Hepatitis C, HCV/HIV Co-Infection, and HIV PREP

November 2015
History – Hep C discovered in 1989

VIRAL HEPATITIS
HISTORICAL PERSPECTIVE

“Infectious” → A → Enterically transmitted
Viral hepatitis

“NANB” → E → Enterically transmitted

“Serum” → B → Parenterally transmitted

D → Parenterally transmitted

other
HCV Background

• Epidemiology of chronic HCV infection in the United States
  • Prevalence
    • Approximately 3.2 million persons have chronic HCV infection
    • Infection is most prevalent among those born during 1945–1965
      • likely infected during the 1970s and 1980s
  • Incidence
    • CDC estimates > 20,000 cases per year
    • Persons newly infected with HCV are usually asymptomatic
      • under recognized and under reported
        • acute cases of hepatitis C reported only 1,229 to 1,778
HCV Background

- Risk factors for HCV infection
  - Current or former injection drug users
    - including those who injected “*only once many years ago*”
  - Blood/Organ Recipients
    - clotting factor concentrates before 1987
    - blood transfusions or solid organ transplants before July 1992
    - Now 1 in 2 million units transfused
  - Chronic hemodialysis patients
  - Health care workers after needlesticks
    - 1-10% if source HCV infected
  - Children born to HCV-positive mothers
  - Persons with HIV infection
  - Other
    - Intranasal drug use, non-sterile tattoos, other blood exposure
HCV Background

• Natural hx of HCV infection:
  • 20%–30% develop acute symptoms
    • symptoms resolve on own in about a month
  • 15%–25% of persons clear the virus from their bodies without treatment
    • do not develop chronic infection
    • reasons for this are not well known
    • can be re-infected
  • 75%–85% becomes chronic
    • often no symptoms for decades
HCV Background

• Natural hx of HCV infection
  • For every 100 persons infected with HCV:
    • 75–85 will go on to develop chronic infection
    • 60–70 will go on to develop chronic liver disease
    • 5–20 will go on to develop cirrhosis over a period of 20–30 years
    • 1–5 will die from the consequences of chronic infection (liver cancer or cirrhosis)
  • 15,106 deaths caused by HCV in 2007
  • Chronic HCV infection is the leading indication for liver transplants in the United States
HCV Background

*Mortality Rates = HBV, HCV, HIV listed as cause of death
Because of decedent can have multiple causes of death, a record listing more than 1 type of infection was counted for each type of infection
HCV Background

• HCV transmission
  • Most efficiently through large or repeated percutaneous exposures to infectious blood
    • Injection drug use
      • Young (aged 18–30 years) IDUs - 1/3rd are HCV-infected
      • Older IDUs (needle use in 1970's-80's) - approximately 70%–90%
  • Inefficient
    • Sex with an HCV-infected person
      • MSM > heterosexual
    • Sharing personal items contaminated with infectious blood
      • razors or toothbrushes
HCV Background

• Signs and symptoms
  • Acute HCV infection
    • Only occurs in 20%–30% of those newly infected with HCV
      • time period from exposure to symptom onset is 4–12 weeks
  • Non-specific
    • Fever, Fatigue, Abdominal pain, Loss of appetite, Nausea, Vomiting, Joint pain
  • Some Liver related
    • Dark urine, Clay-colored stool, Jaundice
HCV Background

• Signs and symptoms
  • Chronic HCV infection
    • Most are asymptomatic
      • fatigue
      • elevated liver enzymes detected during routine examinations
        • may have periodic returns to normal levels; can remain normal despite chronic liver disease
  • Chronic liver disease
  • Cirrhosis
    • Cytopenias, GI bleeding, ascites/swelling, encephalopathy
  • Liver cancer
HCV Background

• Testing – Who?
  • Persons born from 1945 through 1965 (screening)
  • Persons who have ever injected illegal drugs
  • Recipients of clotting factor concentrates made before 1987
  • Recipients of blood transfusions or solid organ transplants before 1992
  • Patients who have received long-term hemodialysis
  • Persons with known exposures to HCV
  • Patients with signs or symptoms of liver disease
  • Children born to HCV-positive mothers
  • All persons with HIV infection
HCV Background

