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Hepatitis C Update
CURABLE

Most common blood borne infection

75-85% of those exposed will develop chronic infection

50-75% of those infected not yet diagnosed

Maximum impact 2010-2020 (NHANES III-1988-94)

Leading indication for liver transplants

No vaccine available
More deaths report than those with HIV/AIDS

HCV Mortality
» Small, enveloped single-stranded RNA virus
» HCV RNA is first detectable in the serum days to 8 weeks after exposure
» Approximately 8-9 weeks from exposure to seroconversion for antibodies
» Cytotoxic lymphocytes contribute to liver injury as it attempts to eradicate the virus
» 20% of people will develop cirrhosis after 20 years and that rate continues to rise after that timeframe.

Pathogenesis
» Blood Exposure only
» IV/Intranasal drug use (needles, cottons, spoons etc)
» Blood transfusion/blood products, organ transplant before 1992
» Tattoo/piercings in non-sterile environments
» Healthcare/emergency professionals
» Sexual 3-5%
  > Women in monogamous relationships: no recommendation for changes in sexual practices, higher rates in MSM
» Maternal-Child 3-5%
  > Increased risk of perinatal transmission with coinfection of HIV and high maternal viral loads

Transmission Risk
Birth Cohort - persons born between 1945-1965
  - Baby boomers have higher rates of HCV

Blood exposure risk - especially in populations of IVDU/INDU
  - 92.5% of the IVDU population tests positive for HCV

Screening
Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection

- **HCV antibody**
  - **Nonreactive**
    - No HCV antibody detected
    - **STOP**
  - **Reactive**
    - **HCV RNA**
      - **No Detected**
        - No current HCV infection
      - **Detected**
        - Current HCV infection
        - Additional testing as appropriate
        - Link to care

* 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.


Diagnostic Labs
First 6 months after exposure
Typically asymptomatic
  > May experience nausea, jaundice, dark urine, RUQ pain
  > Symptoms 2-26 weeks after exposure and can last 2-12 weeks
Elevated aminotransferase levels 10-20 times ULN
  > May go undetected in asymptomatic patient
No treatment recommended during acute hepatitis in the era of DAA (directing acting antivirals), wait to see if spontaneous clearance, if not, refer for consideration for treatment.
» Fatigue is the most common complaint and can lead to decreased quality of life
» Arthralgia/Joint pain
» Extrahepatic Manifestations:
  > Diabetes
  > Chronic dermatology conditions
  > Renal disease
  > Cryoglobulinemia/porphyria
» Transmission risk
» Long term complications
» Alcohol reduction or abstinence
» Vaccinations for Hepatitis A and B
» Dispelling myths and addressing psychosocial issues regarding transmission risks

HCV Education
» AUDIT-C
  > 10 questions screening tool for alcohol use disorder

» CAGE-AID
  > 4 question screening tool for alcohol or drug use disorder
» HCV RNA and HCV Genotype
» CBC & CMP
» Iron profile & Ferritin
» PT/INR
» AFP tumor marker & HIV
» Hepatitis A Antibody
» Hepatitis B Antibody, Antigen, Core
» Liver ultrasound

Referral Diagnostics
Guidance AASLD/ IDSA (evolving document)

Decisions based on:
1. Genotype 1-6
   - GT 1 is most common in US, geographically diverse worldwide
2. Liver fibrosis staging 0-4
3. Treatment experience
4. Insurance

HCV Treatment
» Direct Acting Antivirals (DAA’s)
» Harvoni, Epclusa, Zepatier, Viekira Pak + ribavirn
» 8-12 weeks
» Side effects
» fatigue, headache, nausea, insomnia

» Goal of treatment is Sustained Viral Response (SVR)
  > obtaining a negative HCV RNA 3 months after treatment is complete.

