INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X
Impact Factor: 6.078

(Volume 7, Issue 2 - V7I2-1279)
Available online at: https://www.ijariit.com

Review on Hepatitis C

Pawan Admane
admanepawan4@gmail.com
D. Y. Patil International University, Pune, Maharashtra

Shahabaz Pinjari
pinshaha1412@gmail.com
D. Y. Patil International University, Pune, Maharashtra

Apurwa Singh
singhapurwa2510@gmail.com
D. Y. Patil International University, Pune, Maharashtra

Ayushi Mathew
ayushimathew007@gmail.com
D. Y. Patil International University, Pune, Maharashtra

ABSTRACT

A blood-borne virus causes hepatitis C. The epidemic has a strong global influence on the health, epidemiology, and economy. In 60 percent to 80 percent of cases hepatitis C virus (HCV) infections can become chronic, and can be serious, such as liver cirrhosis and primary hepatitis carcinoma. In Germany it is estimated that there are about 400,000 to 500,000 people who are chronically infected. Since 1990, a compulsory blood and plasma donation monitoring has significantly decreased, and is extremely low, the risk of viral transmission through blood products. However, the injecting of opioid consumers is a significant risk group. In recent years, opioid treatment efficacy has dramatically increased for chronic infection of hepatitis C virus. In 50% to 75% of patients according to HCV genotype, continuous viral clearance is achieved. A large percentage of the global population is estimated to have a chronic virus infection. The virus has major heterogeneity, which interferes directly with the management of diseases. Therapy reaction depends on the genotype and subtype of HCV. Continuous variant generation (quassis) helps the virus to avoid antiviral regulation. In the past, the only treatment choice of the condition was a mixture of ribavirin and interferon therapy. Several alternative medical options are now being established and are available to a substantial portion of the population affected. Moreover, the hunt for novel anti-HCV substances begins, predicting potential therapeutic changes. The mutation ability of the virus and other factors affecting therapeutic outcomes should be considered by researchers.

Keywords: *Hepatitis, HCV Virus*

1. INTRODUCTION

Hepatitis C is a hepatitis C virus (HCV) infectious disease that mainly affects the liver. People often experience mild to no signs after their initial infection. Often there is fever, black urine, stomach pain and tinged yellow skin. In about 75% to 85% of those previously infected, the infection remains in the liver. Normally there are no signs at an early stage of chronic infection. But it also results in liver cancer and even cirrhosis for several years. In certain cases, cirrhosis causes severe problems in the stomach and oesophagus, such as liver disease, liver cancer, or expanded blood vessels.

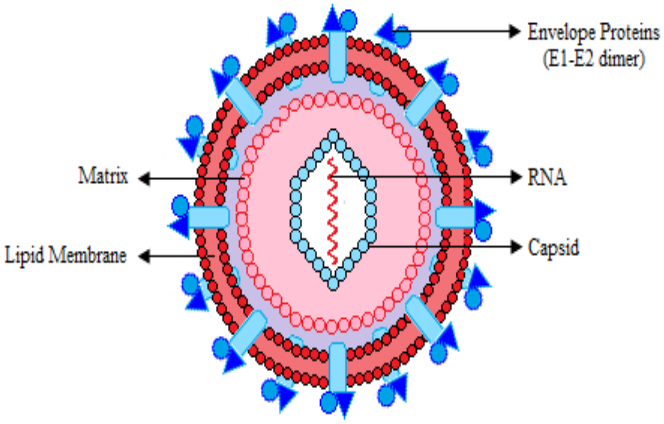
The virus of hepatitis C is both acute and chronic. Normal asymptomatic infections are fresh HCV infection. Any people undergo acute hepatitis that is not life-threatening. Around 30% (15-45%) of infected individuals voluntarily expel the virus without treatment within 6 months of diagnosis.

The rest of 70% (55–85%) of people are afflicted with chronic HCV. The risk of cirrhosis ranges from 15% to 30% in 20 months of those with chronic HCV infection.

2. STRUCTURE OF HCV VIRUS

The structure belongs to Hepacivirus genus which is a member of the family Flaviviridae. It is a enveloped, positive strand RNA virus. The HCV particles are spherical and heterogenous in size which ranges from 40-80nm in diameter. There is total 7 HCV genotypes and 80 subtypes. The structure consists of lipid layer envelop which is 55-65nm in diameter. Inside the lipid layer

envelope contains two viral envelope glycoproteins i.e., E1 and E2 which take part in viral attachment and entry into the cells. an icosahedral core is present inside the envelope which is 33 to 40nm in diameter, and inside this icosahedral core RNA material of the virus is present.



Envelope

The envelope consists of two types of glycoproteins E1 and E2 which are associated as heterodimers. These glycoproteins are embedded in the host derived lipid membrane and together forms a HCV envelope. These glycoproteins form higher order oligomeric structure consisting of three group of heterodimers, the trimers can then group together into pentamers. The Hypervariable region, HVR1 are found in E2 proteins. They are flexible and quite accessible to the surrounding molecules. It prevents CD81 from holding onto its respective receptor of the virus. Structurally, the hypervariable region in the E2 protein which shields the E1 protein from the immune system. The HVR1 is quite different in amino acid sequence, but this region has similar chemical, physical, and conformational characteristics across many E2 glycoproteins. The major role of envelope protein includes host receptor binding, endosome lipid membrane fusion and assembly. The length of the E1 protein is approximately 192 amino acids and of E2 protein is 363 amino acids. The host membrane lipid layer of the envelop consist of cholesterol, cholesteryl esters, phosphatidylcholine, and sphingomyelin.

Lipid membrane

The lipid membrane consist of cholesterol, cholesteryl esters, phosphatidylcholine, and sphingomyelin. The cholesterol content in the HCV particle is slightly higher when compared with host cell membrane. The HCV membrane has a very high amount of embedded cholesterol, which gives it a structure that resembles human very-low-density lipoprotein (VLDL) (VLDL). The specific ratios of lipids in HCV membranes specifically separates it from other viruses and from host cells. It appears that cholesterol and sphingolipid both play a role in the entry of HCV into host cells.