• Testing – Who?
  • Routine HCV Testing is of “uncertain need”
    • Recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, sperm)
    • Long-term steady sex partners of HCV-positive persons
    • Persons with a history of tattooing or body piercing
    • Intranasal cocaine and other non-injecting illegal drug users
    • Persons with a history of multiple sex partners or sexually transmitted diseases
HCV Background

• Testing – Who?
  • Routine HCV Testing Is **Not** Recommended
    • Health-care, emergency medical, and public safety workers
    • Pregnant women
    • Household (nonsexual) contacts of HCV-positive persons
    • General population
HCV Background

• Testing – How?
  • Screening tests
    • Test for antibody to HCV (anti-HCV)
    • Ab can be detected 4–10 weeks after infection
    • Detected in >97% of persons by 6 months
  • Confirmatory tests
    • Detect presence or absence of virus
    • HCV RNA polymerase chain reaction [PCR]
      • Often done quantitative to determine viral load
      • HCV RNA appears in blood and can be detected as early as 2–3 weeks after infection
HCV Background

• Management:
  • Education on:
    • Natural hx of disease
      • “decades, not days”
    • Transmission
      • Low but present risk for transmission to sex partners (1%/year)
      • Avoid sharing personal items (toothbrushes or razors)
      • Cuts and sores on the skin should be covered
      • Should not Donate blood, organs, tissue, or semen

  • NOT spread by sneezing, hugging, holding hands, coughing, sharing utensils or drinking glasses, or through food or water
HCV Background

• Management:
  • Evaluation for possible treatment:
    • **NEW** -- treatment recommended for *all patients with chronic HCV infection*
      • except short life expectancies that cannot be remediated by treating HCV or transplantation
    • Abandon “triage approach”
      • degree of liver disease, extra-hepatic manifestations, risk of transmission
    • Other issues to consider:
      • Capacity to comply with treatment
      • Risk of re-infection
      • Medication interactions
      • Access to medication (insurance)
HCV Background

• Management:
  • Evaluation for possible treatment:
  
  • The risk of liver-related morbidity and mortality in an individual HCV-infected patient increases with the severity of liver fibrosis
    • Fibrosis stage (METAVIR system)
      • F0, no fibrosis
      • F1, portal fibrosis without septa
      • F2, portal fibrosis with few septa
      • F3, numerous septa without cirrhosis
      • F4, cirrhosis

  • Recent paradigm was to prioritize patients treatment based on stage of fibrosis
    • F0-F2 - wait for future therapies
    • F3/F4 - therapy should be offered
  
  • This approach may still be enforced by insurers
    • goes against current guidelines to treat everyone (barrier to care)
HCV Background

• Management:
  • Evaluation for possible treatment:

• Modalities to evaluate for severity of chronic liver disease
  • Liver imaging
  • Biopsy
  • Special blood tests (Fibrosure)
  • Ultrasound based Elastography

• Determination of HCV genotypes
  • needed to determine particular medications used for treatment
  • genotypes 1–6
    • genotype 1 is the most common in the United States
HCV Background

• Management:
  • Look for Co-infection (and vaccinate if applicable)
    • Hepatitis A and Hepatitis B
    • HIV testing
    • RPR testing
  • Look for other liver diseases
  • **Advised to avoid alcohol**
    • accelerates cirrhosis
  • Consideration of *underlying risk factor (i.e. drug addiction)*
    • (this is what kills people most! – see next slide)
HCV Background

  • the authors looked at the cause of death in patients with Hepatitis C
    • They showed that the leading cause of death in the patients with Hepatitis C group was not liver-related illnesses.
    • 72% of deaths were the result of drug overdose or suicide

• Providing a patient’s with ready access and information about how to overcome addiction is vital
HCV Background

• Management:
  • Look for extrahepatic manifestation:
    • Chronic Hepatitis C issues outside the liver
      • endocrine, joints, skin, kidney, CNS, etc (fatigue)
    • Examples:
      • Diabetes mellitus
      • Glomerulonephritis
      • Essential mixed cryoglobulinemia and other vasculitis
      • Porphyria cutanea tarda
      • Non-Hodgkins lymphoma
      • Arthritis (may be rheumatoid like)
HCV Background

