

# Psychopharmacology and the HIV-Positive Patient

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# Course Objectives

- Understanding the effects of HIV and HIV-related medications on mental health
- Appreciation for the myriad of drug-drug interactions, and those to avoid
- Familiarity with applying the biopsychosocial model in treating the HIV-positive patient
- Knowledge about drugs of abuse in HIV

# HIV

# HIV

- Rapidly-mutating retrovirus contracted through exchange of bodily fluids (blood, semen, mother's milk, vaginal secretions)
- Compromises human immune system, notably through destruction of CD4+ t cells, creating vulnerability to viral, fungal, and parasitic infections

# HIV and the Brain

HIV enters CNS early, via macrophages;  
Macrophages and microglial cells  
responsible for CNS replication  
Subcortical structures targeted

# CNS Implications of CD4 Count

- >500 lymphocytes/microliter
  - Acute retroviral syndrome (ARS)
  - Persistent generalized lymphadenopathy (PGL)
  - Aseptic meningitis

# CNS Implications of CD4 Count

- 200-500 lymphocytes/microliter
  - Pneumonia - bacterial
  - Kaposi's Sarcoma (KS)
  - B-cell lymphoma
  - Anemia

# CNS Implications of CD4 Count

- <200 lymphocytes/microliter
  - *Pneumocystis Carinii* Pneumonia (PCP)
  - Disseminated Histoplasmosis and Coccidioidomycosis
  - Extrapulmonary tuberculosis
  - Progressive Multifocal Leukoencephalopathy (PML)
  - Wasting
  - Neuropathy
  - HIV Dementia
  - Non-Hodgkin's Lymphoma (NHL)

# CNS Implications of CD4 Count

- <100 lymphocytes/microliter
  - Toxoplasmosis
  - Cryptococcosis

# CNS Implications of CD4 Count

- <50 lymphocytes/microliter
  - Disseminated Cytomegalovirus (CMV)
  - Disseminated Mycobacterium avium complex (MAC)
  - CNS Lymphoma

# Treatment

- Interrupts the HIV lifecycle by introducing drugs into vulnerable points (mainly enzymes) in the viral replication system
  - reverse transcriptase
  - protease
  - fusion

# Nucleoside-Analogue Reverse Transcriptase Inhibitors

- Includes AZT(Retrovir<sup>TM</sup>), ddI(Videx<sup>TM</sup>), ddC(Hivid<sup>TM</sup>), d4T(Epivir<sup>TM</sup>), ABC(Ziagen<sup>TM</sup>)
- Primarily eliminated by the kidneys
- CNS Penetration 10-40% (AZT 60%)

# Non-Nucleoside Reverse Transcriptase Inhibitors

- Includes NVP(Viramune<sup>TM</sup>), DLV(Rescriptor<sup>TM</sup>), EFV(Sustiva<sup>TM</sup>)
- Many interactions possible due to CYP450 metabolism: substrates, inhibitors, and inducers
- Mental status changes possible

# Considerations with Sustiva™

- Most severe side effects occur during first month
- Generally subside by the end of 4 weeks
- Include nervousness, dizziness, depression, mania, psychosis, suicidality, insomnia

# Nucleotide Reverse Transcriptase Inhibitors

- Tenofovir (Viread™)
  - renally eliminated; possibility of competition for active tubular secretion

# Protease Inhibitors

- Includes IDV(Crixivan<sup>TM</sup>), RTV(Norvir<sup>TM</sup>), SQV (Invirase<sup>TM</sup>,Fortovase<sup>TM</sup>), NFV(Viracept<sup>TM</sup>), APV(Agenerase<sup>TM</sup>), LPV/RTV(Kaletra<sup>TM</sup>)
- Poor-Moderate CNS penetration
- Many serious drug interactions possible, especially involving CYP450

# Fusion Inhibitors

- T20 (Fuzeon<sup>TM</sup>)
  - bid subcutaneous injections
  - peptide; metabolism likely not an issue

# Other HIV-related medications to consider

- Antifungals
  - very potent 3A4 inhibitors
- IFN- $\alpha$  (Hepatitis treatment)
  - mental status changes possible

# Standard of Care - Lab Data

- Routine
  - Viral load
  - CD4+ T cells count (absolute and percent)
  - Liver function tests
  - Renal function, electrolytes
  - Complete blood cell count
- Specialized
  - Resistance testing
  - Therapeutic Drug Monitoring - Investigative

# HIV and Mental Illness

# HIV and Mental Health

- Incidence of mental illness in HIV -- before and after infection
- Incidence of substance abuse in HIV
- Mental health considerations in the selection of antiretrovirals
  - some antiretrovirals have potentially severe CNS side effects, including suicidality
- Non-Adherence
  - risk factors predominately psychosocial

