Dr. Zevin pointed out that educational materials often describe "hepatitis c is asymptomatic...." This is false for many people with hepatitis C infection. The spectrum of symptoms and manifestations of hepatitis C is wide. The presentation presented an overview of extrahepatic syndromes related to hepatitis C, the harm and disability they cause, and some suggested approaches to dealing with them. Dr. Zevin talked from his experiences as a physician who has worked with homeless people and substance users for the past 15 years. This session described the effects of hepatitis C from head to toe (confusion to neuropathy), and from inside out (abdominal pain to skin rashes), and everything in between (bone thinning, blood problems, fatigue,...). The goal of this presentation was to teach the participants how to advocate for recognition of these symptoms from health care providers and disability assessors. The presentation reviewed approaches to avoiding symptoms, treating symptoms, and the role of anti-viral treatment.

Hepatitis C and Skin

There are many extrahepatic conditions associated with hepatitis C that affect the skin. Porphyria cutanea tarda, Palpable purpura/leukocytoclastic vasculitis, lichen planus, urticaria, pruritus, pruigo nodularis, psoriasis and more.

**Porphyria Cutanea Tarda (PCT)** is a skin condition where the skin is easily bruised and blistered. In addition the pigmentation of the skin may be increased or decreased. The causes of PCT include hepatitis C, iron overload, alcoholic liver disease, and estrogen exposure for people with an underlying genetic predisposition. PCT can be treated with therapeutic phlebotomy (if caused by iron overload) and successful treatment of the underlying HCV disease. In addition, other measures can be taken to control this condition such as avoiding exposure to the sun (use sunscreen), avoid or reduce alcohol use, and avoid or minimize estrogen exposure.

**Palpable purpura/leukocytoclastic vasculitis** is a skin condition associated with Mixed Cryoglobulinemia (discussed later). Symptoms usually include arthralgia (joint pain) and other rheumatologic symptoms. Rarely Systemic Vasculitis is seen in people with HCV. Purpura is characterized by hemorrhages of the skin that shows up as red, darkening into purple, then brownish-yellow and may disappear after 2-3 weeks unless the area is under pressure. Usually purpura are on the lower extremities of the body and may eventually ulcerate. The diagnosed of purpura is made by recognition of rash, a skin biopsy and follow up with tests for associated conditions. Treatment usually consists of treating the underlying cause such as hepatitis C or with immunosuppressive agents.

**Lichen planus** is a skin disorder that begins with pin-sized papules (small elevated bumps or pimples) that usually appear on flexor surfaces (the muscle that bring to bones closer together, causing flexion of the part) arms, trunk and genitals. Consultation with a dermatologist is recommend with skin biopsy if necessary. Treatment consists of controlling itching with corticosteroid creams or if severe injections of corticosteroids.

**Rheumatology** associated with hepatitis C presents with symptoms such as arthralgia (joint pain), myalgia
(muscle pain) are frequently seen in patients with hepatitis C that may affect a few or many joints/muscles. In some, muscle and joint pain can be severe and quite disabling. Patients usually describe symptoms as aching or sharp pains and should be checked for true arthritis, hemochromatosis and/or Mixed Cryoglobulinemia.

The most effective treatment or relief from these the symptoms are gentle stretching and exercise. Many people use complimentary medicine approaches such as acupuncture, osteopathic or chiropractic medicine. Acetaminophen (Tylenol) in doses less than 2 grams per day may be better than NSAID’s (aspirin, ibuprofen, etc). Opiates may be difficult to use in people with underlying addiction but are appropriate in severe cases. Identify and treat depression which has a tendency to cause increased symptoms.

**Mixed Cryoglobulinemia Type II and III** is caused by cryoglobulins that are a type of abnormal antibody circulating in the bloodstream. Cryoglobulins in the blood are exceedingly common in people with hepatitis C but disease symptoms are less common and usually moderate. Symptoms can include vasculitis (inflammation of the blood vessels), peripheral neuropathy (usually sensory, rarely motor), joint pain and inflammation, Reynaud’s Phenomenon (hands that are sensitive to cold temperature and turn white, red, blue) and can affect the kidneys. There is a blood test to specifically identify cryoglobulinemia. The blood test must be done under special conditions and therefore the blood drawing can usually only be done at a lab. Treatment usually consists of treating the underlying disease (hepatitis C), immunosuppressive measures, and plasmapheresis (blood is taken from the body, processed and returned to the body). People with cryoglobulinemia should be evaluated for lymphoma.

