An Overview of HIV Infection and Associated Co-Infections

Steve Randall, PA

The Medical Practice Association of KUSM-W - HIV Program
And
HIV Educator, The Kansas AIDS Education and Training Center
The University of Kansas School of Medicine - Wichita
HIV Transmission

- Contact with infected body fluids
  (blood, semen, vaginal fluid, breast milk)
- Unprotected sex
- Sharing needles
- Mother to fetus
Now, why would you have a stamp like that? I mean, what if you lick it and get infected?
This May Be the Most Dangerous Time Yet!

Confusion  Hysteria  Ignorance  Complacency

1980  2007
A global view of HIV infection 2006

39.5 living with HIV
Newly Infected with HIV - 2006

<table>
<thead>
<tr>
<th>Region</th>
<th>New Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>43,000</td>
</tr>
<tr>
<td>Caribbean</td>
<td>27,000</td>
</tr>
<tr>
<td>North Africa and Middle East</td>
<td>68,000</td>
</tr>
<tr>
<td>Latin America</td>
<td>140,000</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>2.8 million</td>
</tr>
<tr>
<td>Eastern Europe and Central Asia</td>
<td>270,000</td>
</tr>
<tr>
<td>East Asia</td>
<td>100,000</td>
</tr>
<tr>
<td>South and South-East Asia</td>
<td>860,000</td>
</tr>
<tr>
<td>Oceania</td>
<td>7,100</td>
</tr>
</tbody>
</table>

**Total Estimated Number of People Newly Infected with HIV in 2006:** 4.3 million
Global Estimates: End of 2006

- 39.5 million people are living with HIV
  - 17.7 million women
  - 2.3 million children under age 15
- 2.9 million AIDS deaths
- 3.8 million were newly infected

Source - http://www.avert.org/worldstats.htm
United States 2007

- There are currently an estimated 40,000 new HIV infections per year in the United States.
- More than half of new HIV infections now occur in persons under 25 years old.
- The estimated lifetime medical costs are an average of $200,655.
- Each new infection results in a loss of approximately 23.9 quality-adjusted life years.
Epidemiology of HIV in US

- 17% increase in prevalence 2001-2004
- Main risk factor: Sexual contact for both men and women
  - Women: 71% heterosexual; 27% IDU
- Disproportionate impact on Blacks & Hispanics
  - 48% of HIV+; 13% of US Black population
  - Hispanics slightly over 4 times higher than whites

Campsmith M, et al. XVI IAC Toronto, Canada, Aug. 13-18, 2006; Abst. MOPE0551
Estimated Prevalence Rates for Adults and Adolescents Living with AIDS (per 100,000 population), 2005—United States and Dependent Areas

Note: Data have been adjusted for reporting delays.
* Includes persons whose area of residence is unknown or missing.

Revised June 2007
Proportion of AIDS Cases among Adults and Adolescents, by Sex and Transmission Category Diagnosed in 2005—50 States and DC

**Males**
- Male-to-male sexual contact: 58%
- Injection drug use: 18%
- High-risk heterosexual contact*: 16%
- Other/not identified†: 7%
- Male-to-male sexual contact and IDU: 1%

**Females**
- Male-to-male sexual contact: 27%
- Injection drug use: 70%
- High-risk heterosexual contact*: 2%
- Other/not identified†: 1%

Note: Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed.

*Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
†Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
“My daughter is not ready yet. Would you like to join me in watching a Short video on AIDS?”
Reported AIDS Cases, by Age and Sex
Cumulative through 2005—United States and Dependent Areas

- Males N* = 769,635
- Females N* = 186,383

* Excludes 1 person of unknown sex.
Living HIV, AIDS Cases Statistics in Kansas, 2006

<table>
<thead>
<tr>
<th>Cases</th>
<th>Total #</th>
<th># Alive</th>
<th>% Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>2691</td>
<td>1236</td>
<td>46%</td>
</tr>
<tr>
<td>HIV</td>
<td>677</td>
<td>657</td>
<td>97%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>3368</td>
<td>1893</td>
<td>56%</td>
</tr>
</tbody>
</table>

Data Source: Kansas HIV/AIDS Surveillance System, analysis by date of report
Cumulative HIV, AIDS Cases Statistics in Kansas, 2006