HCV Capsid

The HCV capsid is the protein shell that encapsulates and covers the HCV RNA, also known as the HCV core. The HCV capsid is completely constituted by the HCV core protein. The proteins on the exterior area of the heart interact with the viral membrane. The internal surface connects with several parts of HCV RNA. On the endoplasmic reticulum, after polypeptide slipping, the core proteins assemble to form the capsid on the cytoplasmic face, caused by interactions with HCV RNA, E1 protein and the surface. The core proteins use HCV RNA as a scaffold for assembling, which is attached to and surrounds the HCV RNA. The HCV capsid is spherical and heterogeneous and about 30 nm in diameter.

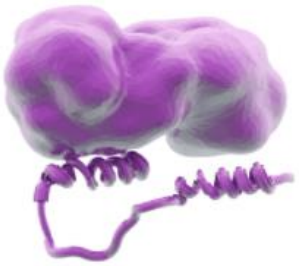
Nucleocapsid

A capsid, composed entirely of HCV nucleocapsid, forms a membrane that embeds and preserves HCV RNA. HCV RNA consists of single-stranded, positive-sense RNA with a length of approximately 9,600 nucleotide bases. The capsid structure is binding to some HCV RNA segments. With an estimated 30 nm diameter, the HCV nucleocapsid is spherical and heterogeneous in size. The HCV RNA (genome) consists of an approximately 9,600 nucleotide bases long, single stranded positive-sense RNA. The HCV genome includes a single, long and open reader frame of 5'' and 3' untranslated areas (3,006-3037 codons) (UTRs). The HCV RNA genome is used both for translation and transcription. The 5' region, which is upstream from the open reading frame, is roughly 340 nucleotides long and consists of 4 closely organized domains. Domain I is made up of a small stem loop (IRES). The IRES is an extremely coordinated regulatory instrument which mediated the binding of the HCV RNA to the host subunits (and cellular factors). The 3' area is around 225 nucleotides and consists of three components: integer, poly-long (U/UC) and 3'X region. The 3'X region is the main element in modifying the transcription of the HCV RNA between translation and RNA.

Lipoviral particles

As a hybrid lipoviral particle composed of lipoproteins closely associated with the HCV particle, HCV can circulate in the bloodstream. The lipoviral particle has specific components including triglycerides, HCV RNA, capsid protein, E1 glycoprotein envelope, E2 envelope glycoprotein, apolipoprotein B and apolipoprotein E. These lipoviral particles are about 100 nm in diameter. Lipoviral particle production enables the insertion of HCV into the hepatocytes and inhibits the neutralization of the antibody by HCV. This lipoviral particles have a density comparable to lipoproteins of medium density (LDLs) and to lipoproteins of extremely low density (VLDLs) that usually circulate throughout the bloodstream.

Core Structure



A host signal peptidase initials cleavage of the heart to produce an immature core protein, 191 amino acids long. A second cleavage of signal peptide peptidase eliminates the signal sequence of C-terminal E1, releasing a mature core protein of 177 amino acids long and weight 21 kDa. The mature core protein consists of two distinct areas: D1 (in the N-terminal) and D2 (at the C-terminal region). The D1 domain is structurally highly flexibly classified into three major (BD) domains: BD1, BD2, and BD3. During assembly, RNA binding and oligomerisation (around the RNA scaffolding) are performed by the D1 domain to form the nuclear capside.This D2 domain includes the regions Helix I and Helix II bound to the lipid membrane via a hydrophobic loop. The D3 domain is the extremity of the cleaved C-terminal, and is thus absent in the mature capsid protein.

Function

The HCV centre is a structural protein aggregating into the viral capsid that covers the virus' genomic RNA and protects it. The central protein is the first HCV-translated protein that consists of three structural HCV-proteins alongside the envelopes glycoproteins (E1 and E2). The mature core protein has the properties as part of the nucleocapside structure to encourage binding to the host-derived lipid membrane and HCV RNA. The HCV genomic RNA is binding to an N-terminal region of the core proteins.

E1 Structure

E1 is a transmembrane protein of type I with a molecular weight of 23 kDa and a length of 192 amino acids. The E1 protein has four major areas: an N-terminal area (NTD), a presumed fusion peptide (pFP) and a C-terminal narrow transmembrane area (TMD). E1 is 4-5 N-linked glycaetes in the protein. Many E1 immune domains in the HCV surface are covered under E2 in the E1-E2, which is why E1 proteins are considerably less immunogenic than E2. In the development of the E1 trimmer the E1 highly-preserved GxxxG motif (Gly354 and Gly358) plays an important role, situated in the transmembrane domain.

Function

The glycoprotein E1 envelope protein is a strongly glycosylic transmembrane protein that forms the envelope glycoprotein E1-E2 heterodimers closely aligned with the E2 glycoprotein. E1 protein has a role to play at many phases of the hydrogen cycle, including host cell binding, fusion, and assembly of endosome-lipid membrane. For E1, binding to host apoproteins or potential CD 36 can be the part of an attachment. Moreover, E1 allows E2 to connect with host receptors, while retaining the receptor-friendly E1-E2 structural conformation. In the endosomal environment, after an endocytosis of the HCV portion of the endosome, the conformational changes in E1 and E2 are induced and the endosomal membrane fused with a viral envelope and the HCV RNA released into the cytoplasm. Recent research also indicate that E1 protein interacts to synchronization of HCV assembly processes with a variety of other viral proteins.

E2 Structure

The molecular weight of the E2 protein is 70 kDa and it has an acidity size of 363. Protein E2 has an intergenotypic vector range 1 (HVR1), HVR2, a stalk region and a Transmembrane (TM) domain. This is known as an E2 protein. This is an important mechanism to correct protein folding and immune escape for E2 proteins, which is glycosylated from N at 9 to 11 sites with 18 retained cysteine reside. The highly glucolized areas of E2 include epitopes for immunoglyzing that are thought to act as immunological decoys to deter more retained epitopes of neutralization. Though genetic variation in the HCV genome can be established, the glycoprotein N-terminus of E2 is highly variable and can vary rapidly even in a patient.