**Sicca syndrome** is characterized by dry mouth, dry eyes, salivary gland lymphocytic infiltration that can cause problems such as cavities and other conditions of the mouth and eyes. There is a test to identify sicca syndrome but usually a history and physical exam will suffice. The most effective ways to improve this condition is by sucking on sugarless hard candies and the use of artificial tears and saliva. It is important to attend to proper dental hygiene including brushing and flossing. Some medications and smoking tobacco and especially cannabis can make this condition worse. It is also important to drink plenty of water to avoid dehydration. Visit [http://www.seattle-dentist.com/xerostomia.htm](http://www.seattle-dentist.com/xerostomia.htm) for information on medications that will make dry mouth worse.

**Hepatitis C and the Nervous System**

There are some nervous system disorders that people with hepatitis C experience such as peripheral neuropathy, some psychiatric conditions and neuro-cognitive impairment.

**Peripheral neuropathy** is characterized of numbness, burning, needles and pins sensations that are most often in the hand and feet. The diagnosis is usually made by history and physical exam, but electro-physiologic studies may be helpful. Cryoglobulins should be measured in cases of severe neuropathy or neuropathy with other signs of vasculitis. Treatment consists of treating the underlying condition (HCV) and avoiding medications which cause or worsen neuropathy. Avoid or reduce alcohol intake and complementary medicine approaches may be useful. There are various anti-epileptics, tricyclic anti-depressants or Vanlafaxine in addition to local measures such as local anesthetic patches used to treat or control this condition. Acetaminophen may be preferable to NSAID’s and opiates should be considered for severe intractable pain.

Some common psychiatric conditions such as depression, anxiety, somatization all seem to be increased in people with hepatitis C compared to other chronic illnesses. These conditions are increased regardless of drug/alcohol users (active or past). Treatments can be effective and can improve quality of life. These conditions can usually be diagnosed by careful history and adequate surveys and questionnaire tools may be helpful. It is helpful to use hints such as amplification of symptoms, fatigue, pain and difficulty concentrating as prompts to take a careful history of depression. The usual treatments of psychotherapy and psychopharmacology are effective, but hepatotoxic medications or medications which can exacerbate
Neuro-cognitive impairment is usually seen as memory loss, difficulty concentrating or thinking clearly. These symptoms seem to occur regardless of the severity of liver damage. Clinical and subclinical hepatic encephalopathy are important in patients with cirrhosis. Cognitive dysfunction can be demonstrated with careful neuro-psychological testing in patients with severe or mild liver disease. Abnormal brain activity on functional (e.g. IH MRS) testing similar to that seen in people with HIV. Brain fog is a common complaint in people with HCV. A careful history related to functional ability (concentration/memory) should be taken along with neuro-psych testing. Other causes of cognitive impairment should be ruled out. The treatment usually consists of treating underlying cause (HCV), and depression. The degree of functional disability should be assessed for disability benefits. Caution should be used with herbs and smart drugs.

Endocrine Conditions – Diabetes, Thyroid, Osteoporosis

There is evidence that indicates that Diabetes (DM) occurs more frequently in people with chronic hepatitis C. However, these individuals have similar risk factors and manifestations as others with Type II DM. It is recommended that people avoid or closely monitor DM drug that are hepatotoxic.

Anti-thyroid antibodies are common in people with HCV, but clinical/subclinical thyroid disease is uncommon except during interferon treatment. TSH should be checked in all patients especially if fatigue and other symptoms are present. Before starting treatment TSH, T4, antithyroid should be checked before starting thyroid therapy.

Osteoporosis is common in cirrhosis and more common in liver disease caused by HCV than other liver diseases and is seen in both men and women. There are currently no recommendations for monitoring and/or testing of osteoporosis in place.

Endocrine effects of cirrhosis can present as decreased testosterone in men with decrease libido, erectile dysfunction, gynecomastia (enlargement of the breast tissue in men). Women can experience amenorrhea (menstrual abnormalities). Insulin resistance and diabetes can occur in the later stage of cirrhosis. Fluids retention and blood pressure should be monitored regularly.

Hepatitis C and Cancer – Hepatocellular Carcinoma, Lymphoma/B-cell lymphoproliferative syndromes

Hepatocellular carcinoma (HCC) is cancer of the liver. In hepatitis C this occurs in the setting of cirrhosis. Patients with cirrhosis should be regularly screen for HCC.