<table>
<thead>
<tr>
<th>Cases</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
<th>M:F Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>2362</td>
<td>329</td>
<td>2691</td>
<td>7.2:1</td>
</tr>
<tr>
<td>HIV</td>
<td>519</td>
<td>158</td>
<td>677</td>
<td>3.3:1</td>
</tr>
</tbody>
</table>

Data Source: Kansas HIV/AIDS Surveillance System, accessed on June 1st 2007, analysis by date of report
PLWHA Cases and Population, Kansas, Through 2006

**PLWHA Cases (N=1893)**

- White: 58%
- African Americans: 14%
- Hispanic: 3%
- Other: 3%

**Population Estimate in 2005 (N=2,744,687)**

- White: 83%
- African Americans: 8%
- Hispanic: 25%
- Other: 3%

Data Source: Kansas HIV/AIDS Surveillance System, analysis by date of report
2005 Population Estimates: Center for Health and Environmental Statistics, KDHE
Estimated Number of AIDS Cases, Deaths, and Persons Living with AIDS, 1985-2003, United States

- AIDS
- Deaths
- Prevalence

Note: Data adjusted for reporting delays.
## Prevalent AIDS Cases by Age

### 2006 Data

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13 Years</td>
<td>6</td>
</tr>
<tr>
<td>13 to 14 Years</td>
<td>1</td>
</tr>
<tr>
<td>15 to 24 Years</td>
<td>84</td>
</tr>
<tr>
<td>25-34 Years</td>
<td>452</td>
</tr>
<tr>
<td>35 to 44 Years</td>
<td>465</td>
</tr>
<tr>
<td>45 to 54 Years</td>
<td>178</td>
</tr>
<tr>
<td>55 to 64 Years</td>
<td>43</td>
</tr>
<tr>
<td>65 Years or older</td>
<td>7</td>
</tr>
</tbody>
</table>

Data source: Kansas HIV/AIDS Bi-Annual Report, December 2006
Prevalent HIV Cases by Age
2006 Data

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13 Years</td>
<td>6</td>
</tr>
<tr>
<td>13 to 14 Years</td>
<td>0</td>
</tr>
<tr>
<td>15 to 24 Years</td>
<td>137</td>
</tr>
<tr>
<td>25-34 Years</td>
<td>238</td>
</tr>
<tr>
<td>35 to 44 Years</td>
<td>178</td>
</tr>
<tr>
<td>45 to 54 Years</td>
<td>78</td>
</tr>
<tr>
<td>55 to 64 Years</td>
<td>18</td>
</tr>
<tr>
<td>65 Years or older</td>
<td>2</td>
</tr>
</tbody>
</table>

Data source: Kansas HIV/AIDS Bi-Annual Report, December 2006
HIV Infection
Time Line of HIV Infection

- Acute Infection
- Asymptomatic HIV Infection: 10-15 Years
- Symptomatic HIV Infection: 3-5 Years
- AIDS: ? Years
- Positive Ab Test result (6 months)
**Typical Course of Untreated HIV Infection**

- **Primary Infection**
  - Possible acute HIV syndrome
  - Wide dissemination of virus
  - Seeding of lymphoid organs

- **Clinical Latency**

- **Opportunistic disease**

- **Constitutional symptoms**

- **Death**

- **Plasma Viremia Titer**

- **CD4 T Cells/mm³**

- **Weeks**
  - 0, 3, 6, 9, 12

- **Years**
  - 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

**Pantaleo et al, NEJM, 1993**
Course of HIV Disease Progression as it Relates to CD4 Lymphocyte Count

CD4 cell count / mm $^3$

- Thrombocytopenia
- Lymphadenopathy
- 500
- Bacterial skin infection
- Herpes simplex, zoster
- Oral, skin fungal infections
- 400
- Hairy leukoplakia
- Tuberculosis
- 300
- Kaposi’s sarcoma
- 200
- PCP
- Cryptococcosis
- Toxoplasmosis
- CMV
- 100
- Lymphoma
- MAC
- 0

Months

Years
Case Study MW

- 42 year old white female who has felt ill since October, 2006.
  - progressive cough with production of clear sputum.
  - fevers, chills, and sweats during this time also.
  - 30 pound weight loss
  - a rash that is a red, scaling, irritated area involving the corners of her mouth, eyelids, and behind her ears.
  - intermittent nausea and vomiting
Case Study MW