Function

The glycoprotein protein E2 is a transmembrane protein which is strongly glycosylated and which in turn interacts with the glycoprotein envelope E1 to form E1-E2 heterodimers. These E1-E2 heterodimers form the HCV envelope and are inserted into the host dependent lipid membrane. E2 is long in form and leads to the binding, feedback and fusion of the host receptor with the endosomal membrane. The E2 protein is related to many surface cell receptors, including a type 1 CD81 and a type B scavenger (SR-B1).

P7 Structure

The molecular weight of the p7 protein is only 7 kDa; only 63 amino acids are available. The protein is made up a region of an N-terminal, transmembrane domain 1 (TM1) and a small loop, transmembrane domain 2 (TM2), and an end of a C-terminal. In both N-terminal and C-term regions of p7, the endoplasmic reticular lumen is oriented, while the narrow, interfering circuit stretches into the cytoplasm. Alpha helixes are TM1 and TM2 domains. Heptameric and hexameric forms of the p7 oligomers have been described.

Function

The p7 protein is a small hydrophobic protein that is used to assemble and unleash the virus. The p7 protein oligomerates as hexamers to form ion channels in host cell membranes — p7 is known as part of the virus protein family, based on this property. P7 is structurally essential within hepatocytes, but it does not constitute a part of the viral particle. P7 proteins are used during assembly to unload core proteins for the assembly and enveloping of the lipid droplets along with other viral proteins at the endoplasmic reticulum. The P7 canal operation will dissipate the low pH of the secretory cell segment to guard against inactivation of the viral glycoprotein

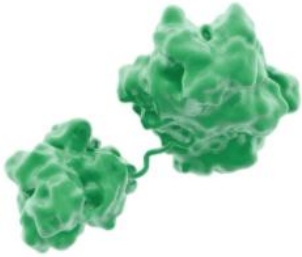
NS2 Structure

The molecular weight of the dimeric NS2 protein is 21 kDa and 217 amino acids are long. NS2 has three domains of transmembrane, a low helix and a protease (that faces the cytosol). The NS2 protein has two active sites and functions as a cysteine Protease with its C-Terminal Domain (the N-Terminal 180 amino acid NS3 junction), which is formed from N-Terminal Alpha helic and Domain-swapped C-Terminal Beta sheets and consists of a dimer of N-Terminal Alpha helical. The protease domain is the catalyst for the catalytic triad C-terminal: its 143, Glu 163 and Cys 184. A area considered to play a central role in HCV particles assembly is the N-terminal transmembrane segment.

Function

The Non-structural Protein 2 (NS2), as a cysteine protease and a cofactor in the assembly phase, has dual roles within the HCV-living period. The protease domain of the NS2 protein serves as cysteine defence for catalysing a single cleavages between the NS2 and NS3 proteins in cooperation with the N-terminal region of NS3. For RNA replication, the NS2 release from NS3 is necessary. The NS2 protein is not essential for HCV RNA replication, but plays a key role in the organization of viral assembly in combination with several other viral proteins. In specific, NS2 tends to collocate near the core proteins and lipid droplet with E1, E2, NS3 and NS5A in viral assembly.

NS3 Structure



The NS3 protein weights 70kDa and has a length of 631 amino acids. The protein has two major domains: (1) in the N-terminal region (180 amino acids long) serine protease domain and (2). the broader, C-terminal region with a 450-acid amino acid length of nucleoside-triphosphatase-dependent RNA helicase domain. A protease catalytic triad at very preservative amino acid positions (Histidine-57, Aspartate-81 and Serine-139) is contained in the N-terminal region. The 54-amino-acidNS4 protein anches on the membrane, and forms together an enzyme complex of the NS3-4A.

Function

The NS3 is a bifunctional enzyme with serine protease and helicase activity. The protein is NS3. Most viral polyprotein clamps that free non-structural protein are the source of the serene-type protease area of NS3. Furthermore, NS3 plays a role in reversing the innate host immune response by proteolytic inactivation of multiple host cell factors that block viral replication. The N3 helicase region potentially plays an important role in the removal of viral RNA and the support of viral replication. The crystal structure for NS3 protease that enabled the production of specific NS3/4A protease inhibitors was one of the first achievements in the development of a direct-action antiviral therapy.

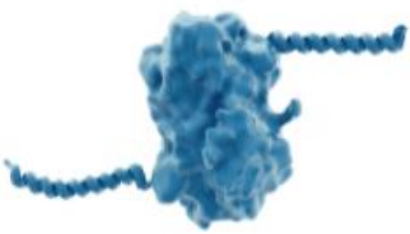
NS4A Structure

NS4A is the smallest of the HCV non-structural proteins, measuring 27 kDa and having a length of 54 amino acids. The NS4A protein has three domains: (1) N-terminal hydrophobic portion that is necessary for a transmembrane-based alpha-helix interaction in the NS3-4A Complex integral membrane; (2) central portion needed for proper fold of NS3; and (3) C-terminal acidic portion that contains a strongly negative α-helix that is involved in the NS5A hyperphosphaelization and viral replicate control.

Function

The smallest of the non-structural HCV proteins is the non-structural protein 4a (NS4A). The NS4A protein has many roles within the HCV longevity cycle, which includes: (1) the anchoring of the NS3-4A complex to the outer leaflet of the endoplasmic and mitochondrial outer membrane; (2) the cofactor for the NS3A serine proteose; (3) the increase in NS3A helicase activity. The interactions between NS4A and NS4B and NS3 and NS4A are critical for the assembly of viruses.