• Management:
  • Pregnancy and HCV Infection
    • Approximately 6 of every 100 infants born to HCV-infected mothers become infected with the virus
    • Transmission occurs at the time of birth
    • No prophylaxis is available to prevent it
    • No evidence that breastfeeding spreads HCV
    • Issues w/ HCV treatment and pregnancy
      • Ribavirin (teratogenicity)
HCV Background

• Treatment for chronic Hepatitis C
  • Until recently pegylated interferon and ribavirin, with possible addition of oral protease inhibitors
  • given for 24-48 weeks
  • treatment resulted in a “sustained virologic response” (SVR)
    • SVR = undetectable HCV RNA in the patient's blood 24 weeks after the end of treatment
      • Now checked 3 months after the end of treatment
    • SVR = Cure
    • SVR in 50%–90% of patients for traditional interferon based treatment
  • Treatment was very challenging to endure
HCV Background
HCV Background

• Treatment for chronic Hepatitis C
  • Now have “direct acting antiviral” drugs
    • treatment times of 8-24 weeks

• Sofosbuvir (Sovaldi™)
• Simeprevir (Olysio™)
• Ledipasvir and Sofosbuvir (Harvoni™)
• Ombitasvir, Paritaprevir, Ritonavir, Dasabuvir tablets (Viekira Pak™)
• Daclatasvir (Daklinza™)
HCV Background

• Treatment for chronic Hepatitis C
  • Direct acting antiviral drugs / interferon-free regimens

• Tolerability / Safety / Convenience
  • Amazing improvement

• Efficacy
  • SVR in high 90%'s for most clinical scenarios

• Cost
  • Has dictated the current approach of triage
    • based on degree of liver disease, extra-hepatic manifestations, risk of transmission, etc.

• See http://www.hcvguidelines.org/
  • website is constantly being updated given rapid evolution / changing treatment paradigms
    • Association for the Study of Liver Diseases (AASLD)
    • Infectious Diseases Society of America (IDSA)
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
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
HCV/HIV Co-infection

• In Men who have sex with men
  • 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
HCV/HIV Co-infection

• **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
HCV/HIV Co-infection

• 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
HCV/HIV Co-infection

• 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)
HCV/HIV Co-infection

- **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)
HCV/HIV Co-infection

• 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 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
HCV/HIV Co-infection

• Effect of ART 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
HCV/HIV Co-infection

• 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
HCV/HIV Co-infection

• 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
HCV/HIV Co-infection

• Treating HCV in setting of HIV co-infection
  • Due to cost concerns of HCV treatments, prioritizing patients who may benefit most from HCV antiviral treatment has been advised (but this approach should be abandoned)
    • Factors:
      • HCV genotype
      • History of prior HCV treatment
      • Stage of underlying liver fibrosis
      • Potential drug interactions between ART and HCV antiviral agents
HCV/HIV Co-infection

• 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
HIV Control

**Strategies to Control HIV**

- Behavior modification
  - safer sex campaigns / education
  - condoms

- Case finding / HIV testing

- Blood supply testing

- Injecting drug users

- Circumcision

**Medical therapies**

- HAART
  - effect on transmission
  - pre-exposure prophylaxis
  - post-exposure prophylaxis
  - prevention of mother to child transmission

- Microbicides
- Treatment of co-infections and STD’s
- HIV vaccines
HIV Control: Medical Therapies

• Pre-Exposure Prophylaxis (PrEP)
  • Using ARVs daily or as needed on HIV *uninfected* individuals to prevent HIV transmission

• Basis:
  • single dose nevirapine to HIV-infected women during labor and to their newborns
    • reduced transmission of HIV by about 50 percent
  • Animal studies

• Concerns:
  • only partially effective
  • antiviral resistance
  • slippery slope thinkers – increased risky behavior
# HIV Control: Medical Therapies

