Hepatitis C in prison settings

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Objectives

- Briefly review the current clinical status of Hepatitis C
- Discuss issues specific to the prison system
- Describe the role of psychiatric co-morbidity in treatment for Hepatitis C
Why are we interested in Hepatitis C?

• Psychiatric co-morbidity is involved in propagation of the virus through behavior
• Psychiatric co-morbidity is the major barrier to successful treatment
• Models of integrated care
• Models of disease co-morbidity
• Models for understanding major depression
## HIV and Hepatitis C

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>Hep C</th>
</tr>
</thead>
<tbody>
<tr>
<td>World prevalence %</td>
<td>0.8 %</td>
<td>3 %</td>
</tr>
<tr>
<td>World prevalence</td>
<td>38,000,000</td>
<td>200,000,000</td>
</tr>
<tr>
<td>Highest prevalence</td>
<td>Swaziland 26 %</td>
<td>Egypt 18 %</td>
</tr>
<tr>
<td>Highest prevalence</td>
<td>South Africa 5.6 mil</td>
<td>China 42 mil</td>
</tr>
<tr>
<td>New infections/day</td>
<td>7,000</td>
<td>11,000</td>
</tr>
</tbody>
</table>
Hepatitis C virus

- Single stranded RNA virus
- Mechanistically never uses DNA
- Transmitted by body fluid contact or freshly contaminated items (razors, needles, straws)
- 5.2 million (2%) in the United States
- Up to 50% of unaware of the infection
- 17,000 new cases/year in the United States
- 15,000 die/year
HCV Infection

Acute Infection, 20-30% with symptoms

Clearance of HCV RNA, 15%-25%

Fulminant Hepatitis, Rare

Chronic Infection, 75%-85%

Extrahepatic Manifestations

Chronic Active Hepatitis

Cirrhosis, 10%-20% over 20 years

 Decompensated Cirrhosis, 5-year survival rate of 50%

HCC, 1%-4% per year
Current issues in HEP C

• Best current result-SVR=cure
• Cure rate 40-80 % with interferon-ribavirin for 1 year depending on genotype
• Addition of direct acting antivirals (now approved) has dramatically improved outcome with 90-100% cure rates “all comers”
• The era of non INF treatment is here with the approval of more “direct acting antivirals”
Hepatitis C in prisoners

• About 30 % with a large range worldwide
  – US large meta-analysis 29 %
• Seroconversion in IVDU 16/100person-years (with broad variation)
• High rates of reinfection after treatment among HIV/HCV-coinfected MSM (9–15 per 100 person-years)
Hepatitis C

Clinical Benefits of SVR: Liver Failure, HCC

- 530 Europeans followed for a median 8.4 years after HCV treatment
- 192 (36%) achieved SVR

HCC Risk After SVR

Nagaoki et al., AASLD 2014; #1977
HCC risk after SVR to IFNa-based therapies (n=2266)

- HCC risk after 10 years: 7% (males 10%)
- HCC risk after 20 years: 17% (males 26%)

Cirrhosis

<table>
<thead>
<tr>
<th></th>
<th>26%</th>
<th>63%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>26%</td>
<td>63%</td>
</tr>
</tbody>
</table>
SVR Decreases All Cause Mortality

General: 18 studies
n=29,269
Avg. FU=4.6 years

Cirrhotic: 9 studies
n=2,734
Avg. FU=6.6 years

HIV/HCV: 5 studies
n=2,560
Avg. FU=5.1 years

% patients after 5 years

5-Year All Cause Mortality

SVR
No SVR

General
10.5%
4.5%

Cirrhotic
11.3%
3.6%

Co-infected
10.0%
1.3%

Saleem, Abst# 44
SVR rates in INF-RBV regimens

SVR Rates by IL28B Genotype
- African Americans
- Hispanic Americans
- European Americans

TT: 17%, 22%, 33%
CT: 19%, 44%, 42%
CC: 53%, 77%, 82%
## To treat or not to treat

### Reasons to treat
- Treatment as prevention
- Cost effective in models
- High likelihood of success
- Concentrated population
- Ease of screening and retention
- Good data capture
- Facilitation of outcome studies

### Reasons not to treat
- Short stays for IVDU who have the highest likelihood of transmission
- Budget and cost
- Reinfection in high risk patients
- Lack of transitional care at release associated with reinfection and loss of prevention assets
### Multi-Class Combination Drugs

