Extrahepatic Manifestations Glossary

Extrahepatic manifestation (EH) means conditions that exist outside the liver. These are conditions that are caused by the hepatitis C virus or are frequently seen in people with hepatitis C. It is important to know about these conditions and that many of these are uncommon. You can read about some of the extrahepatic manifestations in more detail here.

A

Arthralgia (joint pain): a common symptom of hepatitis C, but without inflammation of the joints usually associated with arthritis.

Arthritis: is a condition characterized by inflammation of the joints. Hepatitis C-related arthritis (HCVrA) is estimated to affect about 4% of the HCV population, but it may be much higher. Hepatitis C-related arthritis is classified into two groups – polyarthritis and mono-oligoarthritis. Polyarthritis is similar to rheumatoid arthritis but is less severe. Mono-oligoarthritis affects the medium and large-sized joints – typically the ankles.

B

Bechet's Disease: a disease that presents as ulcerations in the eyes, mouth, and genitals but can also affect any organ of the body. It is caused by coagulation and destruction of arteries and veins. This condition is rare.

Brain Fog: see cognitive dysfunction

C

Canities: a fading of hair pigment leading to white hair that is sometimes viewed as gray. The fading of hair pigment is seen in spots rather than on the entire scalp. This condition is rare.

Cardiovascular Diseases: diseases of the cardiovascular system linked to hepatitis C. However, the link is casual, but the relationship does provide enough information to recommend monitoring people with hepatitis C for cardiovascular disease**.**

Cerebral Vasculitis: a disorder characterized by inflammation and cell death of arteries in the brain. The cause of cerebral vasculitis is unknown, but it is thought to be caused by immune dysfunction. Vasculitis is a condition linked to hepatitis C. Cerebral vasculitis is very rare.

Cognitive Dysfunction: a condition commonly referred to as 'brain fog' that is common in a majority of people with chronic hepatitis C. The symptoms occur regardless of the stage of liver disease. The symptoms include problems with verbal learning, attention, executive functioning*and memory. There have been studies that indicate that HCV crosses the blood-brain barrier and HCV causes inflammation and damage to the brain. Larger studies are required to find out the extent of the damage posed by the hepatitis C virus. It is not known if curing HCV reverses or cures the damage.
**executive function is how to manage time, pay attention, switching focus, plan and organize, remember detail, avoid saying or doing the wrong thing, do things based on your experience*

Corneal Ulceration: an open sore in the outer layer of the cornea of the eye. Rare condition.

Cryoglobulinemia: one of the most common disorders associated with hepatitis C. Cryoglobulinemia is a blood disorder caused by abnormal proteins in the blood called cryoglobulins that precipitate or clump together when blood is chilled, and then proteins dissolve when warmed. The proteins are deposited in the small and medium-sized blood vessels, which restricts blood flow and can lead to further problems.

There is a blood test used to detect cryoglobulinemia, but it is important that the blood sample is kept at room temperature and handled carefully. Even though the markers for cryoglobulinemia are common in people infected with the hepatitis C virus, many people with hepatitis C do not have the symptoms or disorders associated with it.

The symptoms and disorders associated with cryoglobulinemia can be mild, moderate or severe. Symptoms of cryoglobulinemia include red or purple blotching skin and joint and generalized pain. Cryoglobulinemia can affect the skin, kidneys, nerves and joints. Conditions associated with cryoglobulinemia include vasculitis (inflammation of the blood vessels), peripheral neuropathy, Reynaud's Phenomenon (hands that are sensitive to cold temperature and turn white, red, blue), and Non-Hodgkin's lymphoma (cancer of the lymphatic tissues). Treating cryoglobulinemia consists of treatment of the underlying disease (hepatitis C) as well as the administration of medications to suppress the immune system, and plasmapheresis (blood is taken from the body, filtered and returned to the body). Treating the underlying cause – hepatitis C – resolves or improves this condition.

Recent studies have found that treating hepatitis C with direct-acting antiviral medications are safe and effective to treat cryoglobulinemia.

D

Depression: is a mental health illness. The hepatitis C virus is believed to affect the central nervous system and pass through the blood-brain barrier causing inflammation, depression, fatigue and cognitive issues.

Dermatomyositis: a disease characterized by muscle weakness and skin rash. It is an uncommon condition.

