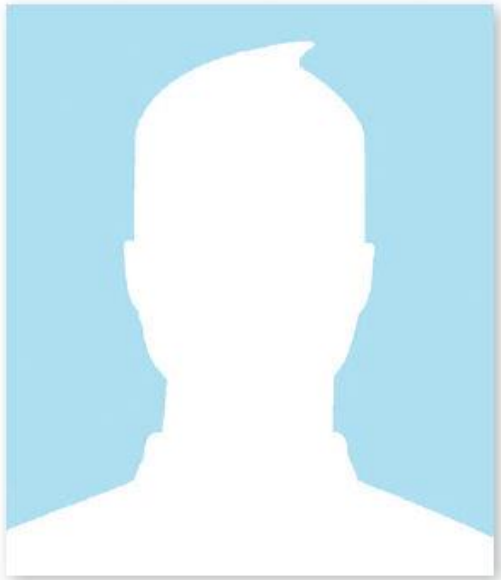


Dr Steve Johnson

Gastroenterologist and Senior Lecturer

Dunedin School of Medicine

Saturday, August 10, 2019

(Plenary)

16:50 - 17:10 Update on HBV and HCV

Hepatitis B and C Review and Update

Steve Johnson, M.D.

“We are not there to be phased by a brilliant international conference speaker, we are there because we are gullible, ignorant and desperate.”

Hepatitis B

- 292 million have chronic HBV worldwide – compared with 71 million with HCV

- Considerable variation in the prevalence for specific regions, towns, ethnic groups, workforce, and age groups within New Zealand

1. Robinson T, Bullen C, Humphries W, et al. The New Zealand Hepatitis B Screening Programme: screening coverage and prevalence of chronic hepatitis B infection. The New Zealand medical journal 2005;118:U1345-U1345.

Hepatitis B

Immune-tolerant phase

Living with the virus, normal ALT (Think baby)

HBeAg-positive immune active phase

Immune system turns on against HBV at around 30 years of age

Inactive chronic hep B phase

A truce is called. Hep B Virus goes into hiding (may be undetectable)

HBeAg-negative immune reactivation

HBV attempts domination again, immune system ready

Immune tolerant

HBeAg+ immune active phase

Inactive Chronic HepB phase

HBeAg negative immune reactivation

Goals of therapy:

The goal of hepatitis B therapy is to improve survival by preventing risk of cirrhosis and end-stage liver disease, and to improve quality of life

How to achieve that goal:

- Sterilizing cure – "It's all gone"
  Loss of HBSAg, HBV DNA, covalently closed circular DNA (cccDNA), and integrated DNA

Ongoing investigation - Numerous trials worldwide (including New Zealand) investigating various methods to stimulate T-cell immunity against HBV

1. Boni C, Janssen HLA, Rossi M, et al. Combined GS-4774 and Tenofovir Therapy can Improve HBV-Specific T-Cell Responses in Patients with Chronic Hepatitis. Gastroenterology 2019.

Functional or immunological cure –

loss of HBsAg with or without loss of development of HBSAb and sustained viral DNA supression

HBsAg

- Positive in acute or chronic infections
- Rapid test for anti-HBSAg – 96-98% specificity, 60-70% sens.
- Dried Blood Spot tests can measure HBsAg

HBsAg

Quantitative HBsAg

- Helpful in distinguishing HBeAg-negative chronic HBV from inactive carriers
- Prediction of mother-to-child transmission
- A high level (>1000 IU/ml) justifies more intense follow-up in HBeAg negative patients
- HCC risk stratification?

Hepatitis B Diagnostic Options

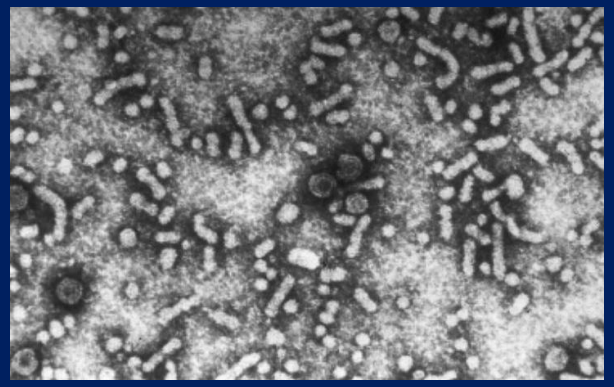
Future

HBsAg is composed of 3 protein subtypes:

- Small
- Medium
- Large

Two non-infectious subviral particals

- Spherical
- Filamentous



The protein patterns with these subtypes will change with the phase of the disease

Hepatitis B Diagnostic Options

- HBSAb – Immunity (natural or vaccination)
- HBcAb – HBV exposure (IgM or IgG)
- HBeAg – High levels of DNA, marker of infectivity

  Rapid test for HBeAg – (not approved) 99% specificity, 96% sens

- Anti-HBe - Associated with lower DNA levels

Hepatitis B Diagnostic Options

- HBV DNA – Phase of infection, need for or response to therapy
- HBV Genotype – only if using peginterferon or epidemiology studies

