HIV/AIDS PSYCHIATRY
A Review of Syndromes and Treatment

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OBJECTIVES

• TO UNDERSTAND THE BIOLOGY OF HIV IN THE CNS

• TO REVIEW COMMON PSYCHIATRIC DISORDERS ASSOCIATED WITH HIV DISEASE AND THEIR TREATMENT

• TO REVIEW IMPORTANT INTERACTIONS BETWEEN PSYCHOTROPIC AND ANTIRETROVIRAL MEDICATIONS
WHAT IS HIV?

- HUMAN RETROVIRUS IDENTIFIED IN 1984
- RNA PLUS REVERSE TRANSCRIPTASE ENZYME
- RAPID REPLICATION AND GENETIC MUTATION
- INFECTS BLOOD T-HELPER (CD4) LYMPHOCYTES, LYMPHOID TISSUE AND CNS
TRANSMISSION OF HIV

- SEXUAL BEHAVIOURS WITH EXCHANGE OF BODY FLUIDS
- INJECTION DRUG USE
- BLOOD TRANSFUSION
- PERINATAL
COFACTORS FOR TRANSMISSION

• PSYCHIATRIC
  MOOD DISORDERS
  BIPOLAR, DEPRESSION, DYSTHYMIA

  PSYCHOTIC DISORDERS
  SCHIZOPHRENIA, SCHIZOAFFECTIVE

  PERSONALITY DISORDERS
  BORDERLINE, HISTRIONIC, NARCISSISTIC, DEPENDENT, ANTISOCIAL

• SUBSTANCE USE / ABUSE / DEPENDENCE

• SOCIAL / GEOGRAPHICAL / FINANCIAL FACTORS
ACUTE PHASE

- 3-6 WEEKS AFTER INFECTION
- BURST OF REPLICATION AND WIDE DISSEMINATION OF VIRUS
- NON-SPECIFIC FLU-LIKE SYMPTOMS
- BODY MOUNTS MASSIVE IMMUNE RESPONSE PRODUCES ANTIBODIES
  POSITIVE SEROCONVERSION AND POSITIVE HIV TEST
ASYMPTOMATIC PHASE

• USUALLY LASTS FOR YEARS

• BALANCE BETWEEN VIRUS REPLICATION/INFECTION OF NEW CD4 CELLS VS PRODUCTION OF NEW CD4 CELLS

• 10 BILLION VIRUS PARTICLES PRODUCED DAILY - PLASMA VIRUS HALF-LIFE OF 6 HOURS

• NOT A DORMANT STATE
ADVANCED STAGE ACQUIRED IMMUNODEFICIENCY SYNDROME AIDS

- PRODUCTION CANNOT KEEP UP WITH DESTRUCTION AND REPLICATION
- FATIGUED IMMUNE RESPONSE SYSTEM
- CD4 < 200
- OPPORTUNISTIC INFECTIONS ARISE
**Biology**

HIV creates chronic, progressive, inflammatory CNS disease
Viral load, CD4 count provide a ‘cross-sectional snapshot’
Serum and CSF viral dynamics may differ
Neuronal dysfunction – neurotoxins, chronic inflammatory state, cytokine and chemokine release
Apoptosis (programmed cell death) in sub-cortical white matter, basal ganglia and frontal lobes
HIV and CNS

- EARLY PENETRATION INTO CNS (DAY 16) VIA MACROPHAGES ACROSS BLOOD-BRAIN BARRIER

- VIRUS INFECTS MACROPHAGES AND MICROGLIAL CELLS, NOT NEURONS

- NEUROTOXINS AND CHRONIC INFLAMMATORY RESPONSE ⇒ NEURONAL DYSFUNCTION/DEATH

- CNS IS A RESERVOIR WITH SEPARATE VIRAL DYNAMICS FROM PERIPHERAL BLOOD

- BRAIN/LIMBIC SYSTEM DYSFUNCTION ⇒ MOOD SYMPTOMS, SLEEP DISTURBANCE, MEMORY AND CONCENTRATION COMPLAINTS, MENTAL SLOWING, AGITATION
ANTIVIRAL THERAPY TARGETS DURING THE HIV REPLICATION CYCLE
HIV MEDICAL TREATMENT CONCERNS