Lymphoma/B-cell lymphoproliferative syndromes many be more common than previously thought especially in the presence of Mixed Cryoglobulins. Treatment of underlying cause (HCV) may cure it.

Hepatitis C and the Digestive Tract

Abnormal pain and nausea are common symptoms at all stages of HCV. Other symptoms may include weight loss, diarrhea, vomiting, and GI bleeding, and should prompt a work up for other conditions. Liver pain is common and due to stretching of Gilsson’s capsule which encases the liver.

Fatigue and Hepatitis C

There are many causes of fatigue but most fatigue seems to be directly attributable to HCV. Some of the underlying causes can be from insignificant sleep, the crash from stimulant use, depression, thyroid dysfunction and other causes. Treat fatigue by optimizing co-occurring conditions. Careful assessment and documentation of fatigue will help guide treatment advice and help patients obtain disability benefits. Additional treatments which may help with improving fatigue are exercising to tolerance level avoiding push-
crash phenomenon, establishing a manageable daily routine. Patients should try body work and acupuncture. Patients should education themselves and family/work/social group about their fatigue and how it affects their daily lives..

Quality of Life

HCV in all stages has been linked to a decrease in quality of life (QOL). Improvements in QOL are seen when extrahepatic manifestations are treated. Improvements are usually seen when HCV treatment is given especially when a sustained virological response is achieved. Finally, decreases in QOL can be dramatic during treatment period.

Recommendations for Liver Care:

- Avoid alcohol and other hepatotoxins
- Low quantity alcohol consumption is clear better than high quantity. Degree to which none is better than a little is unknown
- Care should be used when using acetaminophen (Tylenol):
  - Limit dose to 2 grams and day
  - Alcohol omeprazole, phenytoin, isoniazid may potentiate acetaminophen hepatotoxicity
  - Beware of acetaminophen present in numerous over the counter medications and prescription drugs

Non-prescription products containing acetaminophen

- Actifed®: Cold & Allergy, Sinus
- Alka-Seltzer Plus®: All Products
- Anacin®: Aspirin Free Formula
- Benadryl®: Allergy Sinus Headache; Severe Allergy & Sinus Headache
- Comtrex®: All Products
- Contac®: Severe Cold and Flu Maximum Strength Caplets, Non-Drowsy Caplets, Day & Night Cold & Flu
- Coricidin®: D Cold, Flu & Sinus Tablets, HBP Cold & Flu Tablets
- Dimetapp®: Non-Drowsy Flu Syrup
- Dristan®: Cold Multi-Symptom Formula
- Drixoral®: Allergy Sinus, Cold & Flu Excedrin®: All Products
- Feverall®: Suppositories
- Goody's® Powders: All Products
- Midol®: Maximum Strength Menstrual Formula, Maximum Strength PMS Formula
- NyQuil®/DayQuil®: Cold/Flu Relief Liquid and LiquiCaps
- Pamprin®: All Products
- Percogesic®: All Products
- Robitussin: Cold, Multi-Symptom Cold & Flu, Multi-Symptom Honey Flu Liquid, Nighttime Honey Flu Liquid
- Sinutab® Sinus: Sinus Allergy Medication Maximum Strength Formula
- Sudafed®: Cold & Cough Liquid Caps, Cold & Sinus Liquid Caps, Severe Cold Caplets and Tablets, Sinus Caplets and Tablets
- Tavist®: Sinus Non-Drowsy Coated Caplets
- TheraFlu®: All Regular and Maximum Strength Caplets and Hot Liquid
- Triaminic®: Cold, Cough & Fever Liquid, Cough & Sore Throat Liquid, Cough & Sore Throat Softchews
- Tylenol®: Allergy Sinus Formula, Severe Allergy; Arthritis Pain Extended Relief; Cold Formula, Cold & Flu; Extra Strength Pain Reliever; Flu Formula; Maximum Strength Sore Throat Adult Liquid; PM Pain Reliever/Sleep Aid; Regular Strength; Sinus; Women’s Tylenol
- Vanquish®: Caplets
- Vicks®: Vicks 44M Cough, Cold & Flu Relief Liquid and Liquicaps
NSAIDS