- Seen by multiple physicians between October 2006 and the end of January 2007 for various complaints

- Primary Care Physician appointment on 1/29/07 for increasing dyspnea and was noted to have thrush
Case Study MW

- Rapid HIV test was positive.
- The confirmatory test was positive also.
- The patient was told she was HIV positive and referred to HIV Specialist
- She currently is feeling overwhelmed and depressed.
Case Study MW

Laboratory

- CD4 Absolute – 42
- HIV Quantitative Viral Load – >500,000
HIV Treatment
“That’s the way I treat a virus!”
When to Start Treatment

<table>
<thead>
<tr>
<th>Clinical Category</th>
<th>CD4+ Cell Count</th>
<th>Plasma HIV-1 RNA</th>
<th>General Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS-defining illness or severe symptoms*</td>
<td>Any value</td>
<td>Any value</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&lt; 200</td>
<td>Any value</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>200-350</td>
<td>Any value</td>
<td>Treatment should be offered following full discussion of pros and cons of treatment.</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&gt; 350</td>
<td>≥ 100,000</td>
<td>Most clinicians recommend deferring therapy, but some clinicians will treat.</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&gt; 350</td>
<td>&lt; 100,000</td>
<td>Defer therapy</td>
</tr>
</tbody>
</table>

DHHS Guidelines: 10/10/2006
HIV Replication Cycle and Sites of Drug Activity

1. Attachment
2. Uncoating
3. Reverse Transcription
4. Integration
5. Transcription
6. Translation
7. Assembly and Release

- **Attachment Inhibitors**: CD4 Receptor
- **NNRTIs**: Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
- **Protease Inhibitors**: Capsid proteins and viral RNA
- **HIV Virions**: Viral RNA, Unintegrated double stranded Viral DNA, Integrated viral DNA, Viral mRNA, gag-pol polyprotein
- **Cytokines**: CCR5 or CXCR4 co-receptor
- **New HIV particles**: Viral particles

# Licensure of Antiretroviral Agents by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug / Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>zidovudine (Retrovir)</td>
</tr>
<tr>
<td>1988</td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td>didanosine (Videx)</td>
</tr>
<tr>
<td>1992</td>
<td>zalcitabine (Hivid)</td>
</tr>
<tr>
<td>1993</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>stavudine (Zerit)</td>
</tr>
<tr>
<td>1995</td>
<td>lamivudine (Epivir)</td>
</tr>
<tr>
<td>1996</td>
<td>saquinavir (Invirase)</td>
</tr>
<tr>
<td>1997</td>
<td>ritonavir (Norvir)</td>
</tr>
<tr>
<td></td>
<td>indinavir (Crixivan)</td>
</tr>
<tr>
<td></td>
<td>nevirapine (Viramune)</td>
</tr>
<tr>
<td>1998</td>
<td>nelfinavir (Viracept)</td>
</tr>
<tr>
<td></td>
<td>delavirdine (Rescriptor)</td>
</tr>
<tr>
<td>1999</td>
<td>amprenavir (Agenerase)</td>
</tr>
<tr>
<td>2000</td>
<td>lopinavir/ritonavir (Kaletra)</td>
</tr>
<tr>
<td>2001</td>
<td>tenofovir (Viread)</td>
</tr>
<tr>
<td>2003</td>
<td>enfuvirtide (Fuzeon)</td>
</tr>
<tr>
<td>6/03</td>
<td>atazanavir (Reyataz)</td>
</tr>
<tr>
<td>7/03</td>
<td>emtricitabine (Emtriva)</td>
</tr>
<tr>
<td>8/04</td>
<td>lamivudine/abacavir sulfate (Epzicom)</td>
</tr>
<tr>
<td></td>
<td>emtricitabine / tenofovir disoproxil fumarate (Truvada)</td>
</tr>
<tr>
<td>6/05</td>
<td>tipranavir (Aptivus)</td>
</tr>
<tr>
<td>6/06</td>
<td>darunavir (Prezista)</td>
</tr>
<tr>
<td>7/06</td>
<td>efavirenz/emtricitabine, tenofovir DF (Atripla)</td>
</tr>
<tr>
<td>8/07</td>
<td>maraviroc (Selzentry)</td>
</tr>
</tbody>
</table>

* Fixed dose combinations of existing drugs
New Drugs...New Issues...More $ 

**Selzentry® (maraviroc)**

Entry Inhibitor – Known as CCR5 Inhibitor

- **Pronunciation(s):**
  - sell-ZEN-tree
  - mah-RAV-er-rock

- A new laboratory test called a *tropism assay* will likely be necessary before Selzentry is used, to determine if treatment with the drug will be useful.