<table>
<thead>
<tr>
<th>Location</th>
<th>Sponsor/Funder</th>
<th>Population (mode of exposure)</th>
<th>Intervention Arms</th>
<th>PrEP strategy(ies) being tested</th>
<th>Status/Expected completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>CDC</td>
<td>400 men who have sex with men (penile/rectal)</td>
<td>1</td>
<td>Tenofovir disoproxil fumarate (TDF)</td>
<td>Fully enrolled – Ongoing 2009</td>
</tr>
<tr>
<td>Thailand</td>
<td>CDC</td>
<td>2,400 injecting drug users (parenteral)</td>
<td>1</td>
<td>TDF</td>
<td>Enrolling / 2009</td>
</tr>
<tr>
<td>Botswana</td>
<td>CDC</td>
<td>1,200 heterosexual men and women (penile and vaginal)</td>
<td>1</td>
<td>TDF + entecitabine (FTC) (switched from TDF Q1 2007)</td>
<td>Enrolling / 2010</td>
</tr>
<tr>
<td>Peru, Ecuador, US, additional sites TBD (PrEP Study)</td>
<td>NIH, BMGF</td>
<td>3,000 men who have sex with men (penile/rectal)</td>
<td>1</td>
<td>TDF + FTC</td>
<td>Enrolling / 2010</td>
</tr>
<tr>
<td>Kenya, Uganda (Partners Study)</td>
<td>BMGF</td>
<td>3,900 serodiscordant couples (penile and vaginal)</td>
<td>2</td>
<td>TDF, TDF + FTC</td>
<td>Planning / 2012 Anticipated start Q2/2008</td>
</tr>
<tr>
<td>Malawi, South Africa, Zambia, Zimbabwe (VOICE Study)</td>
<td>MTN, NIH</td>
<td>4,200 sexually active women (vaginal)</td>
<td>3</td>
<td>TDF; TDF + FTC; TDF gel</td>
<td>Planning / 2011 Anticipated start Q4/2008</td>
</tr>
</tbody>
</table>

BMGF – Bill & Melinda Gates Foundation; CDC - US Centers for Disease Control; FHI – Family Health International; MTN – Microbicide Trials Network; NIH – US National Institutes of Health; USAID – United States Agency for International Development
HIV Control: Medical Therapies

- 2499 HIV (-) MSM
- 100 became infected during follow-up (median, 1.2 years)
  - 36 in the pre-exposure prophylaxis group
  - 64 in the placebo group
- 44% reduction in the incidence of HIV
HIV Control: Medical Therapies

• results continued …
  • Does PrEP increase risk behavior?
    • Condom use increased
    • No differences between the treatment / placebo arms in:
      • number of STDs
      • high-risk sexual practices
    • Adherence required
      • drug levels correlated with a protective effect
      • drug was detected in only 9% of participants w/ newly acquired HIV infection vs 51% of participants who did not acquire HIV
  • Sub-study of the trial:
    • protective efficacy of tenofovir-emtricitabine increased to ≥96% for those whose drug levels suggested that they took at least four doses per week
HIV Control: Medical Therapies

• More of PrEP
    • Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women.
      • conducted in heterosexual serodiscordant couples
      • reduced the risk of acquiring HIV infection by 75%
  • The Lancet 2013 June 15
    • Antiretroviral prophylaxis for HIV infection in injecting drug users
  • PROUD study (England)
    • Presented at Conference on Retroviruses and Opportunistic Infections (CROI 2015)
      • effectiveness was 86%
  • Clinical Infectious Diseases; September 2015
    • "No New HIV Infections with Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting"

• Overall take: 50-100% protection
HIV Control: Medical Therapies

- July 16 2012 FDA approval of Emtricitabine/tenofovir for PrEP
  - daily oral antiretroviral drug to reduce the risk of sexual acquisition of HIV

- Issues:
  - Will it increase risk behavior?
  - Resistance?
  - Toxicity long term?
  - Who to treat?
  - Who pays?
HIV Control: Medical Therapies

- Acquired drug resistance during PrEP:
  - emtricitabine
    - the genetic barrier to resistance is low
    - M184V
  - tenofovir
    - the genetic barrier to resistance is high
    - K65R; uncommonly seen in clinical practice