- DRUG-DRUG INTERACTIONS
- LIVER TOXICITY
- DEGREE OF DRUG CNS PENETRATION
- CO-INFECTION WITH HEPATITIS C ⇒ INTERFERON TREATMENT
- SIDE EFFECTS OF ARV THERAPY
ANTIRETROVIRAL MEDICATIONS

- NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTI’s)
- NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NtRTI’s)
- PROTEASE INHIBITORS (PI’s)
- NONNUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI’s)
- RIBONUCLEOTIDE REDUCTASE INHIBITORS
Combination therapy most popular
One pill = 3 or 4 ARV’s
Atripla
Truvada
Kivexa

Raltegravir
Maraviroc
Etravirine
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<tr>
<th>Drug</th>
<th>Brand(s)</th>
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<tbody>
<tr>
<td>Abacavir</td>
<td>Ziagen®</td>
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<tr>
<td>Atazanavir</td>
<td>Reyataz®</td>
</tr>
<tr>
<td>Atripla</td>
<td>Efavirenz, Emtricitabine and Tenofovir in one tablet</td>
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<tr>
<td>Combivir®</td>
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<td>Prezista® - for extended therapy only</td>
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<td>Rescriptor®</td>
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<tr>
<td>Didanosine</td>
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<td>Efavirenz</td>
<td>Sustiva®</td>
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<td><strong>Enfuvirtide</strong></td>
<td>Fuzeon® - for extended therapy only</td>
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<td><strong>Etravirine</strong></td>
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<tr>
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<td>Telzir®</td>
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<tr>
<td>Indinavir</td>
<td>Crixivan®</td>
</tr>
<tr>
<td>Kaletra®</td>
<td>Lopinavir/ritonavir - tablets and liquid</td>
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<tr>
<td>Kivexa®</td>
<td>Abacavir and Lamivudine in one tablet</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>3TC® - tablets and liquid</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Viracept®</td>
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<tr>
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<td>Viramune®</td>
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<tr>
<td><strong>Raltegravir</strong></td>
<td>Isentress® - for extended therapy only</td>
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<tr>
<td>Ritonavir</td>
<td>Norvir® - capsules and liquid</td>
</tr>
<tr>
<td>Saquinavir-HG</td>
<td>Saquinavir hard gels, Invirase®</td>
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<tr>
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<tr>
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<td>Viread®</td>
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<tr>
<td><strong>Tipranavir</strong></td>
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<tr>
<td>Truvada®</td>
<td>Emtricitabine and Tenofovir in one tablet</td>
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<tr>
<td>Zidovudine</td>
<td>Retrovir® - capsules and liquid</td>
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POINTS OF CAUTION

- PROTEASE INHIBITORS GENERALLY INHIBIT METABOLISM OF PSYCHOTROPIC MEDS, ESPECIALLY BUPROPRION, BENZODIAZEPINES AND CLOZAPINE

- MONITOR DOSES, SIDE-EFFECTS, CLINICAL RESPONSE

- RITONAVIR (NORVIR)) AND RITONAVIR / LOPINAVIR (KALETRA) REQUIRES MOST MONITORING

- EFAVIRENZ (SUSTIVA) HAS UP TO 34% CNS PENETRATION
  - FREQUENT CNS / PSYCHIATRIC MANIFESTATIONS
  - CAN HAVE ACUTE ONSET OF MOOD SHIFT, AGITATION, SUICIDALITY
Challenges

- What am I treating?
- What does the patient report as a problem?
- What do other people report as a problem?
- Adherence to ARV RX
- Substances
- Drug interactions
- Delirium
- Vague symptoms
- What is the problem?
PSYCHIATRIC DISORDERS AND HIV DISEASE

