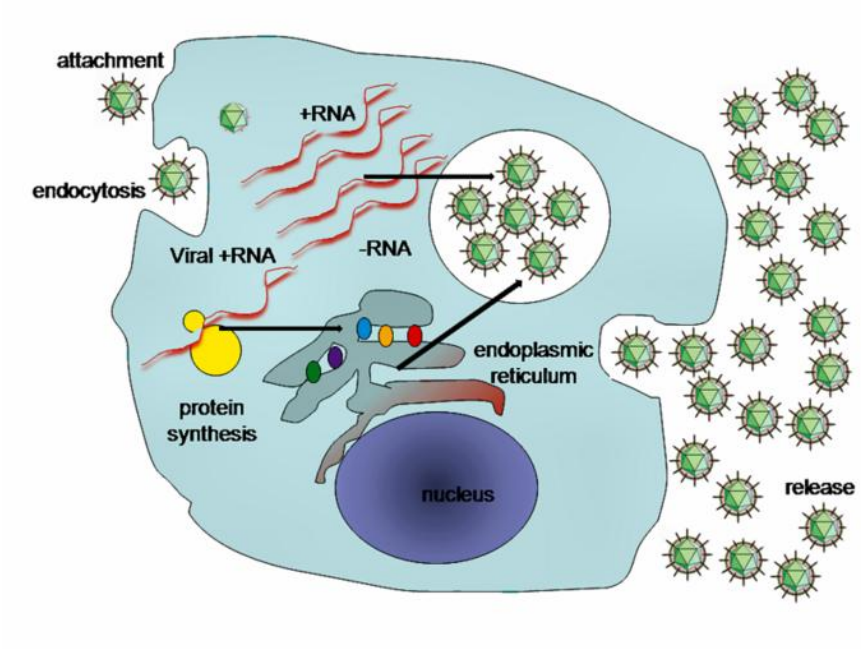

Fig 2: Hepatitis C virus: A simplified diagram of the Hepatitis C virus replication cycle.

5.Self-assembly

Following the structure-mediated self-assembly of the virus particles, some modification of the proteins often occurs. In viruses such as HIV, this modification (sometimes called maturation) occurs after the virus has been released from the host cell.

6.Releasing

Viruses can be released from the host cell by lysis, a process that kills the cell by bursting its membrane and cell wall if present. This is a feature of many bacterial and some animal viruses. Some viruses undergo a lysogenic cycle where the viral genome is incorporated by genetic recombination into a specific place in the host's chromosome. The viral genome is then known as a *provirus* or, in the case of bacteriophages a *prophage*. Whenever the host divides, the viral genome is also replicated. The viral genome is mostly silent within the host; however, at some point the provirus or prophage may give rise to active virus, which may lyse the host cells. Enveloped viruses (e.g., HIV) typically are released from the host cell by budding. During this process the virus acquires its envelope, which is a modified piece of the host's plasma or other internal membrane. The genetic material within virus particles, and the method by which the material is replicated, varies considerably between different types of viruses.