- **Cost** of Tropism Assay --- approx. $1500!!
# The Move Toward Lower Pill Burdens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Daily pill burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996 Zerit/Epivir/Crixivan</td>
<td>10 pills, Q8H</td>
<td></td>
</tr>
<tr>
<td>1998 Retrovir/Epivir/Sustiva</td>
<td>5 pills, BID</td>
<td></td>
</tr>
<tr>
<td>2002 Combivir (AZT/3TC)/EFV</td>
<td>3 pills, BID</td>
<td></td>
</tr>
<tr>
<td>2003 Viread/ Emtriva/Sustiva</td>
<td>3 pills, QD</td>
<td></td>
</tr>
<tr>
<td>2004 Truvada/Sustiva</td>
<td>2 pills, QD</td>
<td></td>
</tr>
</tbody>
</table>
# The Move Toward Lower Pill Burdens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Daily pill burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>1 pill QD</td>
<td></td>
</tr>
<tr>
<td>Atripla</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(efavirenz 600 mg/</td>
<td></td>
</tr>
<tr>
<td></td>
<td>emtricitabine 200 mg/</td>
<td></td>
</tr>
<tr>
<td></td>
<td>tenofovir disoproxil fumarate 300 mg)</td>
<td></td>
</tr>
</tbody>
</table>
"I want you to take one of these with water every four years."
Encourage Healthy Lifestyle Choices

- Quit smoking
- Eliminate / avoid excess alcohol use
- Quit / avoid all drug use – especially crystal methamphetamine
- Good oral health care
- Regular exercise
- Balanced diet
Co-Existing Problems to Consider

- Pregnancy (+/or potential)
- Lipid status
- Diabetic
- Hepatitis B / C
- TB
- Drug and Alcohol Use
Major Toxicities

- Metabolic disorders
  - Lipodystrophy
  - Hyperlipidemia
  - Diabetes
- Renal tubular dysfunction (ADV)
- Anemia (ZDV)
- Kidney stones (IDV)
- Peripheral neuropathy (ddl, ddC, d4T)
- Pancreatitis (ddl)
- Rashes/Stevens-Johnson syndrome (NNRTIs)
- Hypersensitivity (ABC)
- Hepatotoxicity (RTV)
HIV and Hepatitis
# Prevalence- HBV, HCV, HIV

<table>
<thead>
<tr>
<th></th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worldwide</td>
<td>350 million</td>
<td>170 million</td>
<td>40 million</td>
</tr>
<tr>
<td>In U.S.</td>
<td>1.25 million</td>
<td>4.1 million</td>
<td>1 million</td>
</tr>
<tr>
<td>Coinfected-HIV</td>
<td>?&lt;5%,&lt;65,000</td>
<td>5-10%,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>150-300,000</td>
<td></td>
</tr>
<tr>
<td>Coinfected-HCV</td>
<td></td>
<td>15-30%,</td>
<td>15-30%,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150-300,000</td>
<td>150-300,000</td>
</tr>
<tr>
<td>Coinfected-HBV</td>
<td></td>
<td></td>
<td>?5-10%,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50-100,000</td>
</tr>
</tbody>
</table>
Factors Affecting the Liver in HIV

- HCV
- HBV
- HAV
- Opportunistic Infections
- ETOH/IVDU
- HCV Treatment
- NNRTI
- Immune Reconstitution
- Nucleoside Analogues
- Protease Inhibitors
- Diabetes
- Dyslipidemia

Slide courtesy of R. Berggren, MD.
## Epidemiology of Chronic Hepatitis B Infection

