



# **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

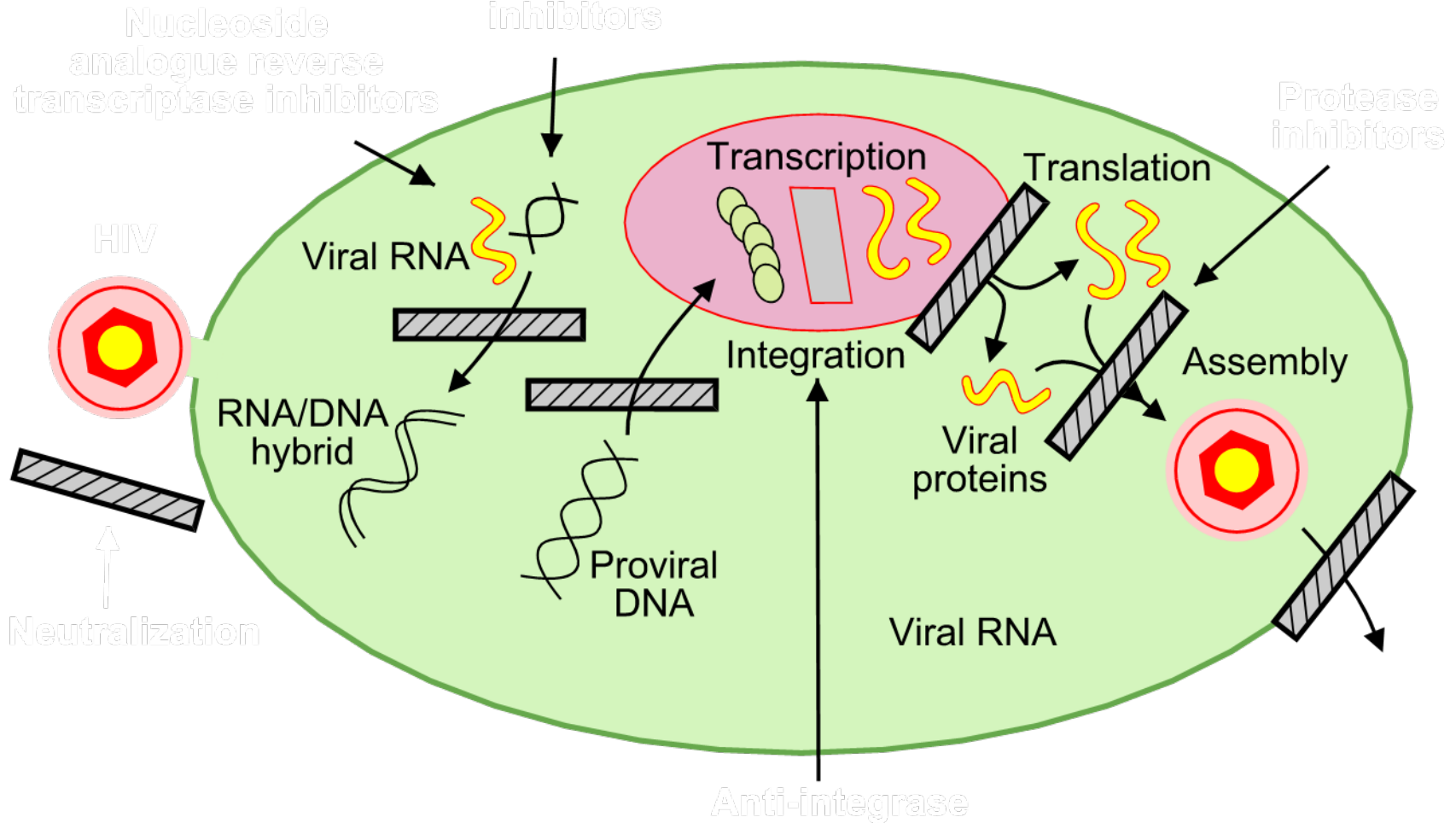
Neuronal dysfunction – neurotoxins, chronic inflammatory state,  
cytokine and chemokine release

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

<b>Abacavir</b>	(Ziagen®)
<b>Atazanavir</b>	(Reyataz®)
<b>Atripla</b>	(Efavirenz, Emtricitabine and Tenofovir in one tablet)
<b>Combivir®</b>	(Zidovudine and Lamivudine in one tablet)
<b>**Darunavir</b>	(Prezista®) - <b>for extended therapy only</b>
<b>Delavirdine</b>	(Rescriptor®)
<b>Didanosine</b>	(Videx-EC®)
<b>Efavirenz</b>	(Sustiva®)
<b>**Enfuvirtide</b>	(Fuzeon®) - <b>for extended therapy only</b>
<b>**Etravirine</b>	(Intelence®) - <b>for extended therapy only</b>
<b>Fosamprenavir</b>	(Telzir®)
<b>Indinavir</b>	(Crixivan®)
<b>Kaletra®</b>	(Lopinavir/ritonavir - tablets and liquid)
<b>Kivexa®</b>	(Abacavir and Lamivudine in one tablet)
<b>Lamivudine</b>	(3TC® - tablets and liquid)
<b>Nelfinavir</b>	(Viracept®)
<b>Nevirapine</b>	(Viramune®)
<b>**Raltegravir</b>	(Isentress®) - <b>for extended therapy only</b>
<b>Ritonavir</b>	(Norvir® - capsules and liquid)
<b>Saquinavir-HG</b>	(Saquinavir hard gelcaps, Invirase®)
<b>Stavudine</b>	(Zerit®)
<b>Tenofovir</b>	(Viread®)
<b>**Tipranavir</b>	(Aptivus®) - <b>for extended therapy only</b>
<b>Trizivir®</b>	(Zidovudine, Lamivudine and Abacavir in one tablet)
<b>Truvada®</b>	(Emtricitabine and Tenofovir in one tablet)
<b>Zidovudine</b>	(Retrovir® - capsules and liquid)

# 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 *H-MCMD*
  - HIV - ASSOCIATED DEMENTIA COMPLEX *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**

# PSYCHIATRIC DISORDERS AND HIV DISEASE

- **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**

# WHY RX?

- **EDUCATE RE:**
  - RISK REDUCTION
  - SEXUAL BEHAVIOURS
  - CO-INFECTION
  
- **ADVOCATE RE:**
  - DISABILITY
  - FAMILY
  - BUREAUCRACY
  
- **ADDRESS DEATH AND DYING ISSUES**

# PSYCHOPHARMACOLOGY

- **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, T<sub>3</sub> (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/PERSONAL 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**