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Status</th>
<th>Pharmaceutical Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvoni</td>
<td>ledipasvir + sofosbuvir (GS-5885 + GS-7977)</td>
<td>Approved</td>
<td>Gilead Sciences</td>
</tr>
<tr>
<td>Technivie (Viekirax)</td>
<td>(ombitasvir + paritaprevir + ritonavir) (ABT 267 + ABT450r)</td>
<td>Approved</td>
<td>AbbVie</td>
</tr>
<tr>
<td>Viekira Pak</td>
<td>(ombitasvir + paritaprevir + ritonavir + dasabuvir) (ABT 267 + ABT450r + ABT 333)</td>
<td>Approved</td>
<td>AbbVie</td>
</tr>
<tr>
<td>n/a</td>
<td>elbasvir + grazoprevir (MK-8742 + MK-5172)</td>
<td>Phase III (submitted to FDA 5/2015)</td>
<td>Merck</td>
</tr>
<tr>
<td>n/a</td>
<td>asunaprevir + beclabuvir + daclatasvir (BMS 650032 + BMS 791325 + BMS 790052)</td>
<td>Phase III</td>
<td>Bristol-Myers Squibb</td>
</tr>
<tr>
<td>n/a</td>
<td>sofosbuvir + velpatasvir (GS-7977 + GS-5816)</td>
<td>Phase III</td>
<td>Gilead Sciences</td>
</tr>
</tbody>
</table>
IAS-USA Guidelines for Hep C Page
Recommended treatment as of August 2015

• www.HCVguidelines.org
HCV genotype 1a infection

• Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1a infection.

• Rating: Class I, Level B (no cirrhosis); Class IIa, Level B (cirrhosis)

*The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.
HCV genotype 1a infection

• Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 1a infection.

• Rating: Class I, Level A
HCV genotype 1a infection

• Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) and weight-based RBV for 12 weeks (no cirrhosis) or 24 weeks (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1a infection.

• Rating: Class I, Level A
HCV genotype 1a infection

- Daily simeprevir (150 mg) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks (cirrhosis without the Q80K polymorphism) with or without weight-based RBV is recommended for treatment-naive patients with HCV genotype 1a infection.

- **Rating:** Class I, Level A
HCV genotype 1b infection.

- Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1b infection.

- **Rating:** Class I, Level B (no cirrhosis); Class IIa, Level B (cirrhosis)

*The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.*
HCV genotype 1b infection.

- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 1b infection.

  - **Rating:** Class I, Level A
HCV genotype 1b infection.

- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 1b infection.
- **Rating:** Class I, Level A
HCV genotype 1b infection.

- Daily simeprevir (150 mg) plus sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1b infection.
- **Rating:** Class I, Level A
HCV genotype 2 infection.

• Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 2 infection who cannot tolerate RBV.
  • Rating: Class IIa, Level B
• Daily sofosbuvir (400 mg) and weight-based RBV for 12 weeks is recommended for treatment-naive patients with HCV genotype 2 infection.
  • Rating: Class I, Level A
• Extending treatment to 16 weeks is recommended in patients with cirrhosis.
  • Rating: Class IIb, Level C

*The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.
HCV genotype 3 infection.

- Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (cirrhosis) is recommended for treatment-naive patients with HCV genotype 3 infection.
- **Rating:** Class I, Level A (no cirrhosis); Class IIa, Level C (cirrhosis)
- Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is recommended for IFN-eligible, treatment-naive patients with HCV genotype 3 infection.
  - **Rating:** Class I, Level A

*The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.*
HCV genotype 3 infection who are IFN-ineligible

- Daily sofosbuvir (400 mg) and weight-based RBV for 24 weeks is an alternative regimen for treatment-naive patients with HCV genotype 3 infection who are IFN-ineligible.

  - **Rating:** Class I, Level A
HCV genotype 4 infection.

- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 4 infection.
  - **Rating:** Class IIb, Level B

- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and weight-based RBV for 12 weeks is recommended for treatment-naive patients with HCV genotype 4 infection.
  - **Rating:** Class I, Level B

- Daily sofosbuvir (400 mg) and weight-based RBV for 24 weeks is recommended for treatment-naive patients with HCV genotype 4 infection.
  - **Rating:** Class IIa, Level B

- **Alternative regimen for treatment-naive patients with HCV genotype 4 infection.**
  - Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an acceptable regimen for treatment-naive patients with HCV genotype 4 infection.
  - **Rating:** Class II, Level B
HCV genotype 5 or 6 infection

- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 5 or 6 infection.
  - Rating: Class IIa, Level B
- Alternative regimen for treatment-naive patients with HCV genotype 5 or 6 infection.
  - Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is an alternative regimen for treatment-naive patients with HCV genotype 5 or 6 infection.
  - Rating: Class IIa, Level B
### Table 5. Characteristics of Direct-Acting Antiviral Drugs and Dose Adjustments for Renal or Hepatic Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Inhibition</th>
<th>Induction</th>
<th>Substrate</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asunaprevir&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Moderate inhibitor of CYP2D6</td>
<td>Weak inhibitor of CYP3A4 and P-gp</td>
<td>Substrate of CYP3A4, P-gp, and OATP1B1</td>
<td>No adjustment needed</td>
<td>Should likely be avoided in patients with CTP class B or C disease</td>
</tr>
<tr>
<td>Daclatasvir&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Moderate inhibitor of P-gp and OATP</td>
<td>NA</td>
<td>Substrate of CYP3A and P-gp</td>
<td>No adjustment needed</td>
<td>No adjustment needed</td>
</tr>
<tr>
<td>Ledipasvir</td>
<td>Mild inhibitor of P-gp, BCRP</td>
<td>NA</td>
<td>Substrate of P-gp</td>
<td>No adjustment needed</td>
<td>No adjustment needed</td>
</tr>
<tr>
<td>Paritaprevir, ritonavir, and ombitasvir plus dasabuvir</td>
<td>Inhibitor of CYP3A4, CYP2D6, P-gp, OATP, and BCRP</td>
<td>Inhibitor of CYP1A2, CYP2C8, CYP2C9, and CYP2C19 (based on ritonavir pharmacokinetics)</td>
<td>Substrate of CYP3A4, CYP2C3, and CYP2D5</td>
<td>Likely no adjustment needed</td>
<td>Not recommended in patients with CTP class B disease, and contraindicated in patients with CTP class C disease</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>Mild inhibitor of intestinal CYP3A and CYP1A2; mild inhibitor of OATP and P-gp</td>
<td>NA</td>
<td>Substrate of CYP3A</td>
<td>No adjustment needed</td>
<td>Should be used with caution in patients with CTP class B or C disease</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>NA</td>
<td>NA</td>
<td>Substrate of P-gp</td>
<td>Not recommended if GFR &lt;30 mL/min/1.73m²</td>
<td>No adjustment needed</td>
</tr>
</tbody>
</table>

Abbreviations: BCRP, breast cancer resistance protein; CTP, Child-Turcotte-Pugh; CYP, cytochrome P450; GFR, glomerular filtration rate; NA, not available; OATP, organic anion-transporting polypeptide; P-gp, P-glycoprotein. Adapted from Kiser et al.<sup>13</sup>  
<sup>a</sup>Investigational drug.

Topics in Antiviral Medicine May/June 2015 (Volume 23, Issue 2) Hepatitis C Virus Direct-Acting Antiviral Drug Interactions and Use in Renal and Hepatic Impairment (PDF)  Lucas Hill, PharmD, AAHIVP.
Sofosbuvir and Amiodarone

• One fatality (cardiac arrest) and nine cases of brady-arrhythmia in patients taking amiodarone who started sofosbuvir +/- ledipasvir, reported this week!

• Seven of the nine patients also taking beta-blockers.

• Amiodarone is a known risk factor for brady-arrhythmia, but these cases occurred within a few hours to a few days after starting sofosbuvir.

• Mechanism unknown.
# Pharmacy costs for Rhode Island correctional facilities

**TABLE 1** Estimated total costs and cure rates per treatment course of HCV treatment guidelines

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>Clinical recommendation&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total estimated cost&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Estimated cure rate&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF+IFN+RBV</td>
<td>GT3; GT4</td>
<td>$93,400</td>
<td>85–90 %</td>
</tr>
<tr>
<td>SMV+IFN+RBV</td>
<td>GT 4</td>
<td>$75,800</td>
<td>93 %</td>
</tr>
<tr>
<td>SOF+RBV</td>
<td>GT2 non-cirrhotic</td>
<td>$84,200</td>
<td>85–95 %</td>
</tr>
<tr>
<td></td>
<td>GT2 cirrhotic</td>
<td>$112,000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GT3, GT4</td>
<td>$168,300</td>
<td></td>
</tr>
<tr>
<td>SOF+SMV</td>
<td>GT1 non-cirrhotic; GT4</td>
<td>$150,400</td>
<td>92 %</td>
</tr>
<tr>
<td></td>
<td>GT1 cirrhotic</td>
<td>$300,700</td>
<td></td>
</tr>
</tbody>
</table>