Diabetes mellitus type 2: a disease that affects the body's ability to produce or use insulin. Insulin is a hormone. Diabetes type 2 prevalence is higher in people with hepatitis C than in people without HCV. Diabetes type 2 is a leading cause of death in the general population and can increase HCV disease progression including liver cancer.

E

Erythema Multiforme: a recurring skin condition associated with certain infections. It is characterized by skin eruptions, raised papules and lesions.

Erythema Nodosum: a form of skin inflammation located in a part of the fatty layer of the skin. It is reddish, tender lumps usually found in the front of the legs below the knees. They may last for weeks to months and when they disappear they may leave a bruised appearance.

F

Fatigue: is the most common symptom of hepatitis C and can range from mild to moderate to debilitating. It is believed to be caused by many factors including the effect of the hepatitis C virus, the immune system and the central nervous system.

Fibromyalgia: a disorder characterized by aches, pain, stiffness, soft tissue tenderness, general fatigue and sleep disturbances. Pain is the most common symptom of fibromyalgia, and it is believed to be confined to muscles and ligaments. Although fibromyalgia has not been directly linked to hepatitis C, it is a condition that is more commonly

found in people with hepatitis C than in the general population. Fibromyalgia is believed to be triggered by viral infections. A comprehensive approach with many different healthcare providers (including the person suffering from Fibro) is the best strategy.

H

Head and Neck Cancers: an association of head and neck cancers were found in people with hepatitis C that begin in and around the throat, and mouth.

Hypertrophic Cardiomyopathy (HCM): a form of heart disease when one chamber of the heart is larger and thicker. The condition is uncommon in people with hepatitis C and is not believed to cause illness.

I

Inclusion Body Myositis (IBM): a progressive group of muscle diseases that usually occurs in people over 60 years old (but not always). In one study IBM was found to be higher in people with hepatitis C than in the general population.

Immune Thrombocytopenic Purpura (ITP): an autoimmune bleeding disorder caused when blood does not clot. Symptoms of ITP are bruising of the skin as well as bruising under the skin that appears as red or purple dots on the skin. In severe cases, bleeding occurs from the nose, gums, and gastrointestinal or urinary systems. Increased prevalence of ITP occurs in people with HCV.

Insulin Resistance (IR): a condition caused by the inability of cells to absorb glucose. This leads to the pancreas releasing more insulin creating an excess of glucose and insulin in the bloodstream. HCV can induce IR. Insulin resistance can increase HCV disease progression. Uncontrolled IR can lead to diabetes.

K

Kidney: the liver and the kidneys work together to remove substances from the body. Mixed cryoglobulinemia can cause kidney damage. Severe HCV disease progression causes damage to the kidneys.

L

Lichen Myxedematous (LM): also known as papular mucinosis. LM is a rare chronic condition that has been linked to HIV infection, hepatitis C infection, and exposure to toxic oil and contaminated L-tryptophan. LM is characterized by small papules (bumps) that affect the face, trunk, and extremities that can progress to skin tightening and hardening.

Lichen Planus: a skin disorder that is characterized by small elevated bumps or pimples that usually appears on flexor surfaces (the muscle that brings two bones together, causing flexion of the part) – arms, trunk, genitals, nails, and scalp. Symptoms include scaling, itching, hair loss, skin lesions, plaque, and pain. Lichen Planus has been found in 16% of hepatitis C patients (WebMD). Hepatitis C-related lichen planus is caused by HCV replication in epithelial (skin) cells. Treatment of LP consists of treating the underlying cause (hepatitis C), but no studies have been conducted with HCV direct acting antiviral medications. Cortisone creams/ointments and cortisone injections are used to manage LP. Avoid substances that can trigger a flare-up including alcohol, tobacco, spicy foods, peppermint, cinnamon, citrus type foods and stressful situations.

Lung Abnormalities and diseases: various diseases triggered by hepatitis C. **Idiopathic Pulmonary Fibrosis** is defined as scarring of the lungs. **Chronic Obstructive Pulmonary Disease (COPD)** involves two diseases – **chronic bronchitis** and **emphysema**. **Asthma** is a chronic disease that inflames and narrows the airways. **Hypoxemia** is a condition in which there is an abnormally low amount of oxygen in the blood due to the inability of the lungs to perform their chief function of gas exchange.