NS4B Structure



The NS4B protein has a size of 27kDa and a length of 261 amino acids. This hydrophobic protein has a complex structure consisting of an endoclosive N-terminal helix, a central region of four-five transmembrane segments, and a cytostic helix C-terminal region. The NS4B is attached with NS4A prior to proteolytic cleavage, with N-terminals as well as C-terminals in the cytosolic lumen (flanking four transmembrane NS4B segments). The N-terminal region is flipped to the endoplasmic reticulum lumen after the NS34A cleavage of NS4A and NS4B.

Function

The NS4B (Nonstructural Protein 4B) is a protein which induces cytoplasmic membrane alternation and mediates host-virus interactions; the protein co-localizes with other non-structural proteins into the endoplasmic reticulum to form a replication complex. The NS4B protein is one of several virus components required for membranous web creation, a viral replication enabling micro-environment within the cytoplasm.

NS5A Structure

The NS5A protein, a 56 kDa in weight and 448 amino acids in length, is a zinc-binding, proline-rich hydrophilic phosphoprotein. The NS5A consists of four major regions: Amphathetic N-terminal, Domain I, Domain II and Domain III and interspersed between three domains of low complexity sequences (LCIS1 and LCIS2). Inside HCV-infected hepatocytes, the NS5A protein is localized to the endoplasmic reticulum (EN) in which the numerous membrane vesicles caused by the virus form; RNA replication complexes and lipid droplets are located in the multi-embryonic network area of the multi-embryonic vesicle.

Function

A main component of the HCV replication complex is non-structural protein 5A (NS5A). NS5a protein interacts in order to control and control viral replication and movement with other primary viral (NS4B, NS5B, RNA) or host cell protein products (cyclophilin A, phosphates etc). The NS5A protein plays a key role in the development and effective viral replication of endoplasmic reticular-derived two-membrane vesicles. The NS5A protein also helps in the pathogenesis of HCV, regulation of pathways of cell signalling, viral spread and response to interferons via the interferon-alpha sensitivity region.

NS5B Structure

The NS5B protein has a weight of 66 kDa and an amino acid length of 591. Similar to other polymerases, NS5B has a conformation that resembles a right hand with finger, palm and thumb subdomains. During RNA synthesis the enzyme complies with a closed structure and is free during RNA elongation. The N-terminal 530 amino acids form the catalytic domain. Structural differentiation is made between HCV NS5B polymerase and cell DNA and RNA polymerase enzymes. In the active site of the NS5B protein is the Gly-Asp-Asp motive which binds magnesium, an important mechanism for enzyme activity, into this region.

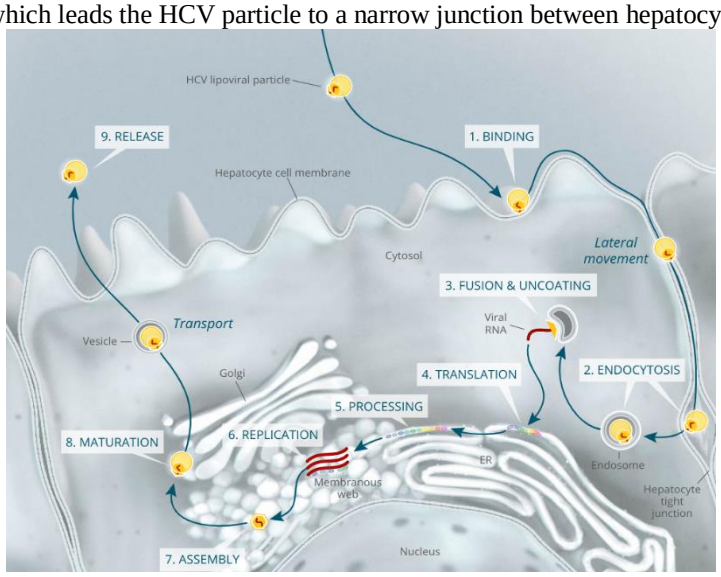
Function

Nonstructural 5B (NS5B) protein is an HCV replication-critical RNA (RdRp) Polymerase. The enzyme's function is to catalyze ribonucleoside triphosphate (RNTP) polymerization during viral replication of the RNA. Two major subclasses of the polymerase inhibitors for the NS5B exist: (1) nucleotide analogs which imitate the natural substrate through which the new RNA integrates chain termination; and (2) non-nucleotide inhibitors, which attach and affect the functionality of the allosteric sites of the enzyme.

3. LIFE CYCLE

Binding

The life cycle of HCV starts with HCV binds to two host receptors on a hepatocyte's surface: the low density lipoprotein receptor (LDLr) and heparin proteoglycanic sulphate receptor (HSPGs). The HCV outer E1/E2 heterodimer membrane protein allows this interaction to bind to the scavenger B1 (SRB1) receptor, and to the tetraspanine CD81 protein. These protein interactions produce a wave in the lipid membrane which leads the HCV particle to a narrow junction between hepatocytes.



Endocytosis

As HCV enter the near crossroad, CD81 interacts with claudin-1 (CLDN1), allowing the viral and hepatocyte cell membranes to pull inside into a clathrin-covered pit-like area. This process creates an internal endosome consisting of a viral particle protected by a host cell membrane, and a clathrin cage covers the entire endosome.

Fusion and uncoating

When the virus enters the cell, the endosome cage is dispersed around the clathrin, leaving the vesicle in the endosoma intact. In the endosome, the acidic pH induces a fusion between the viral membranes and host membranes in a mechanism called endosomal fusion. The event would cause the capsid shell to be uncoated and HCV RNA released to the cytosol in order to be translated and repeated.

Translation

As ribosomal subunits bind to HCV RNA in the rough endoplasmic reticulum, the process of translation of HCV polyproteins is begun. The ribosome-RNA complex is consequently fixed to the endoplasmic membrane of the reticulum and HCV polyprotein is completed. A single polyprotein, around 3,000 amino acids long, is produced during translation.

