HCV Genotypes

Information about hepatitis C genotypes, particularly 1, 2, 3, 4, and 6. This article originally appeared in the HCV Advocate

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This month's column is about hepatitis C (HCV) genotypes. I will discuss genotypes 1, 2, 3, 4, and 6. You will notice that I am not discussing genotype 5 since it was discussed last week. Genotype 7 is also not being discussed because only three people with genotype 7 have been identified—all found to be from the Democratic Republic of Congo.

According to the World Health Organization 130 – 150 million people worldwide have chronic hepatitis C and 350,000 – 500,000 die every year from complications of hepatitis C.

As mentioned above there have been seven genotypes identified but there are likely more that have not yet been found or classified. There is a 30 to 35% viral diversity or difference in the genetic make-up of the nucleotide sites of the virus that are used to classify them as different genotypes. This viral diversity is what makes it so difficult to develop one drug to treat all of the genotypes. There are new drugs called pan-genotypic that work on all of the genotypes that are being developed that might just produce high cure rates across all of the genotypes. The viral diversity i.e. genotype is another reason why it is going to be difficult to develop a therapeutic or a protective vaccine. There has been some early research that is encouraging.

All evidence points to that the hepatitis C virus originated in Africa and spread throughout Africa by various routes including the European colonization of Africa, unsafe medical practices to treat tropical diseases and various cultural practices. HCV spread out of Africa occurred by way of the slave trade throughout the World, needle reuse, organ transplantation, unsafe medical practices, unscreened blood, and injection drug use, etc.

Genotype 1

Genotype 1 is the most common genotype worldwide and accounts for approximately 46% of the total number of people with hepatitis C worldwide —83 million people. The prevalence of genotype 1 expanded greatly during the 20th century due to unsafe blood product/organ transplantation, unsafe medical practices and injection drug use.

Countries with the highest prevalence include East Asia (32,082,000), South Asia (12,889,000), Southeast Asia (4,910,000), Western sub-Sahara Africa (4,427,000), Eastern Europe (4,023,000),

Central Latin America (2,796,000), Central Asia (2,100,000) Genotype 1 has two main subtypes 1a and 1b. Genotype 1a accounts for about 55% of those with genotype 1 in the U.S. and 45% of those with genotype 1b. HCV 1a is more difficult to treat than HCV genotype 1b. The current standard of care for treating HCV genotype 1 can cure up to 90% to 100% of people who take the medications. The current standard of care treatment is HARVONI and VIEKIRA PAK.

Genotype 1 subtypes c through l have been identified but are uncommon

Genotype 2
Genotype 2 is the 3rd most common genotype worldwide and is also the 3rd most common one in the United States. The areas of highest prevalence of genotype 2 worldwide include central Latin America (754,000), high-income Asia Pacific (629,000), Southeast Asia (1,572,000), East Asia (8,444,000), Western sub-Saharan African (1,550,000) and western Europe (583,000).

Genotype 2 accounts for more than 16.5 million people worldwide with hepatitis C. Genotype 2 spread through the slave trade from Africa to the Americas and through trade routes from the Africa, the America and Asia.

The most common subtypes of genotype 2 are 2a, 2b, and 2c, so far there have been another 15 subtypes identified.

The standard of care for treating HCV genotype 2 is the combination of Sovaldi (sofosbuvir) plus ribavirin for a treatment duration of 12 weeks. The cure rates are 88% to 97%.

Genotype 3
Genotype 3 is the second most common genotype in the United States and worldwide. The areas with the highest prevalence of genotype 3 include Australasia (280,000), Central Asia (906,000), East Asia (5,762,000), Eastern Europe (1,881,000), High Income North America (492,000), and South Asia (39,706,000). The total number of people worldwide with genotype 3 is 54 million. Genotype 3 has been found to exist for 200 years.

Genotype 3 causes steatosis (fatty liver), insulin resistance (precursor of type 2 diabetes), and increases the risk of HCV disease progression and liver cancer.

So far there have been 10 genotype 3 subtypes identified—subtype 3a is the most common.

The current standard of care to treat genotype 3 is the combination of Sovaldi and ribavirin for a treatment period of 24 weeks. The cure rates are up to 83%. However, Sovaldi plus ribavirin doesn’t work as well in genotype 3 people with cirrhosis who are treatment experienced. There are, however, very good treatment options (see article in this issue on Sovaldi, pegylated interferon and ribavirin) and many new drugs are being developed to treat genotype 3.

Genotype 4
Genotype 4 is the 4th most common genotype worldwide and accounts for 90% (6,030,000) of the

hepatitis C population in Egypt—The HCV population of Egypt is estimated at 6.7 million. Africa and the Middle East account for the majority of genotype 4 infections. Approximately 1% of the U.S. population has genotype 4. Genotype 4 has many subtypes – a through o.

In Egypt the spread of hepatitis C genotype 4 was the result of a mass campaign in the 1960's through the 1980's to control schistosomiasis infection—a parasitic disease transferred by snails to humans wading in water while working in rice fields. During the 1960's through the 1980's people infected with schistosomiasis were treated with drugs using unsterilized and re-used syringes.

The current standard of care for treating HCV genotype 4 is the combination of Sovaldi (sofosbuvir), pegylated interferon and ribavirin. The treatment duration is 12 weeks and cure rates are up to 96%. There are many drugs that have been developed to treat genotype 4—by AbbVie and Merck—that are likely to be approved in the near future.

Genotype 6

Genotype 6 is mostly seen in Southeast Asia. The estimated number of people who are infected with genotype 6 is about 10,000,000—mostly in Asia. It is the most prevalent genotype in Laos and one of the most common genotypes in Vietnam. Genotype 6 is seen in countries outside of Asia, but mainly in populations that have emigrated from Asian countries.

Genotype 6a is the most common, but there been 26 subtypes identified so far.

There is no standard of care to treat genotype 6. In a study of 25 people who took Harvoni (sofosbuvir plus ledipasvir) for a treatment period of 12 weeks to treat genotype 6 resulted in a cure rate of 82%. The study included people who had never been treated and people who had been treated but had not been cured. There are many other drugs in development to treat genotype 6 including Merck's combination of grazoprevir/elbasvir.

The future is bright for the treatment of hepatitis C with more awareness of all of the HCV genotypes worldwide. There are many drugs under development to treat hepatitis C that are even more effective. Many of the newer drugs in development are pan-genotypic—that is they work against all genotypes and have the potential to cure all genotypes—these drugs could provide cures worldwide if we could only identify and treat everyone.

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