<table>
<thead>
<tr>
<th>Geographical distribution</th>
<th>SE Asia</th>
<th>Mediterranean basin</th>
<th>United States Western Europe Australia New Zealand Middle East</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>China</td>
<td>Eastern Europe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pacific Islands</td>
<td>Central Asia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sub-Saharan Africa</td>
<td>Japan</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Indigenous populations of the Arctic, New Zealand and Australia</td>
<td>Latin America</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>High</th>
<th>Intermediate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrier rate</td>
<td>5–20%</td>
<td>3–5%</td>
<td>0.1–2%</td>
</tr>
<tr>
<td>Mode of transmission</td>
<td>Mother–infant &amp; Percutaneous</td>
<td>Percutaneous Sexual</td>
<td>Percutaneous Sexual</td>
</tr>
<tr>
<td>Usual age at infection</td>
<td>Perinatal &amp; Early childhood</td>
<td>Early childhood</td>
<td>Adult</td>
</tr>
</tbody>
</table>
Epidemiology of HBV: United States

- 1.25 million in US have chronic HBV infection; highest incidence is in Alaska (6.4%)
- Local factors influence incidence and prevalence
  1. Ethnicity
  2. Immigration patterns
  3. IVDA
  4. High-risk sexual activity
- Increased incidence of infection in first generation children of families from high risk area
Impact of Vaccination Schedules in the US

- 1991 CDC published guidelines recommending universal vaccination of infants and children

- In period from 1990-2002, incidence of acute HBV decreased
  - 67% in all age groups
  - 89% in children < 20 years of age

MMWR 2004; 52; 1252
Indications for Therapy

- HBsAg + HBeAg +
  - Elevated ALT
  - HBV DNA > $10^5$ copies

- HBsAg + HBeAg – (pre-core mutant)
  - Elevated ALT
  - HBV DNA > $10^5$ copies

AASLD Practice Guidelines, 2001
Thinking About Hepatitis B Treatment

- Chronic hepatitis B management is more like that of HIV than like that of hepatitis C:
  - Treatment aims at viral suppression more than eradication
  - Declines in HBV load and normalization of LFT’s are seen as favorable markers

- The NIH still mandates that HBV drugs are shown to be efficacious individually, so we have a series of single drug trials and know the effects of drugs individually, but not in combination
Therapy For Hepatitis B

- Interferon
- Lamivudine (Epivir®)
- Adefovir (Preveon® and Hepsera®)
- Tenofovir (Viread®) - most popular agent in 2005 for HIV-HBV, as very effective against both viruses
- Entecavir (Barraclude®) – approved 3/2005
- Telbivudine (Tyzeka®) – approved 1/2007
The HIV-HCV Problem

In parts of the World (Spain), >50% with HIV have HCV

HIV-infected individuals have shared risk factors for hepatitis A, B and C and should be vaccinated against HAV and HBV
Hepatitis C: A Global Health Problem

170 Million Carriers Worldwide, 3-4 MM new cases/year

SOURCE, WHO 1999
Hepatitis C Virus (HCV)

- Discovered in 1989 as a small RNA blood-borne virus with a large reservoir of chronic carriers worldwide
- Major cause of posttransfusion hepatitis prior to 1992
- Major cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma worldwide
- Prevalence is 1.8% of the US population
- 1990-2015: estimated 4-fold increase in the number of patients diagnosed with HCV in the United States

NIH Consensus Development Conference Panel Statement Management of Hepatitis C, 2002
Hepatitis C Basics

- “Chronic hepatitis C” is defined by a positive HCV RNA in a blood test
- 15-25% of people clear hepatitis C spontaneously (don’t have it): negative HCV RNA
- Longer time with HCV, older, heavy alcohol: more liver disease
- Five key genotypes in the U.S., which have variable genetic sequences (1a, 1b, 2a, 2b, 3a)
The HIV-HCV Problem

- Liver disease is a frequent cause of morbidity and mortality

- Underlying liver disease clearly complicates management because:
  - patients likely at increased risk of ART hepatotoxicities
  - Distinction between ART-related ALT abnormalities and hepatitis-associated fluctuations in ALT is problematic
  - Interactions between ribavirin and ART (ddI, d4T)
HCV Genotypes and Subtypes

- Developed countries
- Americas + Western Europe
- South Africa
- Middle East
- North Africa
- IVDU
- Asia

Simmonds P, Journal of Hepatology, 1999
Factors Which Might Influence The Outcome Of Hepatitis C

