Hepatitis C
It’s About More than Liver Disease

May 2, 2018
Housekeeping: GoToWebinar

• Slides and a recording of the webinar will be sent to everyone who registered and posted on our website.

• Please use the question box to submit your questions and comments

• The Q&A session will follow the last presentation
Webinar Overview

• About NVHR
• Project overview
• Speakers:
  – Dr. Zobair Younossi
  – Laura Stillman
  – Dr. Kristen Lee
  – Randy Madara
• Discussion and questions and answer
About NVHR

• National Viral Hepatitis Roundtable
  – working together to eliminate hepatitis B and C in the U.S.

• ~500 coalition members
  – community-based, advocacy, and grassroots groups
  – healthcare providers
  – health departments
  – other government and industry partners

• www.nvhr.org
NVHR’s Program Department

• Capacity-Building and Technical Assistance
  – Support for groups conducting screening in community-based settings
  – Templates and support for implementing routine screening
• Webinars, Fact sheets, online resources
• Working Groups HCV Treaters & Pharmacists
• Community stakeholder engagement in PCORI studies
• Mini-grants
  – Technical assistance and $10K financial support
Inspired by experiences shared by patients and NVHR partners

Recognition that HCV-related conditions occurring outside the liver, also known as extrahepatic manifestations (EHMs), are common

Identified a need to increase attention about these conditions to further emphasize the need for expanded access to early testing and treatment of HCV
Project Objectives

- Raise awareness about HCV conditions that occur outside the liver
- Facilitate discussion with the public health community about these conditions
- Change the conversation about HCV, emphasizing the need to characterize it as a systemic condition
- Broaden the NVHR coalition to expand the number of groups working to eliminate HCV in the U.S.
Project Activities

- Development of fact sheets
  1. Overview of EHMs
  2. Kidney disease, lymphoma
  3. Fatigue, depression, chronic pain
  4. Diabetes, heart disease
  5. Skin conditions

- Engage potential partners

- Webinar
Today’s Speakers

Dr. Zobair Younossi
Chairman, Department of Medicine
Inova Health System

Laura Stillman
Patient and Advocate
Today’s Speakers

Dr. Kristen Lee
Medical Director
HCV Treatment Program
Adult Primary Care Clinic, Boston Medical Center

Randy Madara
Patient, Advocate, and Hep C Peer Counselor
The Extrahepatic Manifestations of HCV Infection

Zobair M Younossi MD, MPH, FAASLD
Chairman and Professor of Medicine
Department of Medicine,
Inova Fairfax Hospital,
Falls Church, VA
The Total Impact of Chronic HCV Infection

• In order to fully understand the comprehensive impact of HCV infection and the benefit of SVR, we must assess:
  – Clinical consequences
  – PRO consequences
  – Economic consequences

DAA, direct-acting antivirals; PRO, patient-reported outcome; SVR, sustained virological response
Consequences of Chronic HCV Infection

- **Endpoints**
  - Hepatic
  - Liver fibrosis
  - Cirrhosis
  - OLT
  - HCC
  - EHM

- **Surrogate markers**
  - HRQoL
  - Functional status
  - Worker
  - Productivity
  - Stigma

- **Economic**
  - Direct costs
  - Indirect costs
  - Intangible costs

- **Outcomes**
  - Survival
  - Patient experience
  - Resource utilisation

- **PRO**

- **Clinical**

- **HCV infection**

- **Surrogate markers**

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EHM, extrahepatic manifestations; HCC, hepatocellular carcinoma; HRQoL, health-related quality of life; OLT, orthotopic liver transplantation; PRO, patient-reported outcome; WP, window phase
The Clinical Manifestations of HCV: The Hepatic and Extra-Hepatic

Cirrhosis, HCC, and liver mortality

Esko Lt, end-stage liver disease; HCC, hepatocellular carcinoma
Systemic vasculitis (polyarteritis nodosa, microscopic polyangiitis)