HBV - Treatment

- **Anyone with cirrhosis**
- **Immune active chronic HBV**
  - HBV DNA >2000 IU/ml (HBeAg neg) with ALT 2x ULN
  - HBV DNA >20,000 IU/ml (HBeAg pos) with ALT 2x ULN

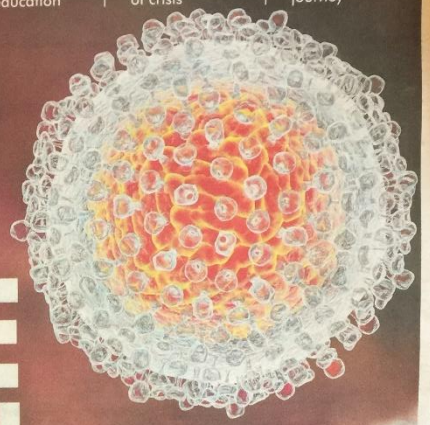
    [AASLD and APASLT recommendation, EASL lower ALT and DNA levels]

HBV - Treatment

Entecavir
Adefovir
Tenofovir
Telbivudine
Lamivudine
Peg-Interferon

Otago Daily Times
July 27, 2019

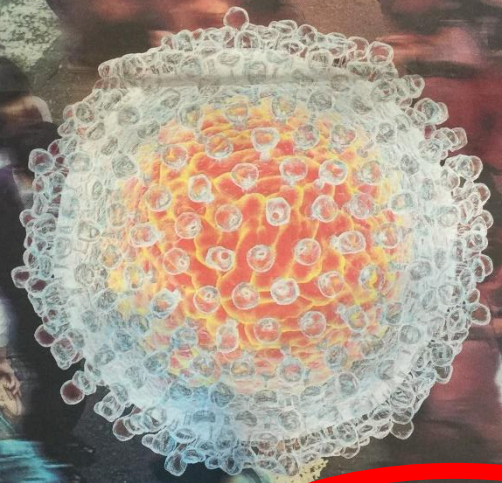
the weekend **mix**



A CURE FOR DEATH

TREATING A SILENT SCOURGE

• p4



Our plastic addiction

• p8

Light in the dark

• p18

PHOTOS: GETTY IMAGES. COVER: MATHEW PATCHETT

HCV Diagnosis

HCV RNA testing remains the gold standard to confirm infection – level unhelpful with prognosis

HCV core antigen is an alternative marker of viral replication (slightly less sensitive – 500-3000 HCV RNA IU/ml - Cheaper

HCV Diagnosis

- HCV Ab for all patients suspected to have HCV infection
- Acute HCV, immunocompromised patients, and those on hemodialysis should be initially tested with HCV RNA
- If HCV antibodies are positive, HCV RNA with a sensitive method (≤15 IU/ml) is next
- If HCV Ab positive and RNA is negative, retest with RNA 12 and 24 weeks later

What's new in diagnosis of HCV?

- HCV point of care testing (not that new) – still requires a trip back to the lab for further testing
- Dried blood spot specimens – easy collection and transport– details, details
- Xpert Viral Load Finger-Stick assay
  - Can accurately detect active infection in one hour on one visit

Lamoury, F. M. J., Bajis, S., Hajarizadeh, B., Marshall, A. D., Martinello, M., Ivanova, E., . . . Grebely, J. (2018). Evaluation of the Xpert HCV Viral Load Finger-Stick Point-of-Care Assay. *The Journal of Infectious Diseases, 217*(12), 1889-1896. doi:10.1093/infdis/jiy114

What's new in treatment of HCV?

Maviret (Gecaprevir/pibrentasvir)

- All genotypes (don't bother getting a genotype anymore)
- Three pills a day for eight weeks (naïve patients)
- Prior treatment : 8-16 weeks
- Childs-Pugh A Cirrhosis: 12 weeks
- Transplant patient: 12 weeks

Maviret (Glecaprevir/pibrentasvir)

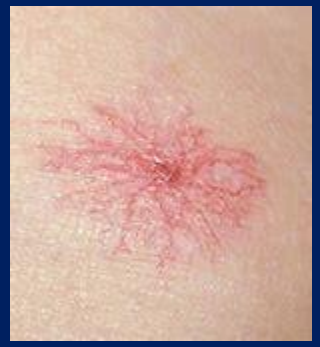
Side effects: Headache, fatigue in 9-17%

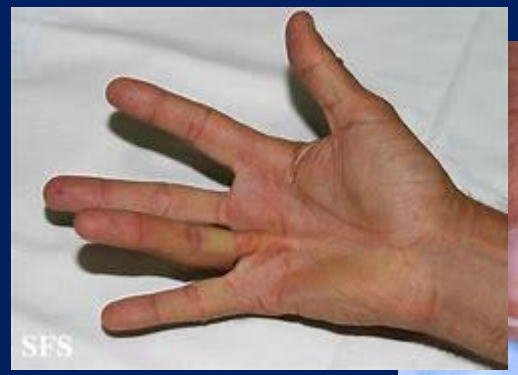
98-100% SVR 12 in treatment naïve
56-94 % SVR in treatment failures