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## Pharmacy costs for Rhode Island correctional facilities

<table>
<thead>
<tr>
<th>Treatment Plan</th>
<th>Duration</th>
<th>Description</th>
<th>Cost</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF+LDV</td>
<td>8 weeks</td>
<td>GT1 non-cirrhotic</td>
<td>$63,000</td>
<td>95–99 %</td>
</tr>
<tr>
<td></td>
<td>12 weeks</td>
<td>GT1 treatment naïve cirrhotic, treatment experienced non-cirrhotic; GT4</td>
<td>$94,500</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 weeks</td>
<td>GT1 treatment experienced cirrhotic</td>
<td>$189,000</td>
<td></td>
</tr>
<tr>
<td>OBV/PTV/r+DSV+RBV</td>
<td>12 weeks</td>
<td>GT1 treatment naïve; GT1 treatment experienced non-cirrhotic; GT1b; GT4</td>
<td>$83,500</td>
<td>95–98 %</td>
</tr>
<tr>
<td>OBV/PTV/r+DSV</td>
<td>24 weeks</td>
<td>GT1a cirrhotic</td>
<td>$167,000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks</td>
<td>GT1b non-cirrhotic</td>
<td>$83,300</td>
<td>90–99 %</td>
</tr>
</tbody>
</table>

Pharmacy costs for Rhode Island correctional facilities

<table>
<thead>
<tr>
<th>TABLE 4 Estimated pharmacy and overall budget impact of HCV treatment guidelines by treatment strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat all</td>
</tr>
<tr>
<td>(n=327)</td>
</tr>
<tr>
<td>Estimated cures</td>
</tr>
<tr>
<td>Estimated total drug costs&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Budget impact&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>RIDOC 2014 pharmacy budget: $2,723,669</td>
</tr>
<tr>
<td>RIDOC 2014 overall healthcare budget: $19,889,269</td>
</tr>
<tr>
<td>Proportion of pharmacy expenditures</td>
</tr>
<tr>
<td>Proportion of overall healthcare expenditures</td>
</tr>
<tr>
<td>Estimated cost per patient cured: $110,000–130,000</td>
</tr>
</tbody>
</table>

<sup>a</sup>Total drug costs estimated from interferon-free regimens (SOF+RBV and SOF/LDV)

<sup>b</sup>Budget impact calculations based on public record of RIDOC 2014 expenditures

What is the Cost of Failure?

1. Monetary
2. Resistance
3. Access to retreatment
   - Data limited
   - Some payer systems may not approve more than one treatment regimen
Psychiatric Disorders

HIV
Hepatitis C

Risk behaviors
Mood disorder
Executive Disorder
Cognitive Disorder
Addiction
Paraphilia
Personality Disorder
Cognitive limitation
Poverty
Poor coping skills
Social Disenfranchisement

Psychological/Social disruption
Drug toxicity
Tissue damage

Mood disorder
Executive Disorder
Cognitive disorder
Addiction
Paraphilia?
Personality Disorder?
Cognitive limitation
Poverty
Poor coping skills?
• The web of psychiatric co-morbidity is so dense that it almost defies description
A web of co-morbidity

- Drug toxicity
- Nerve tissue injury
- Immune dysregulation

- Neuropathy
- Dementia
- Depression
- Disinhibition
- Apathy

- Disability
- Social isolation
- Opiate dependence
- Impoverishment
- Risk Behavior
- Poor adherence
Adherence to Direct-Acting Antivirals

• The high reproductive rate of HIV and Hepatitis C virus (HCV) makes inadequate suppression lead to resistance-associated mutations and decreases the likelihood of treatment success.