Porphyria cutanea tarda

Membranoproliferative glomerulonephritis

Mixed cryoglobulinaemia and cryoglobulinaemic vasculitis

Systemic vasculitis (polyarteritis nodosa, microscopic polyangiitis)

Sjögren (sicca) syndrome

Lymphoproliferative disorders

Porphyria cutanea tarda

Fatigue, depression

Corneal ulcers (Mooren’s ulcer)

Thyroid disease

Lichen planus

Pulmonary fibrosis

Type 2 diabetes

Arthralgias, myalgias, inflammatory polyarthritis

Autoimmune thrombocytopenia

The Extra-Hepatic Consequences of HCV Infection

Mortality from the Extra-Hepatic Consequences of HCV Infection

**Extrahepatic diseases**

- Anti-HCV seropositives, HCV RNA detectable
- Anti-HCV seronegatives

p=0.001 for comparison

**Circulatory system**

- HCV RNA seropositives
- Anti-HCV seronegatives

p=0.005 for comparison among three groups

**Nephritis, nephrotic syndrome, and nephrosis**

- HCV RNA seropositives
- Anti-HCV seronegatives

p<0.001 for comparison

Clinical Consequences of HCV Infection: All Cause Mortality

Both Hepatic and EHM Lead to Increased All-cause mortality

Cumulative mortality (%)

Follow-up (years)

Anti-HCV seropositives, HCV RNA detectable
Anti-HCV seronegatives, HCV RNA undetectable
Anti-HCV seronegatives

p<0.001 for comparison among three groups
p<0.001 for HCV RNA detectable vs undetectable

EHM: Mixed Cryoglobulinemia

- About 40-50% of HCV patients may have detectable cryoglobulinemia
- About 15% of HCV-infected patients will develop a symptomatic mixed cryoglobulinemia
- Symptoms are manifested as rash, vasculitis, MPGN and CNS involvement with significant consequences

Italian cohort (80 centers), 1,777 HCV infected patients tested for the presence of mixed cryoglobulinemia

Consistent with previous Italian and European studies: Cacoub et al, 2015; Doneda et al, 98; Zignego et al, 2008
EHM: Cryoglobulinemia Vasculitis

Skin Purpura

Glomerulonephritis

Neuropathy

CNS Vasculitis

EHM: B-Cell Lymphoma

- HCV infection increases the risk of developing a B-cell lymphoma (RR=34)

**Antigen-Sensitive B-Cell Proliferation**
- Cytokines (BAFF)
- HCV (E2)
- CD81
- Treg deficit
- Hyper γ-globulinemia
- IgH-bcl2?
- Polyclonal proliferation

**Antigen-Insensitive B-Cell Proliferation**
- IgG
- Anti-E2 IgM/Rheumatoid factor
- Cryoglobulinemia
- Vasculitis
- B-cell lymphoma
- Uncontrolled proliferation

**Other oncogenic events?**

Cacoub P 2018
In a meta-analysis, HCV was associated with:

- increased risk of death from cardiovascular disease
  - Odds ratio vs control group, 1.65, [1.07, 2.56]
- increased risk of stroke
  - Odds ratio vs control group, 1.30, [1.10, 1.55]
- increased risk of a carotid artery plaque, a well-known risk factor of stroke
  - Odds ratio vs control group, 2.27, [1.76, 2.94]

EHM: Insulin Resistance and Type 2 DM

1. Negro F. J Hepatol 2014; 61:S69–S78;

Confirmed by other studies
- Cho/Cr ↑
- ml/Cr ↑
- NAA/Cr ↓
- Correlated to neuropsy tests

Consequences: Neurocognitive deficits, depression and fatigue

PROs As a Part Of The Spectrum Of Outcomes

- HbA1c, glycosylated haemoglobin; HOMA, homeostasis model assessment; HRQoL, health-related quality of life; PRO, patient-reported outcome
The interaction of HCV infection with PROs

- PROs: patient-reported outcomes
- SVR: sustained virological response
- HCV disease-related
- HCV treatment-related
- PRO Are Measured by Validated Questionnaires

- AE: adverse event
- PRO: patient-reported outcomes
- SVR: sustained virological response
- Sx: symptom

Modified from Younossi Z et al. Hepatology 2007;45:806–816
PRO Scores in HCV-infected Patients

SF-36, Short Form-36; WPAI, Work Productivity and Activity Impairment
Economic Burden of HCV Liver Disease in the U.S.

