“Psychiatric Diagnosis & Management of HIV/AIDS” 2 Simposium Internacional Psiquiatria & VIH Barcelona 07 05 09

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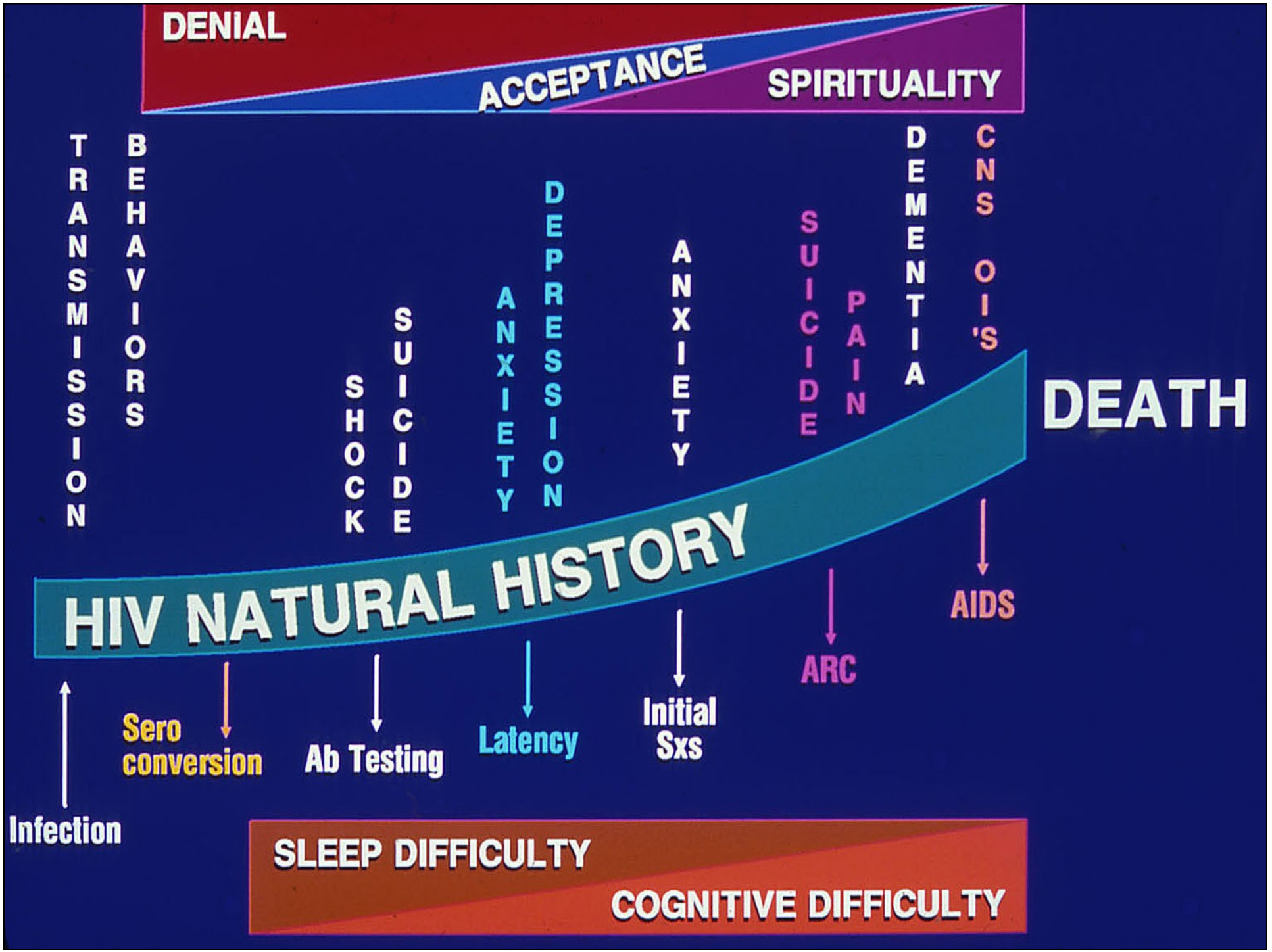

DENIAL
ACCEPTANCE
SPIRITUALITY
TRANSMISSION
BEHAVIORS
SHOCK
SUICIDE
ANXIETY
DEPRESSION
ANXIETY
SUICIDE
PAIN
DEMENTIA
CNS
OI'S
DEATH
HIV NATURAL HISTORY
AIDS
ARC
Infection
Sero conversion
Ab Testing
Latency
Initial Sxs
SLEEP DIFFICULTY
COGNITIVE DIFFICULTY

PSYCHIATRIC ILLNESS IN HIV

- Mental disorders are highly prevalent in HIV-1 infection and AIDS
  - Dual Diagnosis → coexisting substance abuse and psychiatric disorders
  - Triple Diagnosis → coexisting medical illness with substance abuse and psychiatric disorders

Psychiatric Illness in HIV: Medical Differential Diagnosis of Psychiatric Disorders in HIV Disease

- CNS opportunistic illnesses and cancers
- Substance abuse
- Medication effects
- Endocrine abnormalities (hypogonadism, adrenal insufficiency)
- CNS HIV cognitive disorders (MCMD & HAD)