• This becomes more of an issue now with decreasing dependence on interferon and the increasing use of direct-acting viral inhibitors for Hep C that are extremely expensive.
Adherence as a model of co-morbidity

Taking medication is a behavior

environmental exposure  \[\rightarrow\]  increase  \[\rightarrow\]  positive

Behavior

decrease  \[\leftarrow\]  environmental response  \[\leftarrow\]  negative
Depression
Dementia
Delirium

Intellectual endowment
Temperament

Addictions
Life experiences
Social organization and support

Medication taking behavior
Role of Life story

• Institutional health care may have a negative effect on the way patients view treatment
• Cultural and personal assumptions strongly influence the way patients behave
• Behavior profoundly influences the outcome of medical care interventions
Beliefs about illness
Immediate life issues
Health awareness and commitment

**Negative and positive experiences with healthcare and medications**

Cultural attitude toward medical care
Social organization and support

Medication taking behavior
Role of Comorbid Mental Illness

• Depression leads to poor adherence
  – Treatment reverses this
  – Treatment of depression models successful treatment to help patients get ready for HCV and HIV treatment

• Schizophrenia and bipolar illness are both associated with poor outcomes and poor adherence
  – Collaborative treatment can reverse this
Interventions for Improved Adherence in patients with life story issues

- Frequent short visits with positive reinforcement for desired behaviors, and careful avoidance of reinforcing undesirable (non-adherent) behavior
- Understanding the validity of the influences and previous experiences of the patient
- Interventions at meaning (insight), assumptions (cognitive), behavior (behavioral), and experience (your response to the behavior) targeted at improved adherence
Hepatitis C and Depression

• Depression in 40-50%
  – Probably both as a consequence of depression induced risk as well as depression caused by Hepatitis C

• Interferon treatment causes depression

• Antidepressant treatment is effective

• Prophylaxis with antidepressants may be effective
## Elevated rates of Depression in Patients with Hepatitis C

<table>
<thead>
<tr>
<th>Rate of depression</th>
<th>Tavakkoli</th>
<th>Nelligan</th>
<th>Basseri</th>
<th>Lee</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 %</td>
<td>34 %</td>
<td>29.3 %</td>
<td>4 x control</td>
<td></td>
</tr>
</tbody>
</table>
Hepatitis C

Decreased reward sensitivity
Cytokines?
Stress transmitters
Immune system disregulation
(Poor adherence and treatment failure)

Depression

Cytokines
Stress transmitters
Interferon
Immune system activation
(Poor adherence and treatment failure)
The Role of Temperament

- Consequence avoidance vs reward seeking
- Now vs future focus
- Feeling vs function
- Cooperativeness vs disagreeableness
- Distrust (paranoia) vs trust (gullibility)
- Conscientiousness vs spontaneously directed
Simplified model of disposition

- Introversion:
  - Punishment avoidant
  - Future directed
  - Function directed

- Extraversion:
  - Reward directed
  - Present directed
  - Feeling directed
- Population-Disposition

Stability-Instability

Introversion-Extroversion
Increased patient satisfaction correlates with increased mortality

Cultural factors

• Our patients with vulnerable temperaments and cognitive limitations are particularly affected by cultural factors
Interventions to Improve Adherence in patients with temperament issues

• Reframe goals into those that fit the patient’s temperament
• Help patients to see the strengths of their endowments
• Rewards that will come from taking medications rather than problems with not taking medications
• Conspiring with the patient to get better despite the system that keeps them ill
Role of Substance Abuse

• Current alcohol abuse and drug use is associated with poorer outcomes and incomplete HCV treatment
• Addiction associated with viral resistance and increased mortality
• Collaborative treatment improves outcomes
• For opiate addiction, substitution therapy is the best studied intervention and has been shown to have improved outcomes in HCV and HIV
Interventions to Improve Adherence in patients with substance abuse

- Ongoing assessment of substance abuse
- In some cases, ongoing toxicology screens
- Collaborative arrangements for substance abuse treatment (if possible within the clinic)
- Opiate substitution therapy (eg, buprenorphine and naloxone) is extremely helpful
- Helping the patient find and initiate 12-step–based treatments (ie, AA, NA) which are free and often effective
Behavior → Reward
Addiction

Behavior

HIV and HEP C
Inflammation and Cytokines
Sympathetic activation and stress
Decreased reward sensitivity

Depression

Increase in stimulus seeking
Decreased self preservation
Day night cycle disruption
Interferon

Reward
Conclusions

• Hepatitis C is a psychiatric epidemic
• Without collaborative treatment, expense is higher, outcome is poorer, and transmission increases
• The CNS effects of chronic infection are a useful model for understanding pathophysiology