- Total HCV cost (2011): $6.5 bln but will peak in 2024 at $9.1 bln.
- Lifetime cost of an HCV infected in 2011 was estimated at $64,490

Razavi H. et al Hepatology 2013 Jun;57(6):2164-70
### Economic Burden of the Extrahepatic Manifestations of HCV in USA

<table>
<thead>
<tr>
<th>Extrahepatic condition</th>
<th>Total yearly cost</th>
<th>Sensitivity analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed cryoglobulinemia</td>
<td>$184,074,755</td>
<td>$122,716,503</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>$17,540,307</td>
<td>$11,507,658</td>
</tr>
<tr>
<td>ESRD</td>
<td>$94,018,775</td>
<td>$11,266,713</td>
</tr>
<tr>
<td>Porphyría cutanea tarda</td>
<td>$174,133,095</td>
<td>$58,044,365</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>$14,724,777</td>
<td>$6,203,494</td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>$430,942,233</td>
<td>$129,127,095</td>
</tr>
<tr>
<td>Depression</td>
<td>$562,214,412</td>
<td>$140,406,117</td>
</tr>
<tr>
<td>RA-like arthritis</td>
<td>$252,071,869</td>
<td>$189,053,902</td>
</tr>
<tr>
<td><strong>Total extrahepatic burden *)</strong></td>
<td>$1,729,720,221</td>
<td>$668,325,847</td>
</tr>
<tr>
<td>PPPY</td>
<td>$645.42</td>
<td>$249.38</td>
</tr>
</tbody>
</table>

*PPPY: Per Patient Per Year

*Younossi Z et al, Gastroenterology 2016*
The Impact of HCV Cure on the Comprehensive Outcomes

- IFN, interferon; PEG, P1; SVR, sustained virological response

<table>
<thead>
<tr>
<th>Year</th>
<th>SVR (%)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>2</td>
<td>IFN 6m</td>
</tr>
<tr>
<td>1999</td>
<td>10</td>
<td>IFN 12m</td>
</tr>
<tr>
<td>2001</td>
<td>15</td>
<td>IFN/RBV 6m</td>
</tr>
<tr>
<td>2011</td>
<td>25</td>
<td>IFN/RBV 12m</td>
</tr>
<tr>
<td>2017</td>
<td>40</td>
<td>PEG/RBV 12m</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>PEG/P1 6-12m</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>PEG/R/P1 6-12m</td>
</tr>
<tr>
<td></td>
<td>98-100</td>
<td>All oral DAA8-12w</td>
</tr>
</tbody>
</table>
**Improvement of Clinical Outcomes After SVR: Liver-related Outcomes and Mortality**

![Bar Chart: 10-year cumulative incidence of outcomes in cohort with advanced fibrosis (n=530)](chart.png)

- **All-cause mortality**: 8.9% (SVR), 26.0% (Non-SVR)
- **Liver-related mortality**: 1.9% (SVR), 27.4% (Non-SVR)
- **Liver failure**: 2.1% (SVR), 29.9% (Non-SVR)
- **HCC**: 5.1% (SVR), 21.8% (Non-SVR)

- HCC, hepatocellular carcinoma; SVR, sustained virological response
Impact of Treatment on the Extrahepatic Manifestation

- SVR rates
- Reduction in risk of EHM with SVR
- Reduction in EHM associated Mortality
HCV-CryоВаскулитis: Вирологический Репонз с Лечение

SVR (%)