Proteolytic processing

In the rough endoplasmic reticulum, a viral proteolytic processing takes place. Initially, cellular proteases separated the main proteins E1, E2, and p7. The NS2 cysteine protease cleaves NS2 from NS3, along with the N-terminal end of the NS3 enzyme. NS3 then forms the protease complex NS3-4A, aided by the membran bound NS4A, and cleanses the remaining proteins (NS3, NS4A, NS4B, NS5A, NS5B). The end product is a mixture of 10 mature HCV proteins, structural and nonstructural.

RNA Replication

A variety of HCV proteins, perhaps in combination with host factors, allow the host-cell membranes to rearrange themselves into the membranous network — a combination of double-diaphragm vesicles. The NS5B RNA-dependent RNA polymerase catalyzes in the membrane-based network the synthesis of an intermediate, negative-sense RNA (template) for several copies of the HCV RNA positive-sensory progeny, which either are integrated into nuclear particles or used for RNA translation/replication. Multiple HCV nonstructural proteins help the RNA replication phase (replication complex).

Assembly

HCV particles form a nuclear cappuccin composed of core proteins in the HCV RNA. HCV particles assemble in close proximity to cytosolic lipid droplet (cLDL) and, with the aid of a host diacylglycerol acetyltransferase-1 (DGAT1) enzyme, form a nuclear capsule that consists of core proteins surrounding HCV RNA. At the same time, the ER synthesizes proteins from pre-very-low-density (pre-VLDLs) and the pre-VLDL transit to Golgi where they mature before packaging is brought.

Maturation

In Golgi, pre-VLDLs are thought to fuse to form VLDLs with large lipid golets of Triacylglycerol (TG). The VLDLs then fuse to form the HCV lipoviral particle with the high-density HCV precursors. In the specialist transportation vehicles known as multivarious species, this low-density lipovic H CV particle release the trans Golgi network (TGN). Multivisular bodies are transferred onto the cell surface by the cellular machinery. In the multivesicular body development, and in other post-assembly stages leading to the transition into the cell surface and release of lipoviral particle, the endosomal-sorting complex necessary for transportation (ESCRT) is of crucial importance.

Release
The lipoviral vesicles unite with the hepatocyte membrane after transportation through the cell surface of the multivariates containing the HCV lipoviral particles. The HCV lipoviral particle development is combined with the cellular VLDL pathway, which releases both the HCV lipoviral particles and the VLDL particles into the extracellular compartment during this process.

Transmission
Exposure to contaminated blood and blood products is a source of HCV transmission. A blood-transfusion, injection drug use, sexual intercourse, procedure and tattooing may cause HCV infection. A positive HCV antibody test suggests the presence of HCV RNA and anti-HCV antibodies in the serum and plasma and may signify a past or current infection. A positive HCV RNA test reveals that HCV infections are present. HCV may also be transferred from an infected mother to her son, although these are less frequent. Hepatitis C is not transmitted through breast milk, diet, liquids, or casual contact, such as hugs, kissing, and food or drinks.

Complications
The hepatitis C chronic stage can last for decades. Steatosis (chronic fat build up) and fibrosis (progressive tissue scarring) can damage the liver during this period. Both diseases often grow silently with little to no symptoms of disease in most patients. Final stage liver disease defined as the degree of significant damage to the liver that cannot function. Symptoms at this level are normally widely visible and frequently affect many structures of the organs such as the brain, kidney and upper digestive tract. 10 to 15% of those with a chronic infection of hepatitis C will develop an irreversible disease, known as cirrhosis, in which fibrose damage is such that it reduces blood flow to and from the liver.
Cirrhosis21 is classified according to the degree of impairment:
• Compensation Cirrhosis
• Decompensated Cirrhosis

Cirrhosis compensates for the liver's comparatively good function and can also show mild symptoms. Symptoms can include skin, muscles and joints, when the blood flow is limited and induces a rise in localized blood pressure called portal hypertension and the growth of bile and other toxins. Cirrhosis decompensated is a significant issue in which it is seriously weakened and unable to function due to a gradual scaring of the liver.

Stages of illness
After initial infection, the effect of HCV in the body changes over time. This is mainly because the virus proliferates, and can replicate inside the body and create multiple copies of itself. The development is also linked to the cumulative effect on the liver of the virus.

HCV infection stages:
• **Incubation period:** you might have been infected by the virus during this time, but you most probably have no symptoms. If you have symptoms, headache, tiredness or stomach discomfort may be included.
• **Acute hepatitis:** HCV can cause mild to severe disease from two to 12 months after the virus invades the body. About 15-20% of people exposed to the virus show acute infection symptoms. Presentation is often fluid and has little signs of liver damage. Every fourth individual will battle the virus successfully during this point.
Chronic hepatitis: most people with HCV are suffering from chronic hepatitis (hepatitis). Chronic infection occurs when the hepatitis C (HCV) virus does not vanish and persists in the body spontaneously. Some people experience chronic virus symptoms years after infection, without acute symptoms of hepatitis.
End Stage Hepatitis (EPH) - More complex disease type, including kidney failure and liver cancer, manifests with liver failure and a series of severe complications.

Hepatic damage testing
Doctors usually use one or more of the tests below to determine hepatitis C damage to the liver.
Magnetic resonance Elastography (MRE). M REM incorporates magnetic resonance imaging technology with sound wave patterns bouncing off the liver to create a visual map showing gradients of rigidity in the liver, which is non-inventive alternative to liver biopsy (see below). The hepatitis C chronic hepatitis C reveals the presence of liver scarring (fibrosis).
• **Transient Elastography**. Another non-invasive test is a form of ultrasound that transmits vibrations into the liver and tests the speed of its spread through the liver tissue for its rigidity to be estimated.
• **Liver biopsy**. This procedure involves inserting a fine night through the abdominal wall to extract a small sample of liver tissue for lab testing. This test is usually performed using ultrasound guidance.
• **Blood test**. The level of fibrosis in your liver is shown in a variety of blood tests.