**NSAID’s are associated with non predictable idiosyncratic hepatotoxicity**

- Aspirin, diclofenac, sulindac may be worst
- COX2 (Celebrex, Vioxx, Bextra ) inhibitors are also associated with hepatotoxicity
- Avoiding all NSAID’S in patients with Cirrhosis may be advised due to tendency to increase GI bleeding and perturb fluid balances

**Non-prescription Drugs containing NSAID’S**

**Advil®**: Cold and Sinus Caplets and Tablets; Ibuprofen Tablets, Caplets, and Gel Caplets; Flu and Body Ache Caplets; Migraine Liquigels

**Aleve®**: Tablets, Caplets, and Gelcaps; Cold and Sinus Caplets

**Alka-Seltzer®**: Original, Extra Strength, Cherry, and Lemon/Lime Effervescent Antacid and Pain Reliever; Alka-Seltzer PM

**Bayer®**: Regular Strength, Extra Strength Tablets

**Anacin®**: Extra Strength Tablets & Caplets, Extra Strength Plus Aspirin Caplets, Extra Strength PM Aspirin Plus Sleep Aid, Extra Strength Arthritis Pain Regimen Formula, Extra Strength Aspirin Caplets & Tablets, VANQUISH Caplets

**BC®**: Arthritis Strength Powder, Allergy Sinus Cold Powder, BC Powder, Sinus Cold Powder

**Bufferin®**: All Products

**Dristan®**: Sinus Pain Formula

**Ecotrin®**: Enteric Coated Aspirin Regular Strength, Enteric Coated Aspirin Maximum Strength

**Excedrin®**: Extra Strength Migraine Caplets, Geltabs, Tablets; Migraine Tablets

**Goody's®**: Body Pain Formula Powder; Extra Strength Headache Powder; Extra Strength Pain Relief Tablets

**Halfprin®**: Tablets

**Midol®**: Maximum Strength Cramp Formula Tablets

**Motrin®**: IB Caplets, Tablets, and Gelcaps; IB Pain Reliever/Fever Reducer Tablets, Caplets, and Gelcaps; Migraine Pain Caplets; Sinus/Headache Caplets

**Orudis®**: KT Tablets

**Prescription Products Containing NSAID's***

Alor®5/500 Tablets
Anaprox®Tablets, DS Tablets
Ansaid®Tablets
Arthrotec®
ASA w/Codeine
Butalbital, Aspirin, Caffeine, and Codeine Phosphate Capsules
Carisoprodol and Aspirin Tablets
Cataflam®Tablets
Celebrex®Capsules
Choline Magnesium Trisalicylate Tablets, Liquid
Clinoril®Tablets
Darvon®Compound-65, Pulvules®
Daypro®Caplets
Diclofenac Potassium Tablets
Diclofenac Sodium, XR Tablets
Disalcid™ Capsules and Tablets
Dolobid®Tablets
Easprin®Tablets
EC-Naprosyn®Delayed Release-Tablets
Possible Hepatotoxins - Other medications

◆ Iron – avoid iron and iron containing supplements
  ■ OK if definitely iron deficient from bleeding
◆ Lipid-lowering agents: statins, nicotinic acid (niacin; Nicolar)
◆ Antidiabetic agents: acarbose (Precose), pioglitazone (Actos), sulfonylureas
◆ Antibiotics: amoxicillin clavulanate potassium (Augmentin), erythromycin, isoniazid (INH), nitrofurantoin (Furadantin), tetracycline
◆ Antifungal agents: fluconazole (Diflucan), itraconazole (Sporanox), ketoconazole (Nizoral)
◆ Antiviral agents: neveripine, efavirenz, PI’s, AZT, DDI
◆ Retinoids: etretinate (Tegison)
◆ Anticonvulsant agents: phenytoin (Dilantin), valproic acid (Depakene)
Psychotropic agents: nefazadone (Serzone), bupropion (Wellbutrin), chlorpromazine (Thorazine), tricyclic antidepressants
Hormones: tamoxifen (Nolvadex), testosterone
Others: halothane (Fluothane), methotrexate (Rheumatrex)

Possible Toxicities - Herbals / Vitamins

- Amanita species
- Asafetida
- "Bush" herbal teas
- Chaparral
- Comfrey
- Echinacea
- Gentian
- Germander
- Iron
- Jin bu huan
- Kalms tablets
- Mistletoe
- Nicotinic acid (niacin; Nicolar)
- Pennyroyal oil
- Senna fruit extracts
- Valerian
- Vitamin A