M

Membranoproliferative Glomerulonephritis (MPGN): a condition affecting the kidneys usually (but not always) associated with cryoglobulinemia. Symptoms include weakness, edema (swelling of the extremities) and arterial hypertension (high blood pressure in the arteries that go to the heart and lungs). Treatment consists of treating the underlying cause – hepatitis C. However, if there is severe kidney impairment, ribavirin should be avoided.

Membranous Nephropathy: a kidney disease associated with hepatitis C but not with cryoglobulinemia. It is caused by circulating HCV antibodies and viral particles deposited in the kidneys. Treatment consists of treating the underlying disease –hepatitis C. If there is severe kidney damage then the use of ribavirin is usually avoided.

Mooren Corneal Ulceration: a disease that can cause pain, inflammation, tearing and loss of sight. The association between Mooren Corneal Ulceration and hepatitis C has not been established. A disease that is uncommon in people with hepatitis C.

Multiple Myeloma: a form of cancer of the plasma cells in the bone marrow that causes excessive growth of the plasma cells. This interferes with the production of red and white blood cells and platelets, and can cause anemia, infections, and bleeding.

N

Neutropenia: is an abnormally low white blood cell (neutrophils, lymphocytes, monocytes, eosinophils, and basophils) count. Decreased production of white blood cells can lead to increased risk for infections.

Non-Hodgkin's Lymphomas (NHL): are cancers of lymphoid tissues. NHL can be low-grade (slow growing) or high-grade (rapidly growing) cancer. NHL is uncommon, but the incidence of NHL is higher in people with hepatitis C than in the general population.

P

Paresthesia: are sensations of tingling, prickling, or numbness of skin. The exact cause of HCV-related paresthesia is unknown, but it has been linked to other conditions more commonly found in people with hepatitis C such as fibromyalgia, peripheral neuropathy, and hypothyroidism.

Parkinson's Disease: a disorder of the central nervous system that affects movement, that usually includes tremors. One large study found an association between hepatitis C and Parkinson's disease.

Peripheral Neuropathy (PN): a disorder characterized by numbness, burning, pins and needles sensations, crawling skin, and itching that occurs most often in the hands and feet, but can appear in other areas of the body. People with HCV-related PN should be tested for Cryoglobulinemia.

One study found that 15.3% of people with HCV had PN. Treatment consists of treating the underlying disease (HCV) to prevent further damage. The damage of PN seldom is reversed. It is helpful to avoid any substances

(medications, alcohol, certain herbs/supplements) that cause or make it worse. Other infections that can cause PN include diabetes, HIV, Lyme disease, shingles, and Epstein-Barr.

Polyarteritis nodosa: is a type of vasculitis. The association between hepatitis C and polyarteritis nodosa has not been established. An uncommon condition.

Polymyositis: is a chronic disease of the muscles. The association between hepatitis C has not been established. An uncommon condition.

Porphyria Cutanea Tarda (PCT): a skin disorder caused by the reduced activity of an enzyme resulting in an overproduction and build-up of the protein uroporphyrinogen in the blood and urine of patients. Hepatitis C has been suggested as one of the causes. Other causes include hereditary hemochromatosis (accumulation of iron in the liver), heavy alcohol use and estrogens. Characteristics of PCT develop in areas that are exposed to the sun with resulting skin lesions (blisters) on the hands, forearms, back of the neck and face. PCT can also cause skin discoloration, either darkening or lightening of the skin, increased facial hair, thickening of the skin, and alopecia (hair loss). Treatment of PCT can involve phlebotomy, dietary iron restriction, reducing alcohol consumption, avoiding exposure to the sun or the use of sunscreen, and avoiding or minimizing estrogen exposure.

Prostate Cancer: Men with hepatitis C were found to be at an increased risk for prostate cancer in one study.

Pruritus: a common symptom reported by people with hepatitis C (15%), but the severe type is more commonly found in persons with the end-stage liver disease. Pruritus is itching that may be localized to a specific part of the body such as hands and feet, but it can also be a generalized itching all over the body. It can be related to high bilirubin levels, autoimmune disease or dry skin, and can be a side effect of treatment. Use of moisturizing lotions, oatmeal baths or lotions, antihistamines, and cortisone creams and opiate drugs can help.