**Virus**
- Load
- Genotype
- Quasispecies

**Host**
- Sex
- Age
- Race
- Genetics
- Immune response

**Environment**
- Alcohol
- HBV
- HIV
- Drugs
- Steatosis
- Iron
- NASH

Alberti, J of Hepatology, 1999
Considerations for Treatment

- Persistently elevated ALTs
- HCV RNA-positive status
- Histologic changes on liver biopsy
  - Necrosis, inflammation, portal or bridging fibrosis
Histologic Staging

Stage 0: No Fibrosis
Stage 1: Portal Fibrosis
Stage 2: Few septa
Stage 3: Numerous septa
Stage 4: Cirrhosis
Hepatitis C Screening and Diagnosis Summary

- Suspect disease on the basis of risk factors, not symptoms
- Positive anti-HCV result indicates current infection until refuted
- Measurement of HCV RNA may be required to establish diagnosis in selected cases
Treatment Definitions

- The **First** aim is to clear HCV RNA from peripheral blood, a necessary, but not sufficient condition to achieve a sustained virological response.

- The **Second** aim is to prevent relapse in patients who cleared HCV RNA during induction, in order to achieve a sustained virological response.

Adapted from Pawlotsky JM, Hepatology vol. 32, #5, 2000
The decision to treat should be individualized, taking the following factors into consideration:

- Patient’s age
- Histologic severity of the disease
- Comorbid conditions
- Efficacy of currently available treatments
Any patient with chronic HCV infection can be treated. Treatment is for 6-12 months and requires weekly subcutaneous injections and 4-6 pills by mouth every day. Treatment has a lot of side effects. The more liver disease a patient has, and if they have genotype 2 or 3 infection, affect how strongly treatment is recommended.

NIH Consensus Development Conference: Management of Hepatitis C 2002 *Hepatology* 36:S1-252
## Interferon Adverse Effects

- **Flu-like symptoms**
  - fever, chills
  - headaches
  - myalgias, arthralgias
- **Fatigue**
- **Anorexia**
- **Nausea/vomiting**
- **Diarrhea**
- **Thrombocytopenia**
- **Neutropenia**
- **Alopecia**
- **Injection site reactions**
- **Depression**
- **Mood swing/irritability**
- **Insomnia**
- **Impaired concentration**
- **Thyroid alterations**
- **Worsening diabetes**
- **Autoimmune disorders**
Summary

- HIV and HCV have similarities but important differences
- HIV/HCV coinfection is common due to shared risk factors for transmission
- HCV infection can lead to cirrhosis, hepatic decompensation, and hepatocellular carcinoma
- Liver biopsy is to HCV what CD4 count is to HIV
- The serious consequences of HCV are becoming more evident, and disease burden is expected to increase
HIV and TB
Tuberculosis

Caused by infection with a bacteria
- *Mycobacterium tuberculosis*
- Spread like the common cold
- Respiratory droplets in the air
- Coughing, sneezing, talking, singing….

1/3 of the world’s population infected with TB

Bacteria live dormantly in the lung - latent TB infection

Only 5-10% actually develop TB disease during their lifetime

9 million new TB cases (2004)
Latent TB infection progresses to disease when body’s immune system weakened
  - Malnutrition
  - HIV
  - Other factors…

TB disease usually affects the lungs (pulmonary TB) but can affect any other part of the body (extrapulmonary TB).

Symptoms
  - persistent cough for > 2-3 weeks
  - weight loss
  - fever
  - night sweats
  - coughing up blood
Tuberculosis cases per 100k population
2004

![Map showing tuberculosis cases per 100k population in 2004. The map is color-coded, with lighter colors indicating lower case numbers (0-24, 25-50, 50-100) and darker colors indicating higher case numbers (100-300, 300+) and no estimate.](image)
Statewide Active TB Distribution 2006

- 1 - 5 Cases
- 8 Cases
- 10 Cases
- 25 Cases
Where are they *from* in 2006?