Therapy
Medicines for antivirals
Infection of Hepatitis C is treated with antiviral drugs to get you rid of the virus. The purpose of your treatment is not to detect a hepatitis C virus within 12 weeks of the completion of your treatment.

Researchers have made considerable progress in hepatitis C treatment using novel antiviral drugs that are "direct-acting" even in conjunction with conventional medicines. As a result, patients have improved results, less side effects and less recovery times—some just 8 weeks. The choice of medications and treatment duration depend on the hepatitis C genotype and the existence of established hepatitis damage.

Recommendations for medicines and treatment regimens change quickly due to the speed of study. Therefore, it is best to speak to a doctor about your procedures.

Your care team will track your medication response during your treatment

4. LIVER TRANSPLANTATION

When you have developed severe hepatitis C-infection complications, liver transplantation could be an option. The surgeon removes the harmed liver and replaces it with a healthy liver during liver transplantation. The bulk of transplanted liver originates from dead donors, but there are only a limited number of living donors who donate part of their liver. Hepatitis C is mostly not treated by a liver transplant alone. The infection will probably return, and antiviral therapy is needed to avoid damage to the transplanted liver. Several studies found that new antiviral medicines that function directly are successful in the cure of hepatitis C after transplant. In correctly chosen patients before liver transplantation, treatment with direct antivirals can also be accomplished.

5. VACCINATION

There is no hepatitis C vaccine, the doctor would possibly prescribe hepatitis A and B vaccine. These viruses are separate, which can also damage the liver and make hepatitis C more difficult to chronic.

6. PREVENTIONS

You would possibly prescribe such lifestyle changes if you have a diagnosis of hepatitis C. These interventions help you stay safe for longer and also protect others' health:

- Avoid alcoholic drinks. The development of liver disease is increased by alcohol.
- Avoid drugs that could harm the liver. Check with your doctor about drugs, like medicines you take, herbal preparedness and dietary supplements. Avoid such drugs may be prescribed by your doctor.
- Help keep other individuals from coming into blood contact. Cover every wound and don't share the toothbrush or raspberry. Don't donate blood, body or semen and let health workers know you've got the virus. Tell your partner before having sex about your infection and always use condoms.

7. RESEARCH ON HEPATITIS C

While progress has been made, populations are difficult to treat and the appearance of resistant virus species indicates that research on new treatment options has been required. Some studies show that caffeine may enhance the hepatic function of patients with chronic HCV infection. Through in vitro research, the efficient inhibition of HCV replication at non-toxic concentrations has allowed caffeine to be a significant new anti-HCV agent. Many researchers use BVDV as a replacement model for HCV studies, since it propagates. Virus virus (BVDV). Similarities in the processes of reproduction, biodiversity and genetics. Many studies have looked for new natural products antiviral compounds. In the Brazilian research, for example, many marine and micro-organisms were isolated from the antiviral activity. This study showed that a Bacillus-given, sponge-isolated extract has antiviral activity and showed 98 percent inhibition and high selectivity rates during viral adsorption. Plant extracts were also tested as potentially producing new compounds for treating HCV. One survey that screened Brazilian plant species, for example, identified four compounds, a natural maytrenusiliifolia isolated alkaloid and three other Peperomia blanda compounds, which could dramatically reduce RNA and viral protein levels while replicating HCV. It has been only several decades since the hepatitis C virus was first identified. In that time, an extraordinary amount of progress has been made in the fight against this virus. Still, much needs to be done. Improved diagnostic tests are needed to identify people infected with HCV more precisely and less expensively than is possible today. Better ways to prevent transmission are urgently needed. With an astonishing 3 percent of the world's population infected with HCV, the most intense research is being done in the area of treatment. Current treatments eliminate the virus in only a little more than half of all patients. The drugs also have unwanted side effects that make it difficult or impossible for some patients to take them. In all these areas, rapid progress is being made. Here's an overview from several fronts in the battle against HCV:

New and more effective treatments

The Food and Drug Administration has approved a new two-drug combo named Harvoni, which combines sofosbuvir and another antiviral drug called ledipasvir, which offers a cure for hepatitis C in as little as eight weeks. Patients taking the new drug run a much lower risk of serious side effects associated with the standard treatment for hepatitis C. Unfortunately, the high cost of the medicine means that some patients who need it may not be eligible for it, but it has been hailed as a major breakthrough in hepatitis C treatment. Scientists are also improving existing drugs in significant ways. The development of pegylated interferon, or peginterferon, significantly increased interferon's effectiveness. By combining peginterferon with ribavirin, doctors are achieving even better results. A new version of ribavirin called viramidine (taribavirin) is under investigation and at least one study has shown that it triggers fewer side effects, including anemia, than the original ribavirin. It has not yet been approved by the Food and Drug Administration, but has shown some promise in clinical trials. Research on a hepatitis C-specific protease inhibitor called telaprevir also forecasts a new era in treatment. The New England Journal of Medicine reported on a study that showed significant improvement in the chances of being cured when telaprevir was added to the current standard therapy, and treatment took only half the time. Telaprevir is marketed under the names Incivek and Incivo.

Another drug that shows promise in clinical trials is the anti-cholesterol medication fluvastatin. A small study of veterans in 2008 found that fluvastatin may help to temporarily reduce hepatitis C levels. Now researchers will look at combining it with standard therapy in an effort to improve cure rates. Meanwhile, entirely new drugs are also being developed to fight HCV. Researchers hope to use the same model that has proved so successful in developing HIV/AIDS therapies -- targeting enzymes that the virus needs to reproduce. The specific drugs that fight HIV don't work against HCV, because the two viruses use different kinds of enzymes, but the same strategies are likely to work in conquering them. Extensive testing remains to be done before some of these new antiviral

drugs are approved. Still, the fact that so many are in the pipeline is encouraging, experts say. As new drugs become available, doctors will be able to create "cocktails" of treatments, much as they do for HIV-infected patients today. By individualizing therapy, doctors will be able to treat patients more effectively and with fewer side effects.