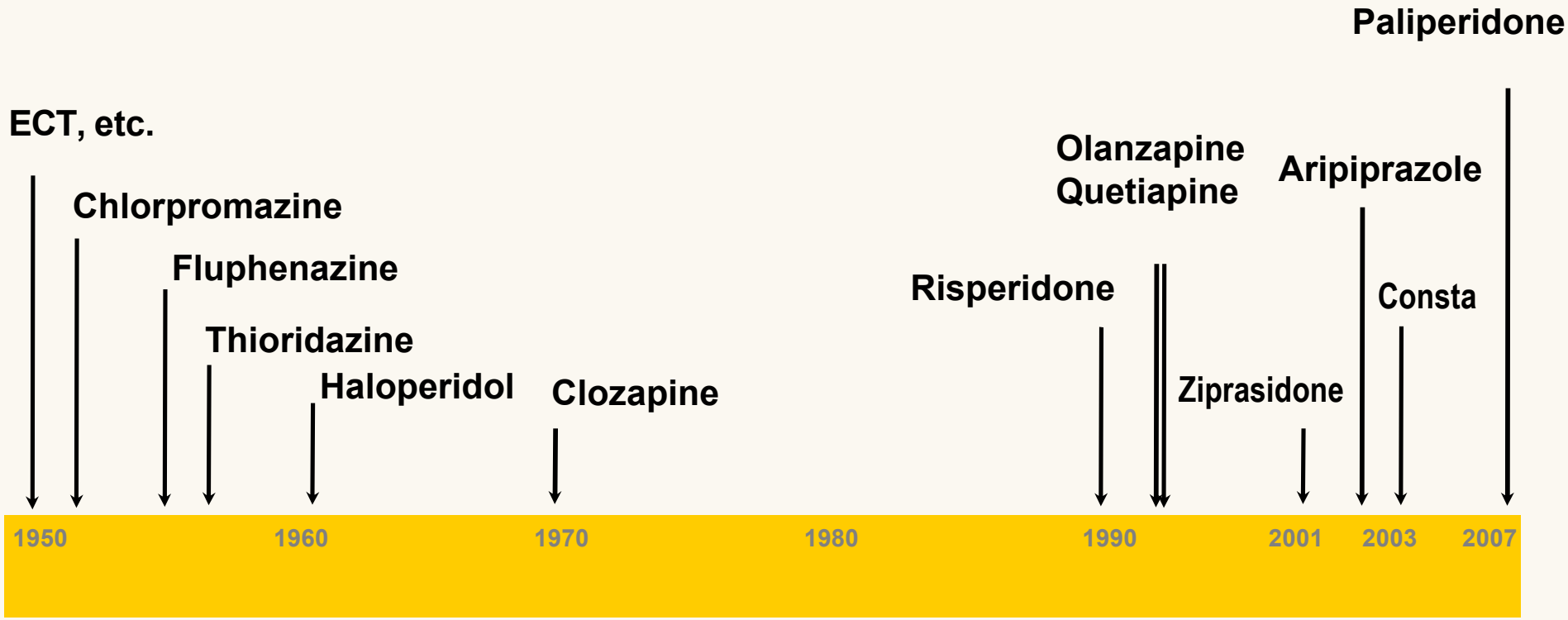
Psychiatric Illness in HIV: Triple Diagnosis

- Patients with triple diagnosis have more frequent and more severe psychiatric symptoms
  - Higher acuity of psychiatric symptoms are associated with negative outcomes in treatment
    - Poor adherence
    - Frequent hospitalizations
    - Increased high risk behaviors

PSYCHOTIC DISORDERS

- Primary disorder
  - Schizophrenia
  - Schizoaffective disorder
  - Delusional disorder
  - Mood disorders
- Substance induced during intoxication or withdrawal
- Medical illness induced
  - must be distinguished from delirium
  - late stage HIV associated dementia

Timeline of Major Antipsychotic Therapies



Consta = Long-acting injectable risperidone

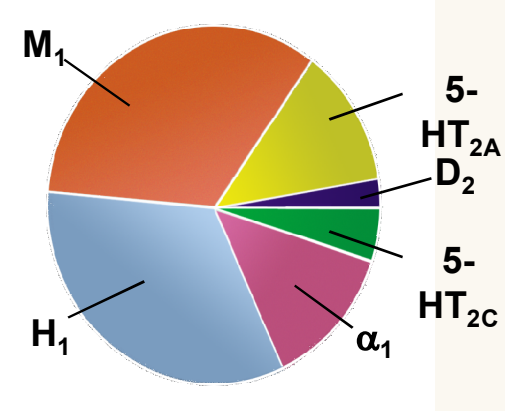
Psychosis Rx: Antipsychotics

- Conventional Antipsychotics
  - Control psychosis
  - Ineffective for cognitive and negative symptoms
  - Poorly tolerated due to neurological symptoms
- Second Generation Atypicals
  - Risperidone, olanzapine, quetiapine, ziprasidone, aripripazole, paliperidone
  - Better tolerated
  - Share some advantages of clozapine

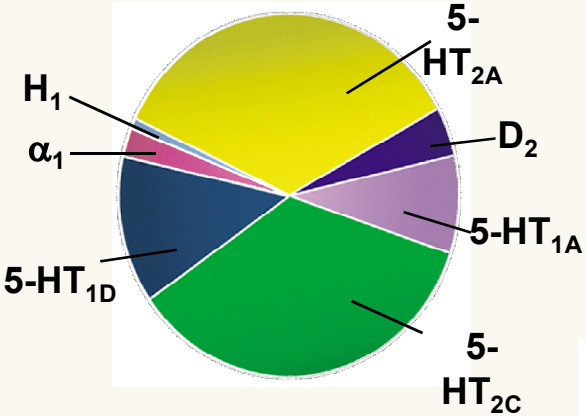
- Clozapine
  - "Gold Standard"
  - More effective for psychosis, negative symptoms and cognitive symptoms
  - Requires weekly blood monitoring