- US Born: 38%
- Foreign Born: 62%
**TB Cases by Selected Characteristics - Kansas, 2006**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>HIV co-Infected cases</td>
</tr>
<tr>
<td>4</td>
<td>case diagnosed at death</td>
</tr>
<tr>
<td>66</td>
<td>Pulmonary, 10 Extrapulmonary, 6 Both</td>
</tr>
<tr>
<td>39</td>
<td>Smear +, 35 Smear -, 8 No smears</td>
</tr>
<tr>
<td>13</td>
<td>Negative Skin Test, 4 normal CXR</td>
</tr>
<tr>
<td>4</td>
<td>Homeless in past year</td>
</tr>
<tr>
<td>4</td>
<td>Correctional inmates at diagnosis</td>
</tr>
</tbody>
</table>
TB Cases by Selected Characteristics - Kansas, 2006

(Continued)

4 Long term facility residents
5 injection drug users
9 non injection drug users
17 excessive alcohol users
29 clinical cases
31 culture confirmed cases
1 MDR
The Links Between HIV & TB

- Often described as the “co-epidemic” or “dual epidemic”
  - HIV affects the immune system and increases the likelihood of people acquiring new TB infection.
  - It also promotes both the progression of latent TB infection to active disease and relapse of the disease in previously treated patients.
  - TB is one of the leading causes of death in HIV-infected people.
An Extensive Problem

- An estimated one-third of the 40 million people living with HIV/AIDS worldwide are co-infected with TB.
- Without proper treatment, approximately 90% of those living with HIV die within months of contracting TB.
- The majority of people who are co-infected with both diseases live in sub-Saharan Africa.
The Impact of TB/HIV Co-infection

- Each disease speeds up the progress of the other
- TB considerably shortens the survival of people with HIV/AIDS.
- TB kills up to half of all AIDS patients worldwide.
- People who are HIV-positive and infected with TB are up to 50 times more likely to develop active TB in a given year than people who are HIV-negative.
The Impact of TB/HIV Co-infection

- TB is harder to diagnose in HIV-positive people.
- TB progresses faster in HIV-infected people.
- TB in HIV-positive people is almost certain to be fatal if undiagnosed or left untreated.
- TB occurs earlier in the course of HIV infection than many other opportunistic infections.
To Treat...We Must Identify

- Mantoux / PPD (Purified Protein Derivative) “TB Skin Testing” – patient must have a return visit to read the test in 48-72 hours.
- QuantiFeron Gold– a blood test to identify
Treatment of TB

TB is treatable and curable, even in people living with HIV

Four antibiotics over 6-8 months
  - Rifampicin
  - Isoniazid
  - Ethambutol
  - Pyrazinamide

To prevent drug resistance
Clinical features 2

Microscopy of specially stained sputum is the main test for diagnosing TB
Test is not as effective in HIV
  - sputum negative TB
  - extrapulmonary TB
X-ray has important role in HIV
Mortality rates are higher with HIV
  - Rapid progression of TB
  - Delays in seeking care
  - Delays in making the diagnosis of TB
New tools to improve diagnosis and treatment urgently needed
TB is treatable and preventable

TB can be prevented in people living with HIV by

- Isoniazid preventive therapy
- Intensified case finding
- Infection control
  - HIV care
  - Prisons
  - Workplace
Drug resistant TB

First line TB drugs
- Rifampicin
- Isoniazid
- Ethambutol
- Pyrazinamide

Multi-drug resistance (MDR)
- at least Rifampicin and Isoniazid

Drug resistant TB results from inadequate TB control
Treat with second-line drugs
Treating MDR TB takes 3-4 times longer and costs 100 times more
Extensively *drug* resistant TB
XDR TB

MDR - TB that is also resistant to 2/3 of the most powerful second line TB drugs

Difficult to diagnose
- Time for culture
- Special laboratories

About 10% of MDR TB is XDR

High fatality rate in people living with HIV

Present in every region of the world
Summary

Drug resistant TB

Drug-resistant TB poses a grave public health threat especially in high HIV prevalence settings.

XDR-TB strains have been found in all regions of the world.

XDR-TB occurs as a result of inadequate TB control programmes.

XDR-TB, if identified early, can be treated and cured but experience limited to low HIV prevalence settings.

Infection control measures must be strengthened.

XDR-TB underlines the need for investment in basic TB control plus development of new TB diagnostics, treatments and vaccines.
Summary

TB is usually treatable in people living with HIV
TB is preventable
XDR TB is preventable
HIV community can play a major role in detecting, treating and preventing TB
TB programmes can help in accelerating towards universal access
TB and HIV communities need to work very closely together to reduce the impact of TB on people living with HIV
“We can’t fight AIDS unless we do much more to fight TB as well.”

Nelson Mandela

Bangkok, July 15, 2004

Source: From the CREATE project
Nelson Mandela, Former President of South Africa and Nobel peace prize winner 1993