- SOF + RBV\(^1\) 24 wk: 74% (17/23)
- SOF + SMV ± RBV\(^2\) 12-24 wk: 83% (10/12)
- SOF + LDV\(^3\) 12 wk: 100% (44/44)
- SOF-based/3D\(^4\) 12-24 wk: 94% (33/35)
- SOF + DCV\(^5\) 12-24 wk: 100% (41/41)

The Effect of Sustained Virological Response on the Risk of HCV Extrahepatic Manifestations

Mahale et al, GUT 2017

HRs were adjusted for age categories (20–39, 40–49, 50–59, 60–69 and 70+ years), sex, race, period of service, average annual number of outpatient visits, body mass index (<25.0, 25 to <30, 30+ kg/m²), smoking and alcohol abuse. Additional adjustments for baseline diabetes mellitus and hypertension were conducted in models for glomerulonephritis, coronary heart disease and stroke.
The Impact of SVR on EHM of HCV

Impact of SVR on HCV Cryoglobulinemia: Complete Clinical Response

<table>
<thead>
<tr>
<th>Study</th>
<th>SVR</th>
<th>non-SVR</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boncompini 2002</td>
<td>6/9</td>
<td>1/4</td>
<td>44.33</td>
<td>[1.4, 1366.05]</td>
</tr>
<tr>
<td>Marchi 2004</td>
<td>0/1</td>
<td>0/1</td>
<td>484.00</td>
<td>[9.89, 27956.02]</td>
</tr>
<tr>
<td>Rizzon 2005</td>
<td>0/1</td>
<td>1/10</td>
<td>467.00</td>
<td>[0.38, 18562.80]</td>
</tr>
<tr>
<td>Sise 2006 (1)</td>
<td>10/12</td>
<td>1/10</td>
<td>463.00</td>
<td>[3.89, 41161.96]</td>
</tr>
<tr>
<td>Saadoun 2005 (1)</td>
<td>17/0</td>
<td>0/16</td>
<td>480.00</td>
<td>[1.46, 660.96]</td>
</tr>
<tr>
<td>Gemperline 2014</td>
<td>16/63</td>
<td>1/6</td>
<td>258.20</td>
<td>[9.15, 7228.85]</td>
</tr>
<tr>
<td>Malaguarnera 2015</td>
<td>4/15</td>
<td>0/16</td>
<td>269.00</td>
<td>[0.76, 32250.87]</td>
</tr>
<tr>
<td>Sise 2016 (1)</td>
<td>9/10</td>
<td>0/2</td>
<td>466.00</td>
<td>[3.37, 7.02]</td>
</tr>
<tr>
<td>Sise 2016 (2)</td>
<td>9/9</td>
<td>0/16</td>
<td>472.00</td>
<td>[0.79, 410.68]</td>
</tr>
<tr>
<td>Bonani 2017</td>
<td>24/10</td>
<td>1/8</td>
<td>42.33</td>
<td>[0.86, 846.41]</td>
</tr>
</tbody>
</table>

All studies (random-effect model)
Heterogeneity Q = 24.85, df = 11, I² = 55.9%
Test for overall effect p<0.001

Study Odds Ratio OR [95% CI]
No. events / No. patients
SVR non SVR non SVR better SVR better

Impact of SVR on Diabetes: Incidence of de novo DM

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<td>Mazzaro 2009</td>
<td>0/5</td>
<td>1/6</td>
<td>29.20</td>
<td>[1.04, 11.03]</td>
</tr>
<tr>
<td>Arcaini 2016 (1)</td>
<td>6/6</td>
<td>20/50</td>
<td>3.53</td>
<td>[0.84, 6.82]</td>
</tr>
<tr>
<td>Alric 2016 (1)</td>
<td>29/51</td>
<td>13/00</td>
<td>14.86</td>
<td>[3.81, 50.08]</td>
</tr>
<tr>
<td>Alric 2016 (2)</td>
<td>0/5</td>
<td>1/1</td>
<td>6.53</td>
<td>[0.09, 45.61]</td>
</tr>
</tbody>
</table>

All studies (random-effect model)
Heterogeneity Q = 6.22, df = 4, I² = 35.7%
Test for overall effect p = 0.0017