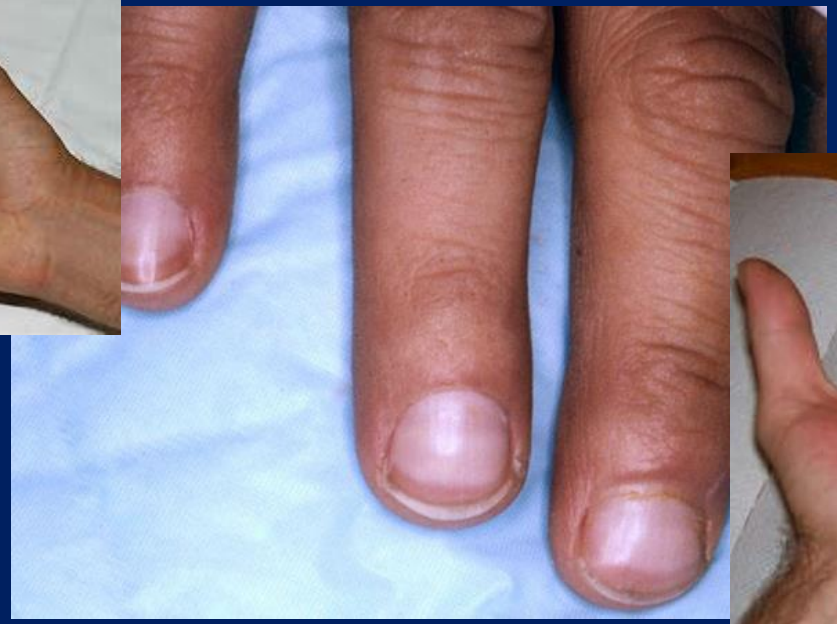
Recheck HCV RNA in 12 weeks (SVR12) – Done!

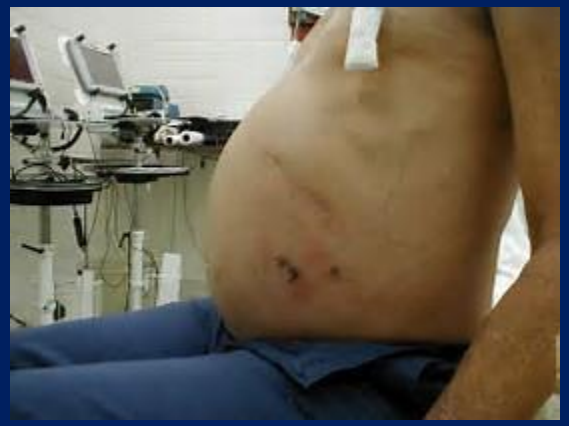
Maviret (Glecaprevir/pibrentasvir)

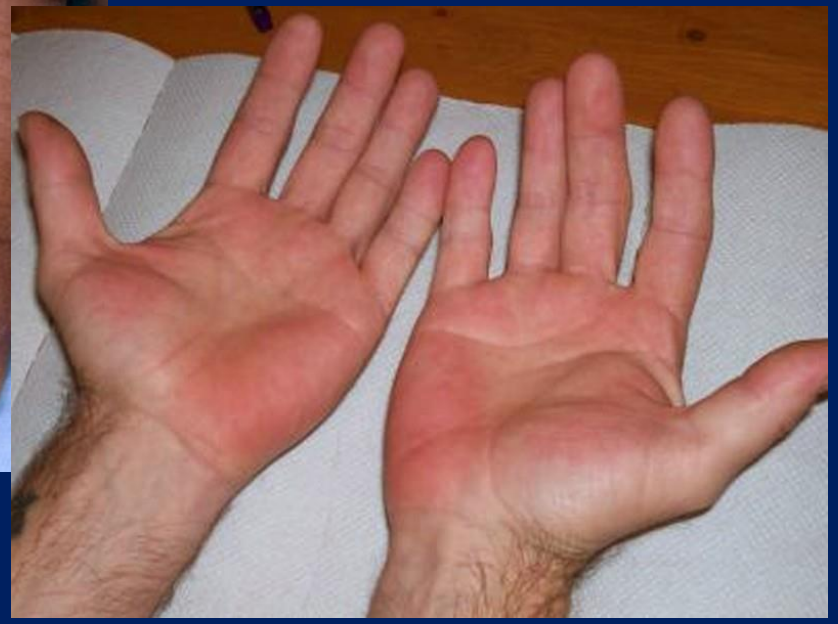
- Advanced Cirrhosis a contraindication- need to screen
  - Physical exam with Fibroscan, SWE, APRI, or Fib-4











Maviret (Glecaprevir/pibrentasvir)

- Untreated HBV – may become fulminant
- Diabetics may suddenly have better glucose control- hypoglycemia
- Drug interactions
    - Statins, cyclosporin, dabigatran, digoxin, St John’s Wort, Tacrolimus


Thank you