Psoriasis: a chronic condition of the immune system that can range from mild to moderate to severe. It is uncommon in people with hepatitis C. The association between hepatitis C and psoriasis has not been established.

R

Raynaud's Syndrome: a disorder that causes the blood vessels in the fingers, toes, ears, and nose to constrict or narrow from sensitively to cold temperatures. Treatment consists of managing the condition since there is no cure for Raynaud's.

Rheumatoid Arthritis (RA): is a type of autoimmune disease that usually affects wrists and hands but can also affect other joints. In people with hepatitis C it is hard to distinguish between hepatitis C-related arthritis and RA, but there are specific tests to identify RA.

S

Sialadenitis: an inflammatory disease that causes dry mouth and eyes. It is associated with hepatitis C infection. Sialadenitis destroys the salivary glands.

Sjogren's Syndrome (SS): is an autoimmune disease that affects the eyes and mouth, making them dry. Although hepatitis C has not been directly linked to SS, it is found more often in people with hepatitis C than in the general population. There is no cure for SS. Treatment consists of managing or lessening the symptoms.

Spider Nevi: small red dots that appear on the skin with radiating lines resembling a spider web. Spider nevi can be found anywhere on the body but usually affects the face and trunk.

Steatosis (Fatty Liver): fatty infiltrates of the liver. Viral steatosis is caused by genotype 3 and may lead to faster HCV disease progression and can lead to liver cancer. Successful HCV treatment that leads to a virologic cure reduces or eliminates fatty liver in people with genotype 3. A common condition in people with hepatitis C and the general population.

Systemic Lupus Erythematosus (SLE): an autoimmune disease. The exact cause of SLE is unknown. An autoimmune disease is when the immune system mistakenly recognizes proteins in the blood as foreign invaders and destroys normal proteins. Symptoms vary widely from patient to patient as do episodic attacks or flare-ups. The disease usually attacks one organ, but over time other organs can be affected and after many years SLE can lead to serious health problems and death. There are many strategies for managing SLE including the use of NSAIDs, acetaminophen, corticosteroids, immunomodulating drugs, and anticoagulants. An uncommon condition in people with hepatitis C.

T

Thrombocytopenia: low platelets defined as a platelet count below 100,000 to 150,000 cells per microliter of blood. The normal range of platelets is between 150,000 and 450,000 cells per microliter of blood. Most studies have found a correlation between the stage of fibrosis and thrombocytopenia in HCV patients. Platelets are proteins that help the blood clot.

Thyroid Disease: are diseases of the thyroid gland caused by different factors including hyperthyroidism (too much thyroid hormone) and hypothyroidism (too little thyroid hormone) released by the thyroid gland. The direct link between hepatitis C and thyroid disease (usually hypothyroidism) is unclear, but thyroid disease is found more commonly in people with hepatitis C than in the general population. Thyroid disease is common in people with hepatitis C.

V

Vasculitis (essential cryoglobulinemic vasculitis): an inflammation of blood and lymphatic vessels and is caused by cryoglobulins – antibodies that precipitate (clump together) under cold conditions and dissolve on rewarming. Vasculitis is associated with hepatitis C-related cryoglobulinemia (see cryoglobulinemia above). Symptoms include purpura (discoloration of the skin caused by bleeding vessels) petechiae, (pinpoint red rash caused by minor hemorrhaging), and usually affects the lower extremities of the body. Other symptoms include fever, itching welts, muscle aches and pain, enlarged lymph nodes as well as peripheral neuropathy. Treatment consists of treating the underlying cause (HCV) with direct-acting antiviral medications with good results. Other treatment options include the use of immunosuppressive drugs. Vasculitis can also affect other organs such as the kidneys, liver, lungs, heart and central nervous system, but this is uncommon. A skin biopsy that shows inflammation of the small blood vessels indicates vasculitis. Another type of vasculitis, leukocytoclastic vasculitis, is also associated with hepatitis C. An uncommon condition.

Vitiligo: a condition in which there is a loss of pigmentation – usually around the mouth, eyes, nose, elbows, knees and wrists. An uncommon condition.

W

Waldenstrom Macroglobulinemia (WM): a chronic type of low-grade cancer of the lymph cells. Treatment of WM depends on the degree of disease progression. An uncommon type of cancer.