- ADJUSTMENT DISORDERS

- ANXIETY DISORDERS

- MOOD DISORDERS
  - DEPRESSION
  - MANIA / HYPOMANIA

- PSYCHOTIC DISORDERS
  - SCHIZOPHRENIA
  - SCHIZOAFFECTIVE
  - BRIEF PSYCHOSIS
PSYCHIATRIC DISORDERS AND HIV DISEASE

- SLEEP DISORDERS

- COGNITIVE DISORDERS
  - HIV - ASSOCIATED MINOR COGNITIVE MOTOR DISORDER  \textit{H-MCMD}
  - HIV - ASSOCIATED DEMENTIA COMPLEX  \textit{H-ADC}

- SUBSTANCE ABUSE / DEPENDENCE

- DELIRIUM
PSYCHIATRIC DISORDERS AND HIV DISEASE

- VERY COMMON

- ELEVATED PREVALENCE OF PSYCHIATRIC DISORDERS PRE-HIV INFECTION

- ALL PERSONS WITH HIV WILL DEVELOP AT LEAST ONE PSYCHIATRIC DISORDER OVER COURSE OF DISEASE

- BIO-PSYCHO-SOCIAL MODEL
- FREQUENT CO-MORBIDITY
- POLYPHARMACY
- DYNAMICS OF ACUTE AND CHRONIC MEDICAL DISEASE
- SOCIALLY MARGINALIZED, LIMITED SUPPORT, ISOLATION FROM FAMILY
WHY RX?

- IMPROVE QUALITY OF LIFE
- FACILITATE ADHERENCE
- INCREASE LEVEL OF FUNCTION
- DECREASE HEALTH CARE COSTS
- IMPROVE RELATIONSHIPS
EDUCATE RE:
  - RISK REDUCTION
  - SEXUAL BEHAVIOURS
  - CO-INFECTION

ADVOCATE RE:
  - DISABILITY
  - FAMILY
  - BUREAUCRACY

ADDRESS DEATH AND DYING ISSUES
- THINK GERIATRIC BRAIN
  - START LOW, GO SLOW

- BALANCE RISKS AND BENEFITS

- POLYPHARMACY

- REVIEW CD4, VIRAL LOAD, ANTIRETROVIRAL (ARV) MEDS, OTHER MEDICATIONS, LFTS
Depression

- Most common disorder
- Cascade of negative consequences
- Under recognized, under treated
- Normalization of Sx by others
- Overlap of HIV physical Sx with mood Sx
- Anhedonia, diurnal variation, early cognitive decline
- Responsive to Rx
Depression Rx

- SRI’s
- SSNRI’s
- Bupropion
- Psychostimulants
- Mirtazepine
- ECT

- No TCA’s, MAOI’s – exceptions include
  - Pain
  - Sleep
  - Augmentation
Augmentation

- Common
- Effective
- Multiple choices – other AD’s, Lithium, T3 (Cytomel), psychostimulants, atypicals
- Caution - Drug-drug interactions
BIPOLAR DISORDERS

- PRE-EXISTING BIPOLAR DISORDER BECOMES MORE FRAGILE WITH HIV

- NEW ONSET MORE LIKELY ASSOCIATED WITH CNS HIV DISEASE OR SUBSTANCE USE THAN FAMILY/PERSOANAL HISTORY

- ? RECENT CHANGE IN ARVs

- MAY DO WELL WITH SUBTHERAPEUTIC DOSES
MEDICATIONS FOR BIPOLAR DISORDERS

- lithium
- valproic acid (EPIVAL)
- gabapentin (NEURONTIN)
- atypical antipsychotics
- avoid carbamazepine (TEGRETOL) and clozapine
  - bone marrow suppression
- ? lamotrigine (LAMICTAL) - Steven’s-Johnson Syndrome
- ? topiramate (TOPAMAX)
PSYCHOTIC DISORDERS

- Pre-existing Axis 1 Disorder may worsen
- Appearance of de-novo psychotic sx suggestive of CNS HIV Disease or substance use
- Preferential use of atypical neuroleptics
- Higher than usual rate of EPS
- Use depots with caution
- Accuphase
Psychosis

