Curing Hepatitis C
in the Indian Health Service

Jonathan Vilasieir Iralu, MD, FACP
Indian Health Service Chief Clinical Consultant
for Infectious Diseases
Case Presentation

An American Indian 52 year-old male restaurant owner comes in to establish primary care with his new IHS physician. He does not drink alcohol but injected drugs once when he was in high school in 1978. He is found to have systolic hypertension, an LDL of 192 and an ALT of 48 after evaluation. Review of the EHR reminders shows that he is due for an influenza vaccine, and HIV serology and a Hepatitis C baby boomer screening test with reflex viral load. He is found to be HIV negative but HCV Antibody positive with a viral load of 150,000 iu/ml.
Forecasted Annual Incident Cases of Decompensated Cirrhosis (DCC), Hepatocellular Carcinoma (HCC), Liver Transplants, and Deaths Associated with Persons with Chronic Hepatitis C Infection and No Liver Cirrhosis in the United States in 2005

Incidence of acute hepatitis C by Race/Ethnicity, U.S., 2000-2010

Source: National Notifiable Diseases Surveillance System (NNDSS)
HCV Boomer Screening IHS

- 29% of boomers screened GPRA 2014 (increase of 278% over prior year)
- Things that work
  - Screening Reminders
  - Standing protocols
  - Nurses run the program, not physicians
Catch up on HCV+ backlog

- Audit of IHS site charts of HCV+ patients
  - About 50% of HCV+ never genotyped
  - About 30% never RNA confirmed
  - Need to identify and contact patients for follow up (confirmation, genotyping, staging for treatment, lifestyle counseling)
Hepatitis C testing

Test of Choice in 2014:
- Screening EIA with reflex Reverse Transcriptase PCR
  - Qualitative PCR- yes no answer
  - Quantitative PCR- how much virus is present preferred
Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection

* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Slide courtesy AASLD Curriculum & Training

Hepatitis C screening recommendations

Risk based screening

- h/o Injection or Intranasal Drug Use
- Hemodialysis
- Tattoo, nonprofessional
- Children of HCV mother
- Transfusion/organ recipients
- Incarcerated
- HIV infected
- Alcoholics
- Unexplained hepatitis
Hepatitis C screening recommendations

New CDC recommendations:

- Screen all Baby Boomers born between 1945 and 1965 (inclusive)
Hepatitis C – Who to treat

- Most likely to benefit
  - Advanced fibrosis F3
  - Compensated cirrhosis F4
  - Liver transplant recipients
- Severe extra hepatic manifestations:
  - Cryoglobulinemia (cutaneous vasculitis)
  - Membranoproliferative GN, proteinuria, nephrotic syndrome
Leukocytoclastic vasculitis
Hepatitis C – Who to treat?

- High risk of complications
  - Fibrosis F2
  - HIV coinfection
  - HBV coinfection
  - Other liver diseases (NASH)
  - Debilitating fatigue
  - DM
  - Porphyria
Porphyria Cutanea Tarda (PCT)
Hepatitis C – Who to treat?

- Transmission risk:
  - MSM
  - IDU
  - Incarcerated
  - Dialysis
Hepatitis C Evaluation

- Obtain the following
  - Hepatitis C viral load
  - Hepatitis C genotype
  - HIV serology
  - Hepatitis B, Hepatitis A antibodies
  - AST/Platelet Ratio (APRI Score)
  - (Consider biopsy/liver elastometry) ➔ Optional in Project ECHO
The Old Drugs…

- Pegelated Interferon (PEG)
  - Given subcutaneously for 6-12 months
  - Side Effects:
    - Flu like illness, depression, anxiety, alopecia, cytopenias

- Ribavirin
  - Given orally BID
  - Side effects:
    - Teratogenic, severe anemia
The New Drugs !!!

- **Sofosbuvir**
  - Once daily oral dosing
  - Inhibits NS 5b Polymerase
  - Side effects: Fatigue, Headache

- **Simepravir**
  - Once daily oral dosing
  - Inhibits NS 3/4a Protease
  - Side Effects: Photosensitivity, rash, pruritus, myalgia, dyspnea, nausea, hyperbilirubinemia
Hepatitis C Treatment

- **Genotype 1:**
  - Peg-Interferon injection, Ribavirin, Sofosbuvir for 12 weeks
  - Simepravir/Sofosbuvir +/- Ribavirin for 12 weeks

- **Genotype 2**
  - Ribavirin plus Sofosbuvir for 12 weeks

- **Genotype 3**
  - Ribavirin plus Sofosbuvir for 24 weeks
Cure Rates (Sustained Virologic Response)

- Genotype 1: Sof/Peg-IFN/RBV, 89%
- Genotype 1: Sof/SIM +/- RBV, 86-96%
- Genotype 2: 94%
- Genotype 3: 68% with cirrhosis, 91% without
Ledipasvir/Sofosbuvir: A Single Tablet Regimen (STR)

- **Ledipasvir**
  - Potency activity against GT 1a and 1b1
  - Once-daily oral, 90 mg

- **Sofosbuvir**
  - Potent activity against GT 1–6
  - High barrier to resistance
  - Once-daily oral, 400-mg tablet

- **Ledipasvir/Sofosbuvir STR**
  - Once-daily oral fixed-dose combination tablet
  - No food effect
  - >2000 patients treated

Priority Review and Breakthrough Status Granted
PDUFA: Oct 10, 2014

ION Phase 3 Program (ION-1, ION-2, ION-3)

Efficacy Summary

- 97% (1886/1952) overall SVR rate

Error bars represent 95% confidence intervals.
What do we get with HCV Treatment?

SVR (cure) of HCV is associated with:

70% Reduction of Liver Cancer
50% Reduction in All-cause Mortality
90% Reduction in Liver Failure

Lok A. NEJM 2012; Ghany M. Hepatol 2009; Van der Meer AJ. JAMA 2012
Treatment Costs

- **Sofosbuvir**: $1,000 per day for 84 days = $84,000 per patient
- **Ribavirin**: $10 per day for 84 days = $840
- **Ledipasvir**: $ ????????????????????????????????????????????????????
Hepatitis C treatment in the IHS

- Treatment offered at many IHS sites for over 10 years
- Treatment often covered by insurance or offered free to low income patients through Patient Support Programs
- Critical to link to a centers of excellence
  - Anchorage Alaska Native Medical Center
  - UNM Project ECHO- IHS HCV ECHO first Wednesday, Noon MT
Hepatitis C Rx:

You can do this!!
Contact us

Jonathan Iralu  MD, FACP
Indian Health Service Chief Clinical Consultant for Infectious Diseases
jonathan.iralu@ihs.gov

Lisa Neel, Acting HIV/AIDS National Consultant
lisa.neel@ihs.gov

Amy Nguyen, Pharm D,  GIMC Hepatitis Coordinator
amy.nguyen@ihs.gov