Pharmacology Of Atypical Antipsychotics

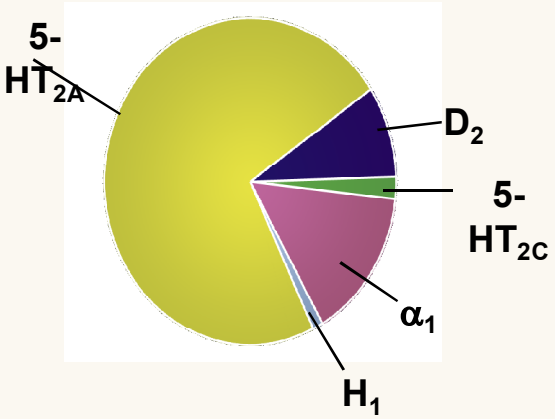
Clozapine



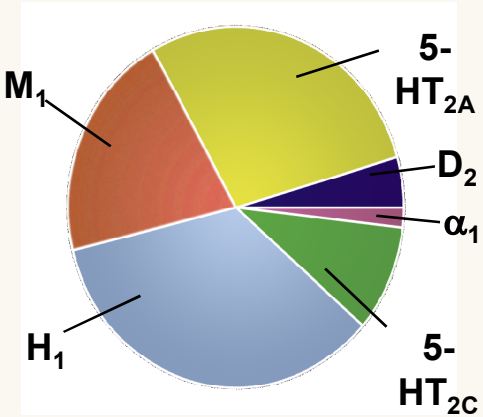
Ziprasidone



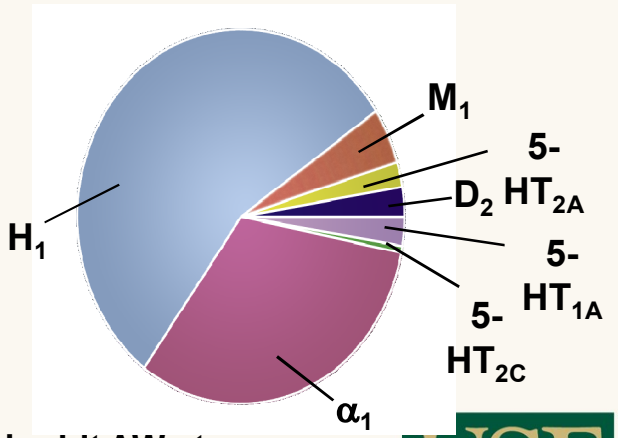
Risperidone



Olanzapine



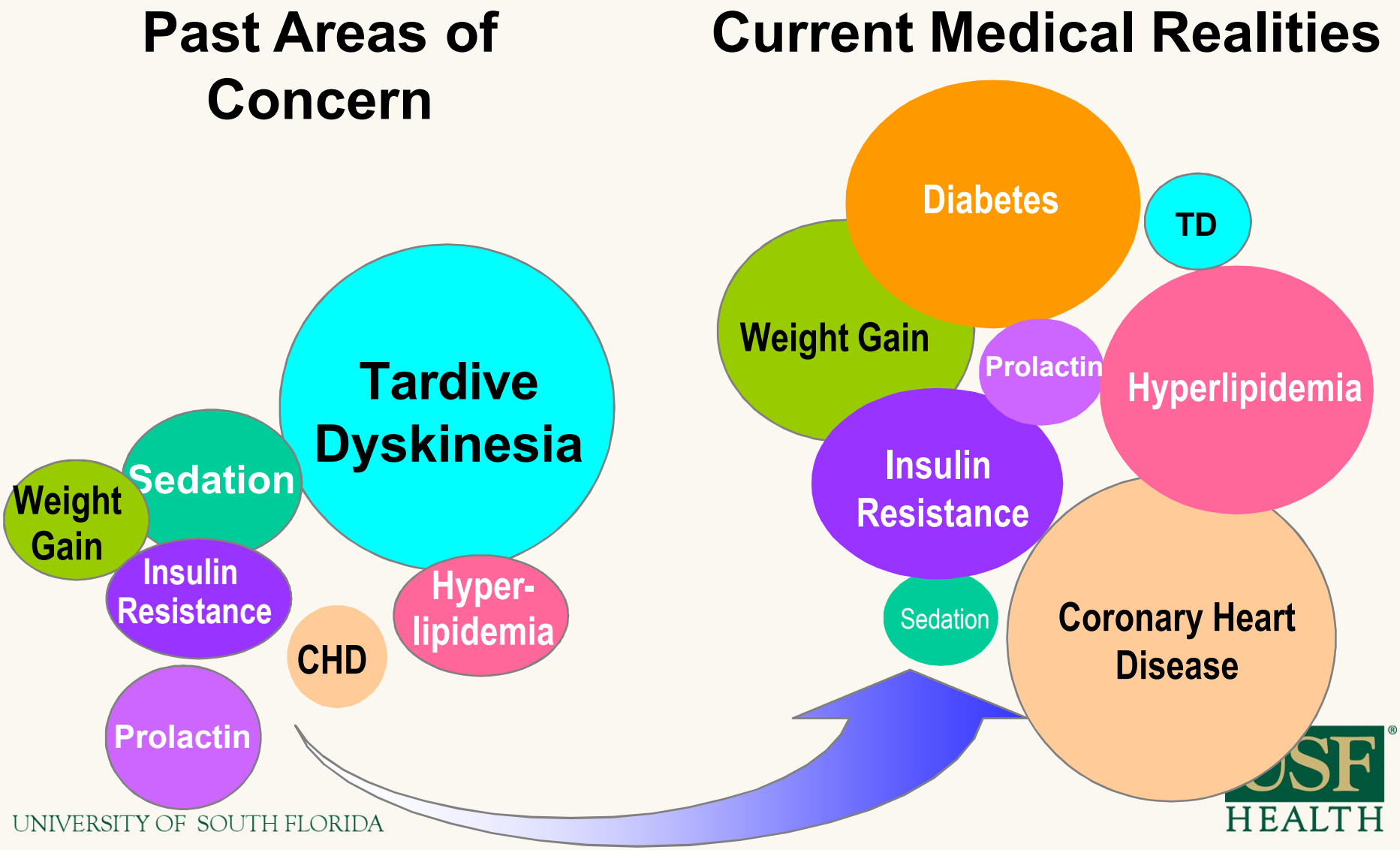
Quetiapine



Zorn SH et al. Interactive Monoaminergic Brain Disorders. 1999:377-393. Schmidt AW et al. Eur J Pharmacol.2001;425:197-201.

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population.