- Delirium or HIV-associated cognitive impairment?
- Organic work-up – CT, MRI, CSF viral load, syphilis
- New or changed ARV RX can precipitate
- Neuropsych testing
- Be Patient
COGNITIVE DISORDERS

- COMMON COMPLAINTS
  - POOR CONCENTRATION, MENTAL SLOWING
  - SHORT TERM MEMORY PROBLEMS,
    - I.E. RECALL OF NAMES, PHONE NUMBERS

  UP TO 90% IS H-MCMD, ONLY 10% H-ADC

- SUBCORTICAL RATHER THAN CORTICAL PROCESS

- RULE OUT MEDICAL CNS PATHOLOGY – CT, MRI, CSF Viral Load
Cognitive Disorders

- Depression?
- The ‘aha’ phenomenon
- Inevitable – mild, moderate, severe
COGNITIVE DISORDERS

- NEURO-PSYCHOLOGICAL TESTING HELPFUL
  - 3MS, MOCA
  - FINGER TAPPING, TRAIL-MAKING, SEQUENCING, VISUAL-SPATIAL

- MMSE IS LESS HELPFUL
TREATMENT FOR COGNITIVE DISORDERS

- MAXIMIZE ARV THERAPY

- ANTIDEPRESSANTS

- PSYCHOSTIMULANTS
  - DEXEDRINE, METHYLPHENIDATE (RITALIN)

- AUGMENTATION
  - ATYPICAL NEUROLEPTICS, MOOD STABILIZERS

- PROMPTS, CUES, STICKY NOTES, DAY PLANNER/CALENDAR, BLISTER PACK MEDS, ALARM FOR MEDS, COMMUNITY NURSING
SLEEP DISORDERS

- VERY COMMON – chronic, refractory
- PRIMARILY INSOMNIA
  - INITIAL, MIDDLE, NON-RESTORATIVE SLEEP
- CENTRALLY MEDIATED
- REVIEW SUBSTANCE USE
- NOT NECESSARILY ASSOCIATED WITH DEPRESSION
MEDICATIONS FOR SLEEP DISORDERS

- OFTEN REQUIRED

- zopiclone (IMOVANE)

- trazodone (DESYREL), amitriptyline (ELAVIL), mirtazapine (REMERON)

- clonazepam (RIVOTRIL), oxazepam (SERAX), lorazepam (ATIVAN)

- ATYPICAL NEUROLEPTICS
OTHER INTERVENTIONS

- PSYCHOTHERAPY
  - SUPPORTIVE, PSYCHODYNAMIC
  - INDIVIDUAL VS GROUP
  - TREATMENT SPECIFIC
    - ANXIETY GROUP, PERSONALITY DISORDERS GROUP, COGNITIVE-BEHAVIOURAL

- ADVOCACY

- EDUCATION

- ADDICTIONS COUNSELLING
OTHER INTERVENTIONS

- COMMUNITY SUPPORT
  - PWA SOCIETY
  - AIDS VANCOUVER
  - FRIENDS FOR LIFE
  - LOVING SPOONFUL
  - POSITIVE WOMEN’S NETWORK
  - OAKTREE CLINIC
  - DR. PETER CENTER
  - VANCOUVER NATIVE HEALTH SOCIETY
  - THREE BRIDGES COMMUNITY MEDICAL CENTER
  - SURREY COMMUNITY SERVICES
  - HEART OF RICHMOND SOCIETY
  - WINGS HOUSING SOCIETY
SUMMARY

- **Psychiatric Disorders Are Very Common in Persons Living with HIV Both Pre-Infection (as a Risk Factor) and Post-Infection (as a Complication)**

- HIV Enters the CNS Early and Eventually Causes Neuronal Dysfunction and Neuronal Death

- **Psychiatric Disorders Usually Respond Very Well to Treatment**

- Be Careful with Dosing and Mindful of Other Meds
  - I.E. ARV Therapy, Interferon, OTCs