Study Odds Ratio OR [95% CI]
No. events / No. patients
SVR non SVR non SVR better SVR better

Impact of SVR on Lymphoproliferative Disease: Hematologic Response (PR+CR)

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All studies (random-effect model)
Heterogeneity Q = 6.22, df = 4, I² = 35.7%
Test for overall effect p = 0.0017

Study Odds Ratio OR [95% CI]
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SVR non SVR non SVR better SVR better

Impact of SVR on insulin resistance in HCV: Patients without insulin resistance at follow up

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<tr>
<td>Impieri 2006</td>
<td>10/32</td>
<td>2/20</td>
<td>6.47</td>
<td>[0.25, 156.6]</td>
</tr>
<tr>
<td>Pile 2005</td>
<td>7/17</td>
<td>4/20</td>
<td>6.47</td>
<td>[0.14, 29.92]</td>
</tr>
<tr>
<td>Agnelli 2012</td>
<td>20/34</td>
<td>2/22</td>
<td>6.51</td>
<td>[0.26, 229.7]</td>
</tr>
<tr>
<td>Thompson 2012</td>
<td>110/284</td>
<td>150/275</td>
<td>6.26</td>
<td>[0.29, 135.9]</td>
</tr>
</tbody>
</table>

All studies (random-effect model)
Heterogeneity Q = 2.67, df = 0, p = 0.15% I² = 66.4%
Test for overall effect p<0.001

Study Odds Ratio OR [95% CI]
No. events / No. patients
SVR non SVR non SVR better SVR better

Impact of SVR on insulin resistance in HCV: Patients without insulin resistance at follow up

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All studies (random-effect model)
Heterogeneity Q = 2.67, df = 0, p = 0.15% I² = 66.4%
Test for overall effect p<0.001

Study Odds Ratio OR [95% CI]
No. events / No. patients
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Impact of SVR on Diabetes: Incidence of de novo DM

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<td>Sise 2009</td>
<td>5/50</td>
<td>5/55</td>
<td>4.87</td>
<td>[1.03, 22.01]</td>
</tr>
<tr>
<td>Gemperline 2010</td>
<td>6/59</td>
<td>15/53</td>
<td>4.12</td>
<td>[0.82, 21.00]</td>
</tr>
<tr>
<td>Malaguarnera 2009</td>
<td>13/115</td>
<td>20/176</td>
<td>3.80</td>
<td>[0.18, 8.49]</td>
</tr>
<tr>
<td>Arcaini 2016</td>
<td>5/57</td>
<td>5/54</td>
<td>3.99</td>
<td>[0.34, 36.06]</td>
</tr>
</tbody>
</table>

All studies (random-effect model)
Heterogeneity Q = 2.67, df = 0, p = 0.15%
Test for overall effect p<0.001

Study Odds Ratio OR [95% CI]
No. events / No. patients
SVR non SVR non SVR better SVR better

Cacoub P et al, Gut 2018
Improvement of Fatigue with SVR

N=1080

Fatigue metric (% of max)

Activity

Fatigue

Vitality

All p-values <0.001

EHM, extrahepatic manifestations; PRO, patient-reported outcome; SVR, sustained virological response

Younossi Z. AASLD 2015
Impact of SVR on Extra-hepatic Mortality In HCV Patients: Incidence of Extra-Hepatic Deaths

<table>
<thead>
<tr>
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<th>No. events / No. patients</th>
<th>Odds Ratio</th>
<th>OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cacoub 2002</td>
<td>0/4 0/9</td>
<td></td>
<td>0.47 [0.01, 27.94]</td>
</tr>
<tr>
<td>Martinez-Macias 2015</td>
<td>2/61 0/13</td>
<td></td>
<td>0.88 [0.04, 19.44]</td>
</tr>
<tr>
<td>Lin 2017</td>
<td>14/745 40/4564</td>
<td></td>
<td>0.46 [0.25, 0.85]</td>
</tr>
<tr>
<td>Nahon 2017</td>
<td>48/1014 13/685</td>
<td></td>
<td>0.40 [0.22, 0.75]</td>
</tr>
</tbody>
</table>