- In the PrEP trials, most cases of drug resistance have occurred in patients who were retrospectively found to have acute HIV infection at enrollment
HIV Control: Medical Therapies

• Adverse event to PrEP:
  • Generally well tolerated in studies to date

• Renal
  • Limit to patients w/ normal renal function
    • in the NEJM published iPrEX trial 10 creatinine elevations led to discontinuation of a study drug
    • all but one elevation resolved with treatment discontinuation

• Bone
  • subclinical bone demineralization
  • no differences in the rate of fracture occurrences

• Caution in Hep B co-infected
  • May induce a flare if adherence an issue
HIV Control: Medical Therapies

• Who should get PrEP?
  • HIV-uninfected sexual partners of an HIV-infected individual (sero-discordant partner)
    • likely not needed if HIV-infected partner has confirmed suppressed HIV RNA
  • MSM who have reported high-risk sexual behaviors in the past 6 months
    • or had a documented sexually transmitted infection
  • Heterosexual men / women who infrequently use condoms and have sex with partners who are at high risk of HIV-infection
    • injection drug users, MSM, partners from areas where there is a high HIV prevalence
  • Individuals who have used post-exposure prophylaxis more than twice in the past year
  • Injection drug users who, in the last six months, report sharing needles/equipment
HIV Control: Medical Therapies

• Cost of PrEP
  • estimated cost of daily emtricitabine-tenofovir is $1425 monthly

• “The cost-effectiveness of pre-exposure prophylaxis for HIV prevention in the United States in men who have sex with men”
  • PrEP was evaluated in both the general MSM population and in high-risk MSM (average of 5 partners per year)
  • use in high-risk MSM compares favorably with other interventions that are considered cost-effective
  • would result in annual PrEP expenditures of more than $4 billion
“On-Demand” PrEP – 86% effective (IPERGAY trial)
HIV Control: Medical Therapies

• “Time for debate on the effectiveness of PrEP is over”
  • DAN GROOVER JANUARY 4, 2015
• Under-utilized:
  • Currently only a few thousand individuals are using PrEP nationwide
  • CDC says that at least 500,000 people could benefit from using it
  • August 2014 study by the Kaiser Family Foundation found that 80% of gay and bisexual men knew “only a little” or “nothing at all” about PrEP
HIV Control

**Strategies to Control HIV**

- Behavior modification
  - safer sex campaigns / education
  - condoms
- Case finding / HIV testing
- Blood supply testing
- Injecting drug users
- Circumcision

**Medical therapies**

- HAART
  - effect on transmission
  - pre-exposure prophylaxis
  - post-exposure prophylaxis
  - prevention of mother to child transmission
- Microbicides
- Treatment of co-infections and STD’s
- HIV vaccines
HIV Control: Medical Therapies

• “Microbicide"
  • topical agent that can be applied vaginally
  • Locally applied “PrEP”
  • Vaginal chemoprophylaxis
  • female-controlled method of prevention

• Various mechanisms:
  • physical barrier
  • non-selective inactivation of the virus
  • specific antiviral activity
HIV Control: Medical Therapies

• Microbicides
  • Currently available spermicides do not protect against transmission of HIV
    • nonoxynol 9 might increase the risk for HIV sexual transmission
      • irritative effects on the vaginal epithelium
  • Others:
    • P3 cellulose sulfate gel halted 2007
      • increased risk of HIV
    • Carraguard microbicide trial 2008
      • showed safety, but no efficacy
HIV Control: Medical Therapies

• Finally success
  • July, 2010 XVII International AIDS Conference
    • Tenofovir Vaginal Gel
      • First Microbicide to Prevent HIV Infections
      • Application of gel or placebo before & after sex
        • high prevalence area (pregnant women 21.0-51.1% HIV positive)
      • 889 sexually active HIV (-) women
        • 38 women in the tenofovir group became HIV-positive
        • 60 women in the placebo group became HIV-positive
    • 39% lower risk of HIV overall
      • 54% reduction if used routinely / correctly

• Ongoing studies w/ topically applied anti-retrovirals
  • Both intravaginal and enema deliver methods
    • Ex. vaginal ring
• QUESTIONS / COMMENTS?