HCV/HIV Co-Infection Overview

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HCV/HIV Co-infection

- **Themes**:
  - Co-infection is common
  - Increased transmission of HCV
    - HCV as an STI when co-infection present
    - Perinatal
  - Accelerated rates of liver damage (fibrosis)
  - Traditional poor response to HCV treatment
    - **Now optimism** w/ new direct acting antivirals
      - Still challenges w/ drug interactions

HCV/HIV Co-infection

- **Epidemiology**
  - Co-infection with HIV and HCV is common
  - share similar routes of transmission
  - In the United States, approximately 25-30 % of patients who are HIV-infected are also co-infected with HCV

- **Rates differ according to risk factor**
  - Example: HCV seroprevalence in HIV-infected in *intravenous drug users* was 73 percent in one large study

HCV/HIV Co-Infection

- **Epidemiology**
- The *sequence* of infections is often different based on *risk factors*:
    - Injection drug users usually acquire HCV before HIV infection
    - Men who have sex with men (MSM) typically are infected with HIV before they acquire HCV infection

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- **In Men who have sex with men (MSM)**
  - HIV-infection associated with a **six-fold** increase in HCV incidence
  - Seroprevalence of HCV in HIV-infected MSM is **increasing**
    - Especially in those whose predominant risk factor is unsafe sex
  - HCV is **sexually transmitted** more commonly among HIV-infected MSM
    - MSM with HIV infection have higher seminal fluid HCV values than HIV-uninfected MSM
      - More likely to transmit HCV
    - HCV is **not** as common among HIV-uninfected MSM

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- **Perinatal transmission**
  - Vertical transmission of HCV appears to be facilitated by HIV co-infection
  - Maternal co-infection increases the odds of vertical HCV transmission by approximately 90 percent compared with maternal HCV infection alone
    - 10.8 versus 5.8 percent in large study published in CID 2014
  - HCV has been isolated from cervicovaginal fluid in HIV-seropositive women, but not in women with HCV alone
    - May explain the higher rates of perinatal HCV transmission observed in the setting of coinfection

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- **Virology**
  - Both RNA viruses
    - HIV (a retrovirus)
    - HCV (a flavivirus)
  - Viral production rates
    - HIV 10(10) virions a day
    - HCV 10(12) virions a day

  - During the chronic stage of either HIV or HCV infection, a relatively stable viral load or "set point" is maintained
    - Usually in the “thousands” for HIV & in the “millions” for HCV

HCV/HIV Co-Infection

- **Virology**
  - HCV RNA levels increase after HIV seroconversion
    - May be related to immunosuppression
    - The envelope protein of HIV (gp120) also increases HCV replication
  - HCV viremia is inversely correlated with lower CD4 counts
  - Higher HCV mutational rates
    - Increased sequence variability of the HCV genome has been noted in HIV/HCV-coinfected individuals
    - Harder on the host immune system to mount effective response

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- **Pathogenesis**
  - HIV/HCV co-infected patients have accelerated rates of fibrosis progression compared with patients with HCV alone
    - Decreased immune response to HCV antigens in HIV-infected patients
  - HIV-associated non-directed immune activation
    - Increased pro-inflammatory cytokines
    - Activated hepatic cells increase collagen formation (fibrosis)

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- **Effect of HIV on the Natural History of HCV**
  - Higher rates of morbidity and mortality related to liver disease
    - Mortality rate, 59 versus 39 per 1000 person-years (co-infected vs mono-infected)
  - Less likely to clear HVC viral infection
    - Less than 10% clear (>90 % become chronic)
  - More rapid rates of liver fibrosis
    - Paired biopsy studies
      - 2.5 years between biopsies, progression of at least one fibrosis stage was observed in 34 percent, and progression of two or more stages was observed in 9 percent
      - Rapid progression to cirrhosis has also been reported
  - Higher risk of hepatic decompensation compared with HCV mono-infected patients
  - Hepatocellular carcinoma (HCC) occurs faster and is associated with shorter survival in HIV/HCV co-infected patients
    - Co-infected patients (after 26 years)
    - HCV mono-infected patients (after 34 years)

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- **Testing for HCV with HIV co-infection**
  - Sensitivity and specificity of third generation HCV Ab ELISA assays approach 99 percent
  - However, patients with severe immunosuppression (CD4 cell counts **<100 cells/ mm3**) *may have a false negative serology*
    - Due to impaired antibody formation
    - Occurs in than less than 5 percent of patients
  - In HIV-infected patient w/ low CD4 consider hepatitis C RNA testing
    - Esp. if has significant risk factors for HCV

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- **Effect of cART on HCV progression**
  - Many studies suggest that ART is beneficial
  - Demonstrated benefits:
    - Decline in liver-related mortality
    - Slower rates of fibrosis progression
    - Lower risk of end-stage liver disease
      - Almost percent lower likelihood of hepatic decompensation
    - Lower rates of hepatocellular carcinoma

  - BUT cART alone is not enough !!!

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- **HCV and Hepatotoxicity with ART**
  - HCV increases the risk of hepatotoxicity from antiretroviral therapy
    - Some ART regimens are more hepatotoxic than others
      - Ex. nevirapine, ritonavir
    - ART-associated hepatotoxicity may be related to immune reconstitution
      - Hepatotoxicity often correlates with a rise in CD4 count
  - Benefit of antiretroviral therapy outweighs the risk of liver injury
    - Close laboratory follow-up is prudent

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- **Treating HCV in setting of HIV co-infection**
  - Interferon based regimens (old news)
    - HIV/HCV co-infected patients traditionally had lower response rates to HCV treatment
    - With peginterferon and ribavirin
      - Overall SVR rates 14 - 35 percent compared with 42 - 46 percent in mono-infected patients
  - Direct Acting antivirals (now):
    - HIV/HCV co-infected patients appear to have comparable SVR rates to mono-infected patients w HCV
      - > 90%
      - **Curative all-oral treatment is a possibility for most patients w/ HIV-infection!**
    - Major issue at this point is potential drug-drug interactions w/ ART and HCV meds
      - Should take into account w/ ART regimen selection

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- **Effect of HCV on the *natural hx of HIV***
  - Various studies that suggest:
    - HCV seropositivity is an independent risk factor for progression to *AIDS and death*
      - AIDS-defining events when HCV-seropositive
        - Relative risk 2.6 of
      - Increased mortality
        - Standardized mortality rate HCV co-infection vs HCV-negative 20.8 compared with 4.8
    - *Lower rate of CD4 cell gains* among patients who had chronic HCV infection
    - Greater rates of *non-hepatic complications*
      - Osteoporosis / bone fractures
      - Chronic kidney disease
      - Possibly additional cardiovascular risk
  - The factors responsible are not well understood
    - May result from generalized immune activation

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- QUESTIONS / COMMENTS?