All studies (random-effect model)
Heterogeneity: $Q = 0.30$, df = 3, $p = 0.95$; $I^2 = 0.0\%$
Test for overall effect: $p=0.001$

SVR better: non SVR better

0.25 1 10 100

Cacoub P et al, Gut 2018
Improvement of clinical outcomes after SVR: Extrahepatic Disease and Mortality

Impact of Treatment on PROs

Superiority of interferon-free regimens: Improvements in work productivity and PROs

AE, adverse event; CLDQ-HCV, Chronic Liver Disease Questionnaire-HCV; EoT, end of treatment; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; IFN, interferon; MCS, mental component score; PCS, physical component score; PRO, patient-reported outcome; SVR, sustained virological response.

Younossi ZM et al. Am J Gastroenterol 2016;111:808–816
The long term patient-reported outcomes benefit of sustained virologic response

- Baseline data was available for 3,486 subjects with SVR-12:
  - Age: 53.2 ± 10.0 years
  - Male: 62%
  - Treatment-naïve: 62%
  - Cirrhotic: 16%
  - HCV: GT1 – 65%, GT2 - 10%, GT3 - 18%, GT4 - 4%
  - Coinfection with HIV: 12%
  - While in the registry, patients completed the Short Form-36 (SF-36) HRQL questionnaire at baseline and then every 24 weeks
The Long-term Impact Of Sustained Virological Response On Patient-reported Outcomes In Cirrhotics

- A prospective study to assess the PROs of HCV patients with cirrhosis (N= 955) who had achieved SVR following a SOF-based regimen without interferon

Improvement in SF-36 vs baseline

- Improvements in PRO scores recorded during follow-up were similar in patients with compensated and decompensated cirrhosis
  - CC patients had mental and physical health scores similar to or higher than population norms
  - DCC patients had mental health scores similar to population norms, but had significant impairments on physical health PROs

365 HCV cirrhotics (CC=295 and DC=70) with SVR-12 with both SF-36 and CLDQ-HCV

Chronic HCV infected patients with cirrhosis who achieve SVR experience continued PRO improvements post-SVR.
Are there PRO benefits in HCV patients with early fibrosis?

- HCV patients with F0-F1 (N=1,548 from 16 Clinical trials)
  - Fibrotest ≤ 0.31 and APRI ≤ 0.7 and no histologic evidence of cirrhosis on a biopsy or transient elastography
- PROs were collected before, during and after treatment using SF-36 V2, FACIT-F, CLDQHCV, and WPAI-HCV.
- The results were validated in a subsample of patients with documented F0-F1 by liver biopsy or TE
- Regimens:
  - IFN-based (N=91) or
  - IFN-free with RBV (N=479) or
  - IFN/RBV-free regimens (N=978)
- At baseline, no PRO differences for the three treatment groups (all p>0.01).
HCV cure with LDV/SOF leads to annual savings of $2.7 billion (US) and €435 million (EU5) due to the improvement in work productivity.
The Extrahepatic Manifestation of HCV
Summary

• The impact of HCV must be assessed in comprehensive manner
  – Clinical: Hepatic and EHM
  – PRO
  – Economic
• In this context, the comprehensive impact of HCV infection is tremendous
• There is evidence that SVR provides clinical, PRO and economic benefit to the patient and the society
• The true benefit of SVR can only be recognized if the comprehensive benefit of HCV cure is assessed
Living with Hepatitis C and Chronic Kidney Disease (CKD)

Laura Stillman
NVHR Webinar
May 2, 2018
About Me

- I am 63 years old and live in San Francisco, California.
- I love dance, crafts, making clothes, and volunteering.
- I was a registered nurse, a caterer, and had other food related jobs until retirement in 2014 due to chronic renal failure.
- I am thankful for my Zen Buddhist community and my boyfriend for their support.
My Hepatitis C / CKD Story

- I first showed elevated liver enzymes in 1990, and my doctor insisted it was because of alcohol (even though I hardly drank).