# Special Topics in HIV Relevant to Mental Health and Psychopharmacology

- Lipodystrophy
  - Disturbing body changes may occur, including deformation of face, limbs, trunk
- Metabolic abnormalities
  - May include insulin resistance, lipid elevations
- Disconnect Syndrome
  - Viral load and CD4 no longer maintain an inverse relationship -> implications for elevated CNS burden of virus and cognitive decline<sup>23</sup>

# Drug-Drug Interactions

# Drug Metabolism in HIV

- Cytochrome P450 System
  - Most major isoenzymes potentially involved in metabolism of HAART
    - 3A4 involved in most serious drug-drug interactions
    - Some antiretrovirals less predictable (e.g., efavirenz both inhibits and induces 3A4)

# Drug Metabolism in HIV

- UGT (uridine diphosphate-glucuronosyltransferase)
  - Consider when prescribing protease inhibitors with some opiate analgesics, tricyclics, lamotrigine, olanzapine, and 3-hydroxysubstituted benzodiazepines

# Drug Metabolism

- Alcohol Dehydrogenase
  - e.g., interaction between abacavir and chloral hydrate
- Renal Elimination
  - consider with tenofovir, nucleoside analog reverse transcriptase inhibitors
- P-Glycoprotein
  - extent of involvement not entirely clear

# **Psychotropic Cautions**

## **Antidepressants**

**Review P450 of psychotropic(s) and HIV-related medications**

## **Anticonvulsants**

**Caution with those that induce P450; immune function considerations**

## **Anxiolytics; sedative-hypnotics**

**P450 and UGT interactions**

## **Antipsychotics**

**Caution with cardiac conduction and immune function**

# **Herbal Medication Cautions**

**St John's Wort**

**Garlic Capsules**

**Milk Thistle**

**Cat's Claw (Uña de Gato)**

# Psychiatric Assessment and Management

# General Assessment for all HIV Psychiatric Patients

- Review current medications: side effects and interactions. Adherence?
- Review physical health. Check labs for abnormalities (in addition to standard of care): thyroid, testosterone, and others as indicated
- Explore substance abuse and STD exposure
- Taking herbals?
- Consider CNS workup if symptoms are new and CD4<200 (I.e., imaging, EEG, LP, additional labs)

# Assessment - Psychosocial

- Psychological
  - Defenses employed
  - Flexibility; resiliency
- Socioeconomic
  - Finances
  - Current relationships
  - Losses
  - Supports
  - Housing situation

# Treatment Approach - Depression

- Biological
  - Screen for bipolar disorder
  - Antidepressants
  - Other pharmacotherapy
  - Substance Abuse treatment
  - Changing HAART
- Psychological Issues
  - Individual, group psychotherapy
  - Supportive versus insight-oriented
- Socioeconomic Issues
  - address losses, finances, employment, housing

# Treatment Approach - Anxiety

- Biological
  - SSRIs
  - Anxiolytics: Benzodiazepines and others
  - Substance Abuse Treatment
  - Changing HAART
- Psychological
  - Individual, Group
  - CBT, supportive, insight-oriented
- Socioeconomic
  - address losses, finances, employment, housing

# Treatment Approach - Insomnia, Vivid Dreams

- Assure patients that vivid dreams very common
- Avoid attempting to interpret dreams
- Review sleep hygiene. Substance abuse?
- Selection of sleep medications depends on etiology of insomnia and concurrent HIV-related medications
  - sedating antidepressants
  - anxiolytics, sedative-hypnotics
  - neuroleptics
  - Other, including changing HAART

# Treatment Approach- Memory Changes

- Biological
  - Maximizing HAART for CNS penetration
  - Assure adherence to HAART
  - Antidepressants
  - Stimulants
  - Transdermal Selegeline (clinical trial stage)

# Treatment Approach- Memory Changes

- Psychological
  - Individual therapy aimed at helping patient cope with losses
- Socioeconomic
  - Assistance at home; making lists
  - Consider safety at work and driving
  - Family involvement
  - Conservatorship if indicated

# Treatment Approach - Agitation, Mood Lability

- Neuroleptics
  - newer atypical preferable due to HIV effects on basal ganglia
- Benzodiazepines
  - caution with interactions, substance abuse, severely medically ill
- Anticonvulsants
- Lithium
  - toxicity may occur rapidly
- Changing HAART if all else fails

# Substance Abuse in HIV

- Alcohol
  - liver disease
- Club Drugs - Methamphetamine, Ketamine, GHB, Ecstasy
  - potentially deadly interactions with HAART
- Cocaine
  - leads to dramatically increased viral load
- Opiates
  - interactions with HAART

# **Review Questions**

- 1) What are the five major classes of antiretroviral medications?**
- 2) What is the significance of the CD4 count? Of the viral load?**
- 3) Which benzodiazepines would be safest for someone taking a potent 3A4 inhibitor?**
- 4) A patient on HAART is recreationally taking crystal methamphetamine. What is your advice?**
- 5) Primary care MD approaches you, “I want to start Charlie on Sustiva™.” What would you want to know about Charlie, and how would you advise this doctor?**