Overcoming psychiatric barriers to effective Hepatitis C treatment

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Psychiatric conditions that increase risk for Hepatitis C and complicate treatment
- Diseases-Depression (Bipolar/Schizophrenia)
- Temperament (Personality disorders/MR)
- Behaviors (Addiction)
- Life experiences (Distrust/Avoidance)
Psychiatric conditions that increase risk for Hepatitis C and complicate treatment
- Diseases - Depression (Bipolar/Schizophrenia)
- Temperament (Personality disorders/MR)
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- Life experiences (Distrust/Avoidance)
Depression diminishes

- Mood - the sense of baseline state of happiness that is usually present
- Vital sense - the sense of being well, healthy, energetic, alert and able
- Self Attitude - the sense of being good, of doing well, of effectiveness and utility to others

Anhedonia

- Loss of reward (pleasure, satiation or satisfaction) associated with behaviors
  - Appetite Directed Behaviors
    - Sleeping
    - Eating
    - Sex
  - Function Directed Behaviors
    - Work
    - Hobbies
    - Exercise

Disturbance of Neurophysiology

- Sleep
  - EARLY MORNING AWAKENING
  - Difficulty falling asleep
  - Disrupted sleep architecture
- Appetite
  - Change in food taste
  - Weight loss or gain
  - Immune function
- G.I. function
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

Hepatitis C

Depression

Reward sensitivity
Cytokines
Stress transmitters
Immune system
(Poor adherence and treatment failure)

Depression is associated with immune activation, the stress system (HPA), and genetic vulnerability of monoamine neurotransmission.

Depression is a disease of subcortical brain function and causes cognitive impairment as well as mood changes and other physiologic symptoms.
IL-6 and 5-HIAA correlate with INF administration and depression

IL-6 and serotonin polymorphisms correlate with INF-induced depression

Alleles for decreased Serotonin transporter are associated with increased risk of INF-induced depression
Interferon induced decreased sleep efficiency is associated with decreased motor speed

Interferon–induced decreased sleep is associated with increased evening cortisol

Depression correlates with subcortical deficits in patients receiving INF
Interferon treatment effect on subcortical speed

![Graph A](image1)

![Graph B](image2)

Poor sleep predicts development of major depression

![Graph](image3)

Rapid Escalation of IFN-Induced Depressive Symptoms: Threshold Effect

![Graph](image4)
Prophylactic Citalopram PEG IFN/RBV-related Depression

- Schaefer et al. AASLD; October 24-28, 2003; Boston, Mass.

<table>
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<th>(n = 11)</th>
<th>(n = 11)</th>
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<tr>
<td>History</td>
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<td>On-therapy antidepressant</td>
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<tr>
<td>Psych history (-)</td>
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<td>Receiving methadone substitution</td>
<td>Citalopram 20 mg QD initiated</td>
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Prophylaxis for depression with INF/RBV therapy

- Gleason et al. 2007 (N=10)
  - OLT
  - Escitalopram prevented depression in at risk subjects

- Raisson et al. 2007 (N = 61)
  - Prospective, DBPC
  - Paroxetine prevented depression in at risk subjects

Antidepressants with demonstrated efficacy in the treatment of depression in Hepatitis C

- Fluoxetine
- Sertraline
- Citalopram
- Escitalopram
- Nortriptyline
- Bupropion
- Mirtazapine
- ECT
Acute Treatment of MDD

Duloxetine 60 mg/d vs Placebo

Mean Change, HRSD Total Score

Treatment Time, weeks

Effect size

Mean Standardized Improvement as a Function of Initial Severity, Treatment Group

Mean Improvement

Initial Severity, baseline HRSD


Patients With ≥50% Improvement on SSRI, TCA, or Placebo

Publication Year

Proportion of Patients Responding


Major Depression  
Demoralization  
Dysthymia  
Depressive Personality  
Chronic Depression  
Sub-syndromal Major Depression  

It is much more important to know what sort of patient has a disease than what sort of disease a patient has.  

William Osler  

Simplified model of disposition  
Percent of population  

- Introversion  
- Extraversion  
- Punishment avoidant  
- Reward directed  
- Future directed  
- Present directed  
- Function directed  
- Feeling directed
• Population-Disposition

Stability-Instability

Introversion-Extroversion

Behavior

environmental exposure → Behavior → environmental response

increase positive

decrease negative