- I was diagnosed with hepatitis C in 1991.

- I was unsuccessfully treated with interferon and ribavirin in 2003-2004. The side effects of that treatment were brutal.
In 2014, I had acute gastrointestinal distress. Blood tests revealed abnormal kidney function.

I was diagnosed with severe kidney disease and told I would need dialysis within 2 months.

My nephrologist recommended off-label treatment with a chemotherapy drug.
My Hepatitis C / CKD Story

- Then I participated in a clinical trial for HCV. After 3 months, my HCV was cured!

- My kidney function improved after treatment. (I also had more energy, and improved mood!)

- However, CKD is a progressive disease so I needed to go on dialysis 2 years after I was cured.
What it’s Like Living with CKD/ESRD

- I have dialysis 3 days per week for 4.5 hours.
- I eat a special diet.
- Side effects of disease and treatment:
  - Fatigue, weakness, muscle cramps, joint pain, shortness of breath
- I am currently on the kidney transplant list at UCSF and UC Davis.
Reflecting on my experience

- I had earlier labs indicating kidney disease, but it was not addressed right away.

- I was told my kidney disease was related to uncontrolled high blood pressure, and the only thing that could be done was to take medication to control my blood pressure.
Reflecting on my experience

- The CKD was caused by uncontrolled high blood pressure and made worse by HCV.

- Communication with my healthcare providers was difficult at times.
Unanswered Questions

- If the HCV-CKD connection was made and I had been treated for my HCV earlier, would it have saved my kidneys?

Regardless of the answer, I am happy to be Hep C free!
My Advice to Others

- Get tested.
- Don't wait to get treatment!
- Read everything you can about HCV; not all doctors are knowledgeable about it.
- Find a Hep C support group – a great source of info.
- Monitor your blood pressure.
Thank you!
Nerve Damage associated with Hepatitis C Infection

Kristen Lee, MD
Boston University School of Medicine

May 2, 2018
NVHR Webinar
Disclosure

- Nothing to disclose
Addressing the Burden of Hepatitis C Infection in Primary Care

- Boston Medical Center (BMC) Adult Primary Care Hepatitis C (HCV) Treatment Program
Our Context

Hepatitis C Rates by Boston Neighborhood, 2015

HCV Prevalence

USA: 2%
BMC: 10%
Primary Care HCV Team at BMC

- Public Health Social Worker/Case Manager
- HCV Providers
  - Attending doctors
  - Residents
  - Nurse practitioners
- Clinical Pharmacist
- Pharmacy Technician
- Other Partners
  - Office Based Addiction Treatment (OBAT)
  - Behavioral Health
  - Specialists
Care Cascade

Process:
- Identified by Screening
- Initial Evaluation
- Treatment Initiated
- Cure

Drop-off:

Barriers to Complete Treatment:
- Loss to follow up
- Treatment not appropriate
- Insurance barriers
- Telephone access
- Declines treatment
- HCV stigma
- Transportation, childcare
- Unstable housing, incarceration
Learning Objectives

- Recognize nerve damage as a complication of hepatitis C (HCV) infection
Case – Initial Presentation

- 45-year-old woman with HCV infection presented with numbness and tingling of her hands and feet after a fall. She denied head trauma.

- Physical exam:
  - Decreased sensation to pinprick and light touch on both hands and feet up to her ankles.
  - Loss of balance while standing with eyes closed
Case – Imaging

- Computed tomography (CAT scan) of her head showed two areas of ballooning of blood vessels in her brain.
Case – Clinical Course

- Underwent brain surgery to fix the ballooning without complication

- However, numbness and tingling significantly worsened over one month causing difficulty walking, bathing and dressing herself. She denied skin rash or joint pain.