New ways to study hepatitis C

Although HCV grows quickly in the human liver, researchers have struggled to find ways to grow the virus in the laboratory. Recently, scientists developed strains of mice that can be infected with HCV, an advance that should help speed progress in understanding the virus and developing treatments. And scientists at the University of California, San Diego announced that they had succeeded in developing the first tissue culture of normal human liver cells that can be infected with the virus in the laboratory. This should facilitate more rapid testing of new drug candidates in the future.

More accurate diagnostic tests

Although existing tests to detect and measure HCV are highly sensitive and specific, they are not perfect. In some cases the tests fail to detect infections (false negatives). In other cases they show positive readings in people not infected, or in people whose bodies have actually eliminated the virus (false positives). Tests that measure the amount of virus in the blood, or viral load, vary widely in quality. Researchers are working on developing more reliable tests that would reduce false negatives and false positives. Another goal is to develop less expensive tests, for use in poorer countries, where cost can make testing prohibitive.

A vaccine against hepatitis C

The transmission of HCV through blood transfusions and organ transplants has been largely stopped, thanks to increasingly sophisticated screening tests. Now more must be done to prevent its spread among drug users. Needle exchange programs and counseling on safe methods to handle syringes could help. Ultimately, the gold standard for disease prevention is a vaccine. Vaccines "prime" the immune system to detect and destroy invading germs before they can gain a foothold. Some vaccines can even be used to treat people already infected with a virus by boosting their immune response. Unfortunately, experts are still far from developing a hepatitis C vaccine. The biggest challenge is the fact that hepatitis C virus is constantly changing its shape to elude immune detection. For this reason a vaccine that protects against one form of the virus may not protect against others. Still, the scientific community is making progress in identifying stable regions of the virus that do not change, and is exploring a variety of new approaches for developing vaccines.

Staying informed in a fast-changing field

The swift progress being made on many fronts offers encouragement to everyone infected with HCV. But rapid developments in medicine can also cause confusion and frustration. Preliminary results often make headlines years before new drugs are available. Popular articles may highlight positive results from studies and then fail to follow up when subsequent tests show problems with a new drug or treatment. Sorting through all the information in a fast-changing field like HCV research can be daunting. Two strategies can help you stay abreast of new developments without becoming overwhelmed: First, find a few reliable sources of information and stick with them. Web sites sponsored by federal health agencies like the National Institutes of Health are a good place to start, as they are frequently updated and experts carefully screen the information posted

8. CONCLUSION

Hepatitis C therapy has made significant progress in recent years, which has resulted in a rise in SVR rats, decreased treatment duration and reduced AEs. In spite of these advancements, however, it is necessary to discuss the drawbacks of available therapies. The fact that population groups are difficult to treat and that resistant viral species are evolving suggests that research on new treatment strategies is still needed. Analysis must also continue to find new substances with possible anti-viral activity and address the limitations of current therapies. Besides care, the importance of prevention and the need for global pacts must always be taken into account, so as to make these services available around the world.

9. REFERENCES

[1] Ly KN, Hughes EM, Jiles RB and Holmberg SD: Rising mortality associated with hepatitis C virus in the United States, 2003-2013. Cli Infect Dis 2016; 62(10): 1287-8.
[2] Allison RD, Tong X, Moorman AC, Ly KN, Rupp L, Xu F, Gordon SC and Holmberg SD: Chronic Hepatitis Cohort Study (CHeCS) Investigators. Increased incidence of cancer and cancer-related mortality among persons with chronic hepatitis C infection 2006-2010. Journal of Hepatology 2015; 63(4): 822-8.
[3] AASLDI: HCV Guidance: Recommendations for Testing. Managing and Treating Hepatitis C 2016.
[4] Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, Jewett A, Baack B, Rein DB, Patel N and Alter M: Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. Morbidity and Mortality Weekly Report: Recommendations and Reports 2012; 61(4): 1-32.
[5] Alter MJ and Margolis HS: Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease.
[6] World Health Organization. http://www. who. int/ mediacentre/factsheets/fs340/en.
[7] De Francesco R, Tomei L, Altamura S, Summa V, Migliaccio G. Approaching a new era for hepatitis C virus therapy: inhibitors of the NS3-4A serine protease and the NS5B RNA-dependent RNA polymerase. Antiviral Research 2003; 58(1): 1-6.
[8] Beaulieu PL and Tsantrizos YS: Inhibitors of the HCV NS5B polymerase: new hope for the treatment of hepatitis C infections. Current Opinion in Investigational Drugs (London, England: 2000) 2004; 5(8): 838-50.
[9] Lindenbach BD, Evans MJ, Syder AJ, Wölk B, Tellinghuisen TL, Liu CC, Maruyama T, Hynes RO, Burton DR, McKeating JA and Rice CM: Complete replication of hepatitis C virus in cell culture. Science 2005; 309(5734): 623-6.