HCV Treatment
» Complex drug interactions that can occur between DAAs and antiretroviral medications

» HIV/HCV-coinfected patients suffer from more liver-related morbidity and mortality, nonhepatic organ dysfunction, and overall mortality than HCV-monoinfected patients

» Even in the potent antiretroviral era, HIV infection remains independently associated with advanced liver disease and cirrhosis in patients co-infected with HCV (Thein, 2008)

Co-infection HCV/HIV
Liver Fibrosis
» Occurs when normal tissue replaced by scarred tissue

» Many Causes: Alcohol, Hepatitis B or C, Fatty liver (NAFLD/NASH), Autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, hereditary hemochromatosis, Alpha 1 antitrypsin
Compensated Cirrhosis
» Extensive fibrosis but liver functions normally

Decompensated Cirrhosis
» Extensive fibrosis causing liver to not function properly
» Signs of liver failure:
» A. Portal hypertension (increased pressure in vessel)
» B. Varices (enlarged blood vessels in esophagus, stomach or other organs)
» C. Ascites (accumulation of fluid in the abdomen)
» D. Jaundice (yellowing of sclera)
» E. Hepatic encephalopathy (inability for liver to filter toxins such as ammonia leading to changes in mental functioning or personality changes)- Serum Ammonia 35-65 mcg/dL
» F. Coma or death
Portal Hypertension and Varices
Fibroscan

» Determines “stiffness” of the liver
» Uses ultrasound technology to send a sound wave into the liver.
» Non invasive, takes 10-15 mins, less expensive, immediate results
» Cannot eat solid foods for 3 hours ahead
» Contraindicated in individuals with battery operated device (pacemakers, bladder stimulators...)
» Covered by most insurances, limited access
Liver biopsy

» Used for grading and staging of liver disease but also necessary for diagnosing other liver conditions (Autoimmune hepatitis, Wilson’s, Liver steatosis)

» Typically interventional radiologist performs ultrasound guided needle biopsy

» Risks: internal bleeding, pneumothorax, bile leak

Patients need to stop blood thinners, can be painful, requires recovery time, and a driver to take the patient home.
APRI (AST Platelet Ratio Index)

- http://www.hepatitisc.uw.edu/page/clinical-calculators/apri
- APRI score greater than 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. In addition, they concluded that APRI score greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.

Fib 4

- http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4
- FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis

Non Invasive Testing
» Hepatocellular Carcinoma (HCC) risk once patient is diagnosed with advanced liver disease. Increases 2-6% per year.

» HCC monitoring for those determined to have Advanced Liver Disease stage 3-4

» Liver imaging/AFP every 6 months

» EGD to screen for esophageal varices if cirrhotic.

» Watch for symptoms of worsening liver disease
  > Jaundice, itching, swelling of abdomen or lower extremities, changes in ability to think clearly
Hepatocellular Carcinoma (HCC)

- Worldwide the greatest risk for getting HCC is from hepatitis B (higher rates in Asia) or hepatitis C (higher rates in US)
- Men have high risk than women
- Higher rates in Asians and Pacific Islanders followed by American Indians/Alaskan Natives, Hispanic/Latinos, African Americans, Whites.
- Increased risk with cirrhosis regardless of cause
  - rates increases 4-6% per year
» **Symptoms:**
» There may be none
» Bloating, RUQ pain, N/V, loss of appetite, weight loss.

» **Diagnosis:**
» Increasing Alphafetoprotein (APF-tumor marker) - >20
» US, Cat Scan or MRI followed by liver biopsy.

» **Treatment:**
» Surgical resection, liver transplant (if no metastasis),
» RFA (Radiofrequency ablation), TACE (Transcatheter Arterial Chemoembolization)
» No clear connection between delivery method and transmitting hepatitis C
   > Annals of Internal Med 2013

» No contradiction in a HCV positive mothers and breast feeding
   > Breast feeding should be postponed if cracked and bleeding nipples
   > Milk should be discarded until nipples are healed
   > CDC and AAP (American Academy of Pediatrics)
» Maternal antibodies at birth to 18 month of age

» Can consider checking HCV RNA 3 months to 18 months

» 40% will clear virus by age 2, check HCV RNA at age 2
  > some clear virus by age 7

» No FDA approved HCV treatment for pediatrics