Shift in Risk Perception of Antipsychotics



The Metabolic Syndrome

Clinical Manifestations

Central obesity
Glucose intolerance
Atherosclerosis
Hypertension

First-degree relative with type 2 diabetes
History of gestational diabetes
Polycystic ovary syndrome
Acanthosis nigricans

Biochemical Abnormalities

CARBOHYDRATE
Glucose intolerance
Hyperinsulinemia
Insulin resistance

LIPID
High TG
Low HDL-C
Small, dense LDL particles

FIBRINOLYSIS
Increased PAI-1

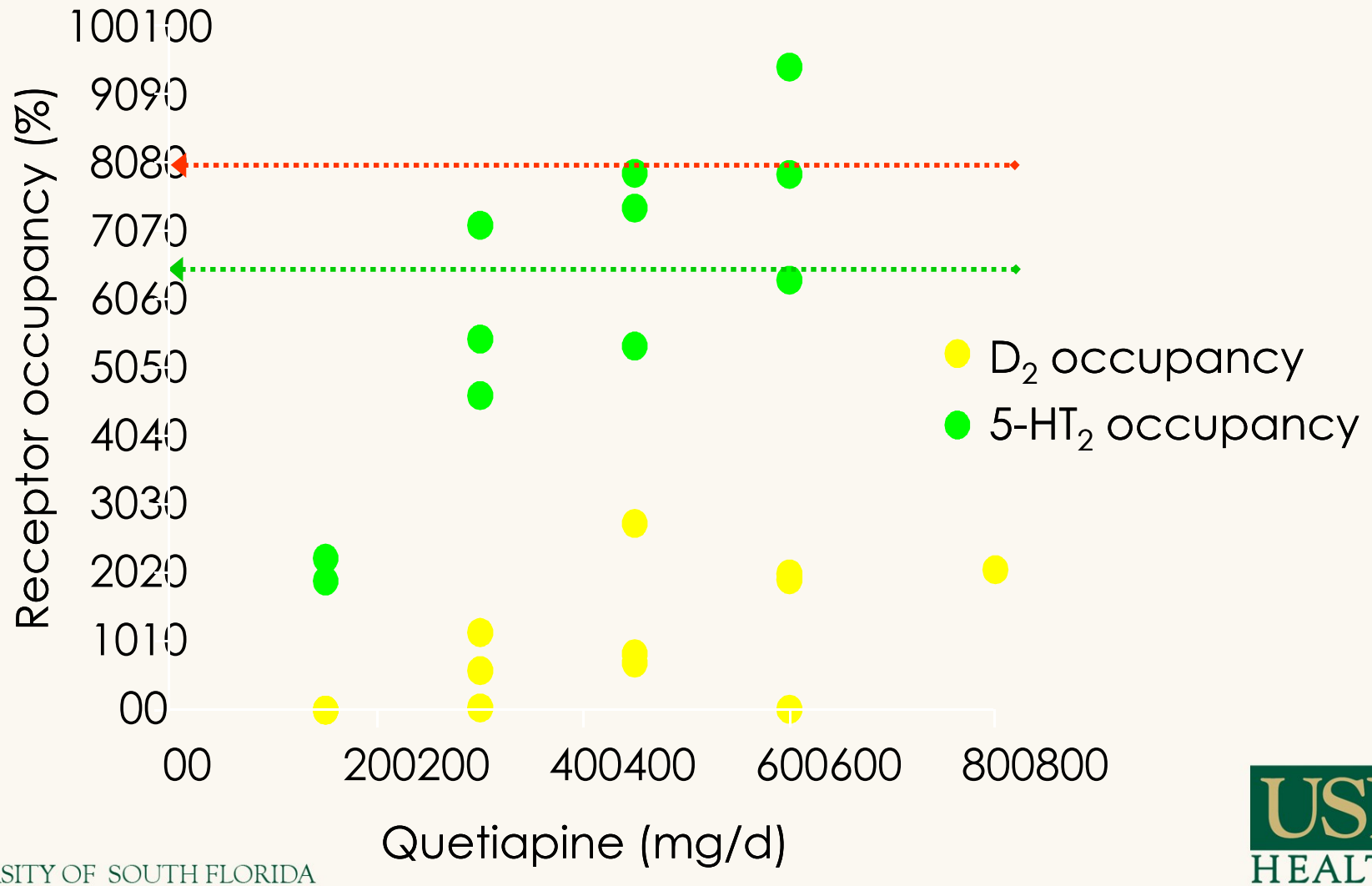
Antipsychotics: Relative Safety and Tolerability

Item	Typ	Clz	Ris	Olz	Qtp	Zip	Ari
EPS	+ to +++	±	± to +++ *	± to + *	±	± to + *	± to +
TD	+++	±	± to +	± (?)	± (?)	± (?)	± (?)
Somnolence	± to +++	+++	±	+	++	±	±
Prolactin	+++	±	+++	±	±	±	±
Weight	± to ++	+++	+	+++	+	±	±
Dyslipidemia	± to +	+++	+	+++	++	±	±
DM	± to +	+++	+	+++	+	±	±
QTc	+	++	+	+	+	++	±
Orthostatic BP↓	± to +++	+++	++	+	++	±	±

* = Dose-related

± = none to minimal; + = mild; ++ = moderate; +++ = marked. Compared to placebo rates.

Quetiapine $5HT_2$ & D2 Occupancy



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Paliperidone (Invega)