- Physical exam:
  - Area of numbness and tingling extended
  - No longer had knee or ankle jerk on exam
Case – Lab

- Blood tests to investigate the cause of nerve damage
  - Vitamin B12 – normal
  - Diabetes test – normal
  - Thyroid hormone tests – normal
  - Syphilis test – normal
  - HIV test - normal
Case – Lab

- Blood tests to investigate the cause of nerve damage
  - Cryoglobulin – positive
Cryoglobulin

- As the immune system fights HCV, it produces proteins that clump together in the blood.

- This buildup of proteins restricts the flow of blood and damages blood vessels.

- This may cause skin rash, joint pain, nerve damage, or kidney problem.
Discussion

- Proposed mechanism of nerve damage by HCV infection (Nemni, et al)
  - Cryoglobulin deposition in the blood vessel near nerve
  - HCV-causing inflammation

- Prevalence of nerve damage among people with HCV infection who tested positive for cryoglobulin in their blood is close to 90% (Adinolfi, et al)
Case - Management

- Consulted neurology and rheumatology

- Initiated a twelve-week course of HCV treatment with ledipasvir-sofosbuvir
Case Follow up

- At three months after treatment completion, she got cured from hepatitis C infection and her numbness and tingling resolved.

- She fully recovered the ability to perform all her activities of daily living.
Lessons Learned

▪ Effects of HCV infection is not limited to the liver

▪ Numbness or tingling of arms and legs can be caused by HCV infection

▪ Treatment of HCV infection can improve symptoms of nerve damage
References


ABOUT ME

• Help-4-Hep peer counselor
• Moderator for HepatitisC.net
• Advocate
• Proud mom & grandma
• I love reading, research, dancing, the beach, and people!
• Hep C patient
NOT FEELING LIKE MYSELF

• “Mack truck” fatigue

• Had to cut back on work hours

• Couldn’t drive

• “Went to sleep” for a couple of years

• Brain fog – couldn’t find words, confusion

• Felt down, withdrew from activities
SEEKING ANSWERS FOR MY SYMPTOMS

- I was misdiagnosed with fibromyalgia, chronic fatigue syndrome
- I wanted to determine the etiology
- I did my own research
- I requested a hepatitis C test
- Sometimes I had to educate my providers
# Health Effects I Experienced

<table>
<thead>
<tr>
<th>Liver Related</th>
<th>Non-Liver Related</th>
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<tbody>
<tr>
<td>Cirrhosis</td>
<td>Fatigue</td>
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<td>Insomnia</td>
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<td>“Brain Fog”</td>
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<td>Joint pain</td>
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<td>Depression</td>
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<td>Muscle cramps</td>
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<td>Weight loss</td>
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<td><em>NOTE – my liver function tests were normal!</em></td>
<td>Gastrointestinal disorders</td>
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<td>Barrett’s esophagus</td>
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<td>Thyroid disorder</td>
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<td>Insulin resistance</td>
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<td>Vitamin D deficiency</td>
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<td>Atherosclerosis</td>
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MY HEPATITIS C EXPERIENCE

• I was infected with hepatitis C for almost 40 years

• I was afraid to get treated

• Finally cured 3 years ago!
LIFE AFTER CURE

• The HCV is gone!
• Some symptoms have gone away
• Others are still there, but are better
• Some have stayed
• Follow-up monitoring and labs
MY ADVICE TO OTHERS

• Don’t walk it alone
• Learn to be your own advocate
• A-S-K
• Have hope, and don’t give up!
Help-4-Hep is a non-profit, peer to peer helpline where counselors work with patients to meet the challenges of Hepatitis C head on. Callers talk one to one with a real person, typically someone who has had Hepatitis C touch their own life.

Our overall goal is to support and empower people by listening, empathizing, educating, navigating to care and building trust relationships by following up with them so they do not have to journey alone from diagnosis through post treatment.

877.435.7443
One call, lots of help – Free – Confidential
Questions?

Please submit questions for any of the presenters via the webinar question function or send an email to tbroder@nvhr.org

Slides and a recording of the webinar will be sent to everyone who registered and posted on our website. http://nvhr.org/program/HCVMoreThanLiverDisease