[10] Fraser CS and Doudna JA: Structural and mechanistic insights into hepatitis C viral translation initiation. Nature Reviews Microbiology 2007; 5(1): 29.
[11] Fukushi S, Katayama K, Kurihara C, Ishiyama N, Hoshino FB, Ando T and Oya A: Complete 5′ noncoding region is necessary for the efficient internal initiation of hepatitis C virus RNA. Biochemical and biophysical research communications 1994; 199(2): 425-32.
[12] Targett-Adams P, Hope G, Boulant S and McLauchlan J: Maturation of hepatitis C virus core protein by signal peptide peptidase is required for virus production. Journal of Biological Chemistry 2008; 283(24): 16850-9.
[13] Ashfaq UA, Javed T, Rehman S, Nawaz Z and Riazuddin S: An overview of HCV molecular biology, replication and immune responses. Virology Journal 2011; 8(1): 161.
[14] Mohd Hanafiah K, Groeger J, Flaxman AD and Wiersma ST: Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013; 57(4): 1333-42.
[15] Roingeard P and Hourioux C: Hepatitis C virus core protein, lipid droplets and steatosis. Journal of viral hepatitis 2008; 15(3): 157-64.
[16] Roingeard P and Depla M: The birth and life of lipid droplets: learning from the hepatitis C virus. Biol Cell 2011; 103: 223-31.
[17] Williamson CD and Colberg-Poley AM: Access of viral proteins to mitochondria *via* mitochondria-associated membranes. Reviews in Med Virol 2009; 19(3): 147-64.
[18] Dubuisson J and Cosset FL: Virology and cell biology of the hepatitis C virus life cycle–an update. Journal of Hepatology 2014; 61(1): S3-13.
[19] Deleersnyder V, Pillez A, Wychowski C, Blight K, Xu J, Hahn YS, Rice CM and Dubuisson J: Formation of native hepatitis C virus glycoprotein complexes. Journal of Virology 1997; 71(1): 697-04.
[20] Weiner AJ, Christopherson C, Hall JE, Bonino F, Saracco G, Brunetto MR, Crawford K, Marion CD, Crawford KA, Venkatakrishna S and Miyamura T: Sequence variation in hepatitis C viral isolates. J of Hepatology 1991; 13: S6-14.
[21] Cocquerel L, Meunier JC, Pillez A, Wychowski C and Dubuisson J: A retention signal necessary and sufficient for endoplasmic reticulum localization maps to the trans-membrane domain of hepatitis C virus glycoprotein E2. Journal of Virology 1998; 72(3): 2183-91.
[22] Farci P, Bukh J and Purcell RH: The quasispecies of hepatitis C virus and the host immune response. In Springer seminars in immunopathology 1997; 19(1): 5-26.
[23] Penin F, Brass V, Appel N, Ramboarina S, Montserret R, Ficheux D, Blum HE, Bartenschlager R and Moradpour D: Structure and function of the membrane anchor domain of hepatitis C virus nonstructural protein 5A. Journal of Biological Chemistry 2004; 279(39): 40835-43.
[24] Flint M and McKeating JA: The role of the hepatitis C virus glycoproteins in infection. Reviews in Medical Virology 2000; 10(2): 101-17.
[25] Barth H, Cerino R, Arcuri M, Hoffmann M, Schürmann P, Adah MI, Gissler B, Zhao X, Ghisetti V, Lavezzo B and Blum HE: Scavenger receptor class B type I and hepatitis C virus infection of primary tupaia hepatocytes. Journal of Virology 2005; 79(9): 5774-85.
[26] Carrère-Kremer S, Montpellier-Pala C, Cocquerel L, Wychowski C, Penin F and Dubuisson J: Subcellular localization and topology of the p7 polypeptide of hepatitis C virus. Journal of virology 2002; 76(8): 3720-30.
[27] Sakai A, Claire MS, Faulk K, Govindarajan S, Emerson SU, Purcell RH and Bukh J: The p7 polypeptide of hepatitis C virus is critical for infectivity and contains functionally important genotype-specific sequences. Proceedings of the National Academy of Sciences 2003; 100(20): 11646-51.
[28] Fan X, Xue B, Dolan PT, LaCount DJ, Kurgan L and Uversky VN: The intrinsic disorder status of the human hepatitis C virus proteome. Molecular Bio Systems 2014; 10(6): 1345-63.
[29] Grakoui A, McCourt DW, Wychowski C, Feinstone SM and Rice CM: Characterization of the hepatitis C virus-encoded serine proteinase: determination of proteinase-dependent polyprotein cleavage sites. J of Virol 1993; 67(5): 2832-43.
[30] Dumoulin FL, von dem Bussche A, Li J, Khamzina L, Wands JR, Sauerbruch T and Spengler U: Hepatitis C virus NS2 protein inhibits gene expression from different cellular and viral promoters in hepatic and nonhepatic cell lines. Virology 2003; 305(2): 260-6.
[31] Erdtmann L, Franck N and Lerat H: The hepatitis C virus NS2 protein is an inhibitor of CIDE-B-induced apoptosis. J Biol Chem 2003; 278: 18256-64.
[32] Pawlotsky JM: Treating hepatitis C in "difficult-to-treat" patients. New England J of Medi 2004; 351(5): 422-3.
[33] Frese M, Pietschmann T, Moradpour D, Haller O and Bartenschlager R: Interferon-α inhibits hepatitis C virus subgenomic RNA replication by an MxA-independent pathway. J of General Virology 2001; 82(4): 723-33.
[34] Lin C, Thomson JA and Rice CM: A central region in the hepatitis C virus NS4A protein allows formation of an active NS3-NS4A serine proteinase complex *in-vivo* and *in-vitro*. Journal of Virology 1995; 69(7): 4373-80.
[35] Foy E, Li K, Wang C, Sumpter R, Ikeda M, Lemon SM and Gale M: Regulation of interferon regulatory factor-3 by the hepatitis C virus serine protease. Science 2003; 300(5622): 1145-8.
[36] Li X, Jeffers LJ, Shao L, Reddy KR, De Medina M, Scheffel J, Moore B and Schiff ER: Identification of hepatitis C virus by immunoelectron microscopy. Journal of Viral Hepatitis 1995; 2(5): 227-34.
[37] Sumpter R, Loo YM, Foy E, Li K, Yoneyama M, Fujita T, Lemon SM and Gale M: Regulating intracellular antiviral defense and permissiveness to hepatitis C virus RNA replication through a cellular RNA helicase, RIG-I. Journal of Virology 2005; 79(5): 2689-99.
[38] Sakamuro D, Furukawa T and Takegami T: Hepatitis C virus nonstructural protein NS3 transforms NIH 3T3 cells. Journal of Virology 1995; 69(6): 3893-6.
[39] Fujita T, Ishido S, Muramatsu S, Itoh M and Hotta H: Suppression of actinomycin D-induced apoptosis by the NS3 protein of hepatitis C virus. Biochemical and Bio-physical Research Communications 1996; 229(3): 825-31.