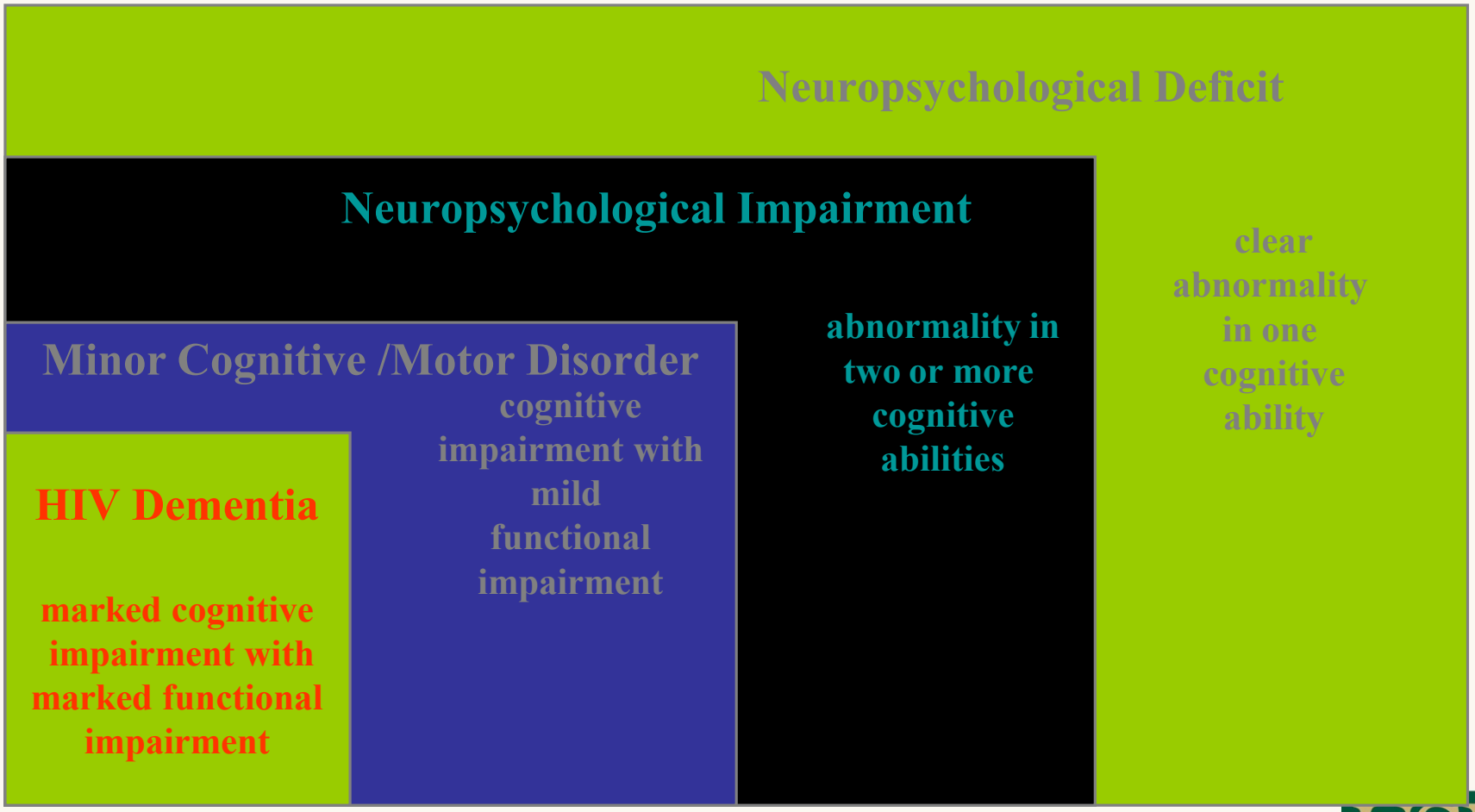
- **Risperidone has also been noted above to be successful in treating psychotic symptoms in HIV infected patients**
  - **Show an effect on initial treatment exposure**
  - **Dosing: 3.29 mg/day**
- **Paliperidone would be expected to offer similar effects.**
  - Paliperidone shows a low extent of enzymatic metabolism.
    - The majority of the paliperidone dose (about 70%) is excreted unchanged, while the remaining 30% is metabolized to four primary inactive metabolites.
    - In contrast, 70-95% of risperidone is metabolized to active and inactive metabolites by the CYP P450 2D6 isoenzyme system, and this is influenced substantially by CPY2D6 genetic polymorphisms
  - Lowest overall propensity to cause metabolic syndrome, EPRs, anticholinergic side effects, drug-drug interactions, and hepatotoxicity.

(Dolder et al., 2008)

Neuropsychiatric vs. Psychiatric Disorders

- Neuropsychiatric syndromes may be confused with Psychiatric Disorders, especially Mood Disorders
- Neuropsychiatric syndrome complaints may mimic
  - Depression: apathy, memory changes, sleep/energy/appetite changes, functional impairment, low mood, social withdrawal, paranoia
  - Mania: restlessness, distractibility, memory changes, decreased sleep, irritability, impaired judgment, paranoia

Range of Cognitive Effects



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Neuropsychiatric vs. Psychiatric Disorders

- Psychiatric Disorders commonly associated with HIV/AIDS
  - Mood Disorders
  - Adjustment Disorders
  - Anxiety Disorders
  - Psychotic Disorders
  - Substance Abuse Disorders
  - Pain Disorders
- HIV Neuropsychiatric complications include
  - AIDS Dementia (HIV-1 associated Dementia)
  - Minor Cognitive-Motor Disorder (MCMD aka "Minor" AIDS Dementia)
  - Delirium
  - Amnestic Disorders

Frascati Consensus Conference

- Original AAN criteria delineated 2 cognitive-motor disorders
  - HAD and MCMD
  - No criterion for asymptomatic neurocognitive impairment
- New criteria
  - De-emphasis of motor and behavioral symptoms (i.e., the "complex")
  - Quantified NP testing to make Dx – not signs/symptoms
  - Quantified functional status testing
  - Severity requirement greater for HAD than MCMD in NP and functional testing
  - Increased differentiation of exclusion/ confounding factors from contributing or secondary factors
  - New category → Asymptomatic NCI

Antinori et al: *Neurology* 2007; 69:1789-1799

HAD

- **Acquired abnormality in at least two of the following cognitive abilities for at least one month:**
  - **Attention/concentration**
  - **Speed of information processing**
  - **Abstraction/reasoning**
  - **Visuospatial skill**
  - **Memory/learning**
  - **Speech/language**
- **At least one of the following:**
  - **Acquired abnormality in motor function**
  - **Decline in motivation or emotional control or change in behavior**
- **Absence of clouding of consciousness (delirium)**
- **No evidence of another etiology**

MCMD

- **Two or more of the following for ≥ 1 month:**
  - **Impaired attention or concentration**
  - **Mental slowing**
  - **Impaired memory**
  - **Slowed movements**
  - **Incoordination**
  - **Personality change, irritability or emotional lability**
- Symptoms must be verified by neurological examination or neuropsychological testing
- Must be accompanied by mild impairment of functional status (eg, work or activities of daily living)
- No evidence of another etiology for symptoms

Temporal

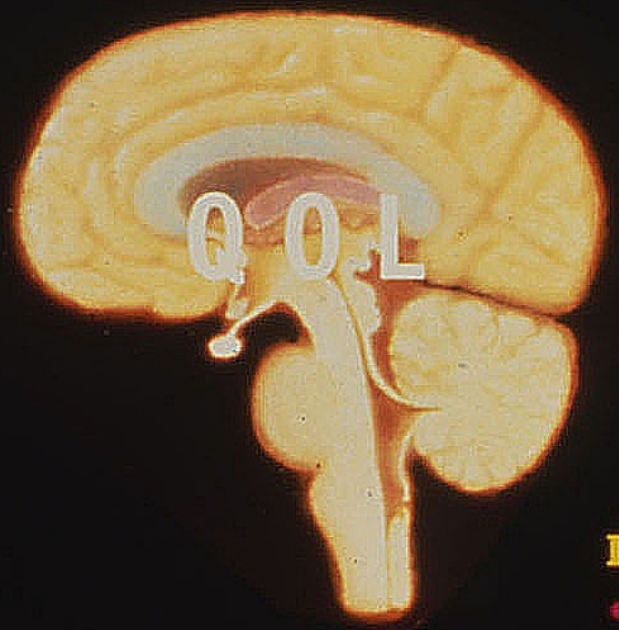
- trajectory of life
- where/when illness struck

Physical dimension

- lack of symptoms
- socioeconomic status

Sociocultural

- ethnicity
- socioeconomic status
- philosophy of life



Spirituality

- intrinsic belief system
- religion
- values/mores

Toxicity

- antineoplastics
- radiotherapy
- surgery

Psychological

- perception of the disease
- body image
- self image
- coping capacity
- goals/hopes/expectations
- limbic set

Interpersonal

- relationships
- libido
- occupations

MCMD Morbidity

- Increased unemployment (Heaton 96, Albert 95)
- Decreased quality of life (Kaplan 95)
- Decreased medication adherence (Albert 99)
- Subjective perception of diminished work performance (Heaton 94)
- Decreased survival (Marder 98, Ellis 97, Sacktor 96)

Distinguishing Neuropsychiatric vs. Psychiatric Disorders

- Assessment includes:
  - careful history mental status
  - neurological exam, neurological work-up may include neuroimaging, LP, labwork,
  - neuropsychological testing
- Differential diagnosis includes
  - CNS complications (HAD, MCMD, delirium, infxns, lymphoma)
  - Medical conditions (endocrine, metabolic disorders)
  - Medication-induced disorders
  - Substance-related disorders

Screening for HIV-Associated Cognitive-Motor Impairment

MOS HIV Cognitive Functional Status Scale

1. Difficulty reasoning and solving problems?
2. Forget things that happened recently?
3. Trouble keeping your attention on any activity for long?
4. Difficulty doing activities involving concentration and thinking?

Validated against NP overall performance

Knippels, Goodkin, Weiss, et al., AIDS, 2002;16:259-267

Pharmacotherapy of HIV Associated Cognitive-Motor Disorders

- Primary Treatments
  - Antiretroviral medications
- Secondary Treatments
  - Immunostimulants and inflammatory mediators
- Palliative Treatments
  - Stimulants (methylphenidate/Ritalin)
  - Neuroprotective agents (selegiline/L-Depryl)
  - Nutraceuticals

What to start with?- A lot to choose from!

>20 current Antiretroviral Medications

NRTI

- Abacavir ABC
- Didanosine DDI
- Emtricitabine FTC
- Lamivudine 3TC
- Stavudine D4T
- Zidovudine ZDV
- Zalcitabine DDC
- Tenofovir TDF

NNRTI

- Delavirdine DLV
- Efavirenz EFV
- Nevirapine NVP

PI

- Amprenavir APV
- Atazanavir ATV
- Fosamprenavir FPV
- Indinavir IDV
- Lopinavir LPV
- Nelfinavir NFV
- Ritonavir RTV
- Saquinavir SQV
  - soft gel SGC
  - hard gel HGC
  - tablet INV
- Tipranavir TPV

Fusion Inhibitor

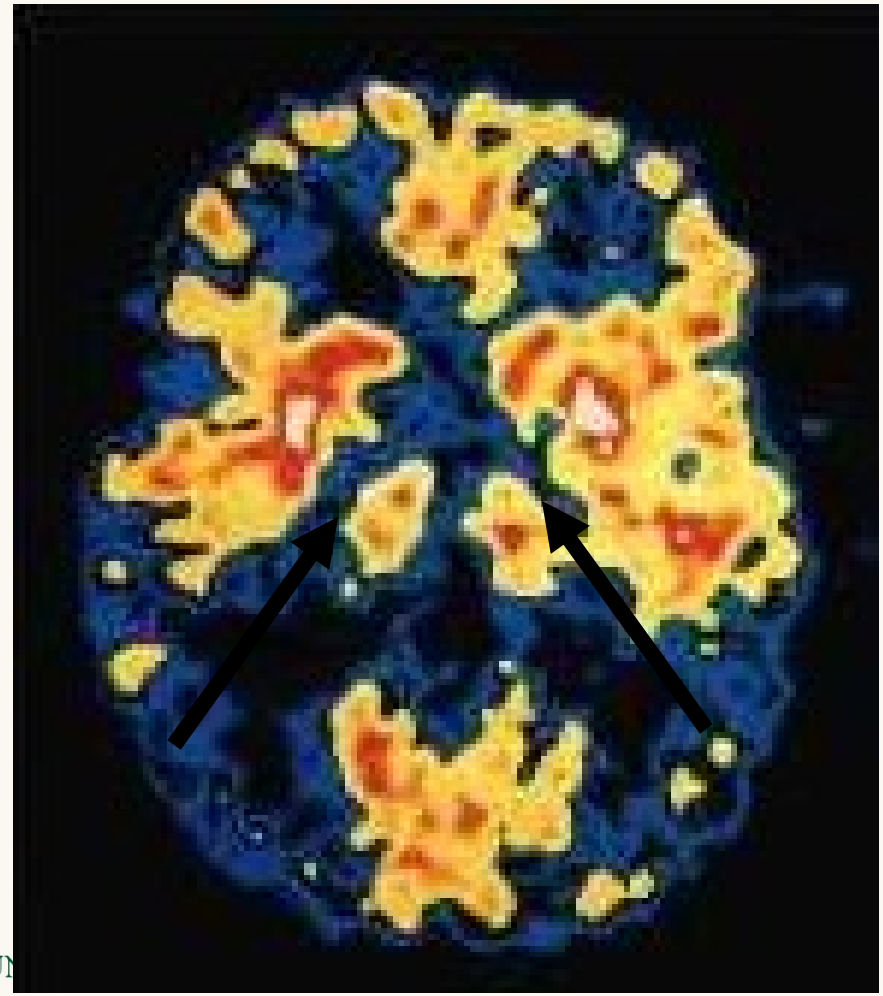
- Enfuvirtide T-20

ZidovudineZidovudine

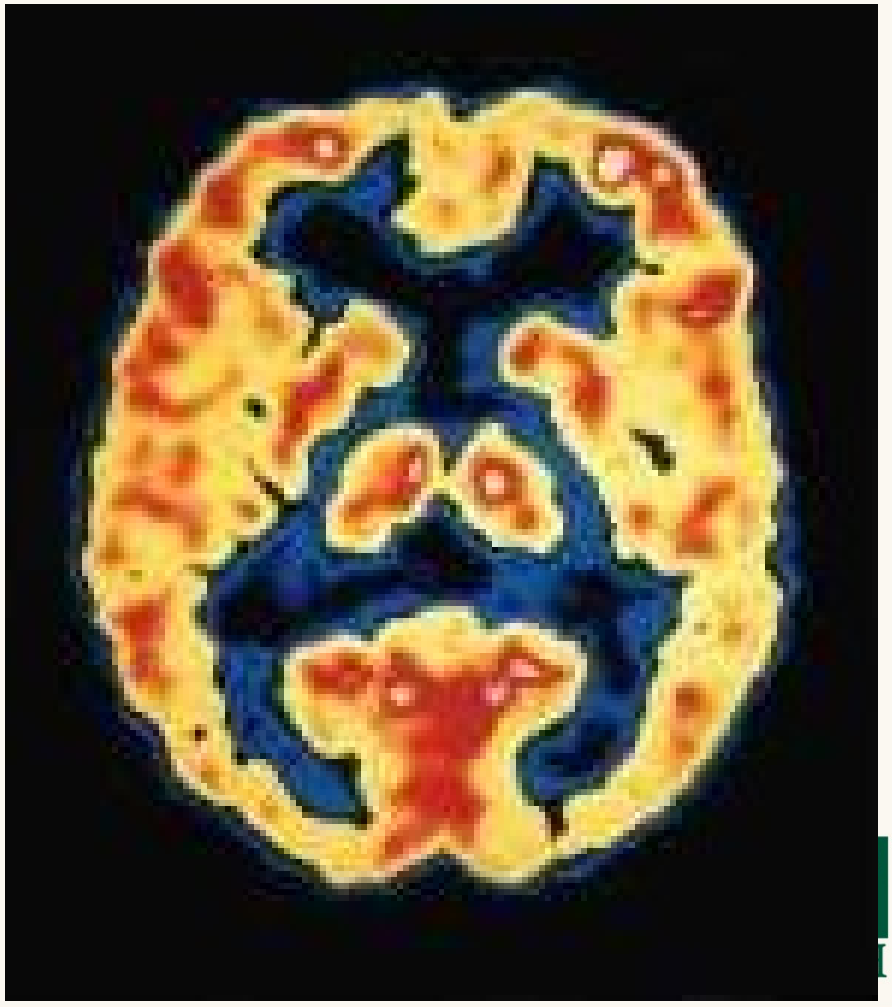
- Relatively good brain penetrance
  - CSF:blood concentration ratio - 0.6
- Only a group receiving a high dose (2,000 mg/day) showed neuropsychological improvement over 16 and 32 weeks
- Shown to decrease quinolinic acid levels in the CSF

Neuroimaging: Pre- and Post-Rx

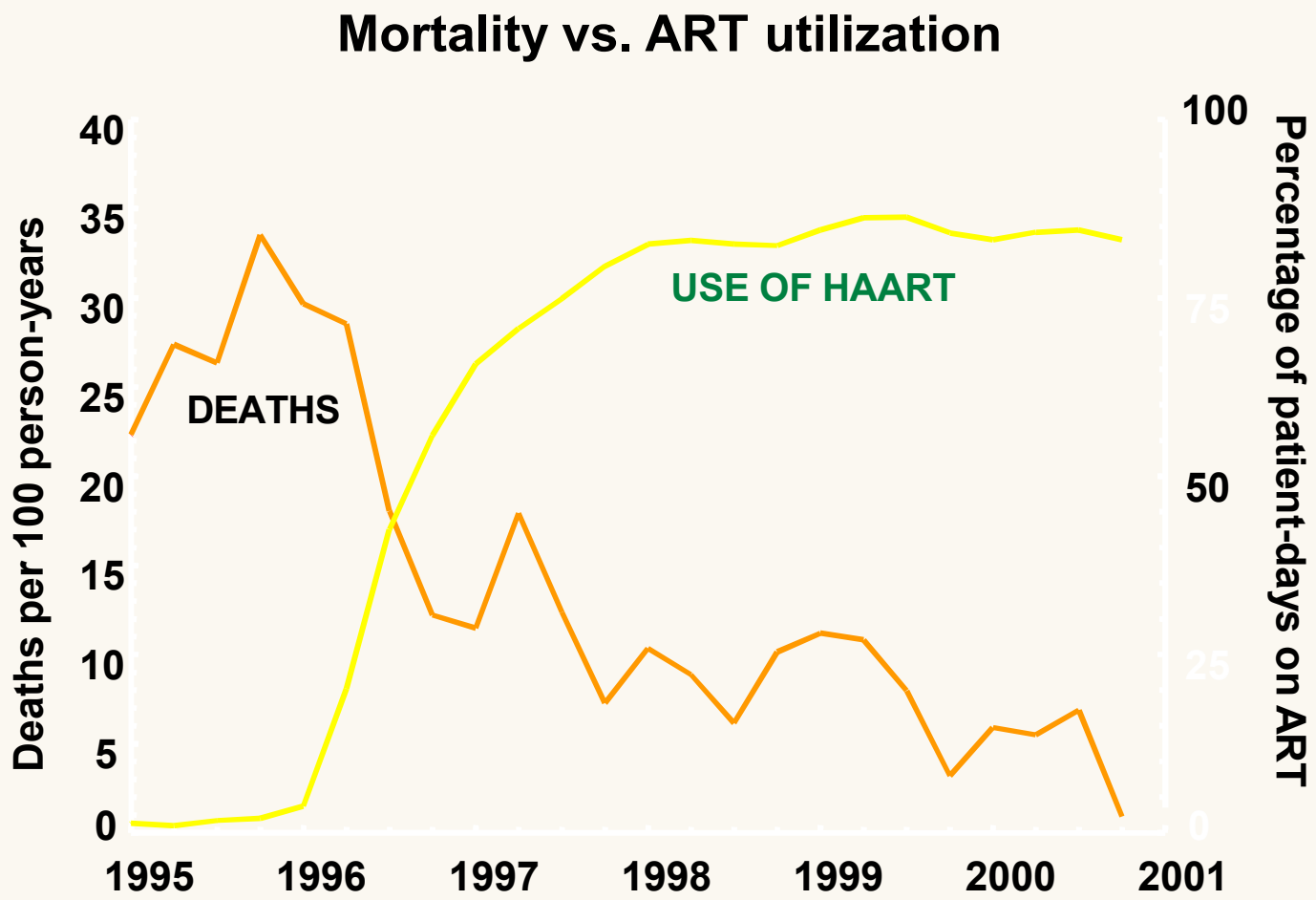
HAD



HAD-ZDV

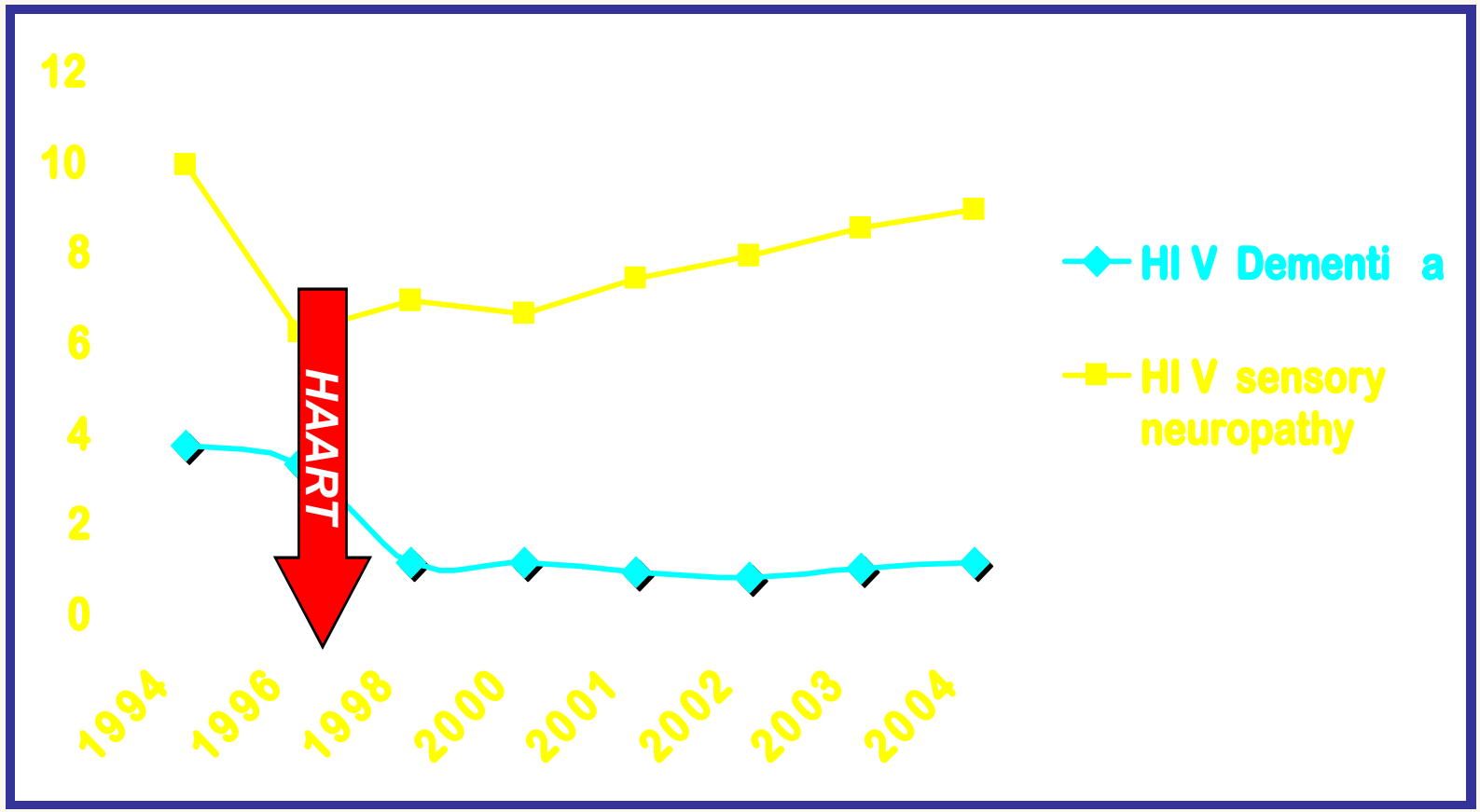


AIDS Mortality Rates: 1996-2001



Palella F *et al*. 8th CROI 2001; abstract 268b.

Incidence of HIV-associated Neurological Conditions



Johns Hopkins HIV Clinical Cohort per 100 person years

Evidence for CSF Effect

CSF penetration

- AZT
- D4T
- Abacavir
- Nevirapine
- Indinavir
- Efavirenz
- 3TC

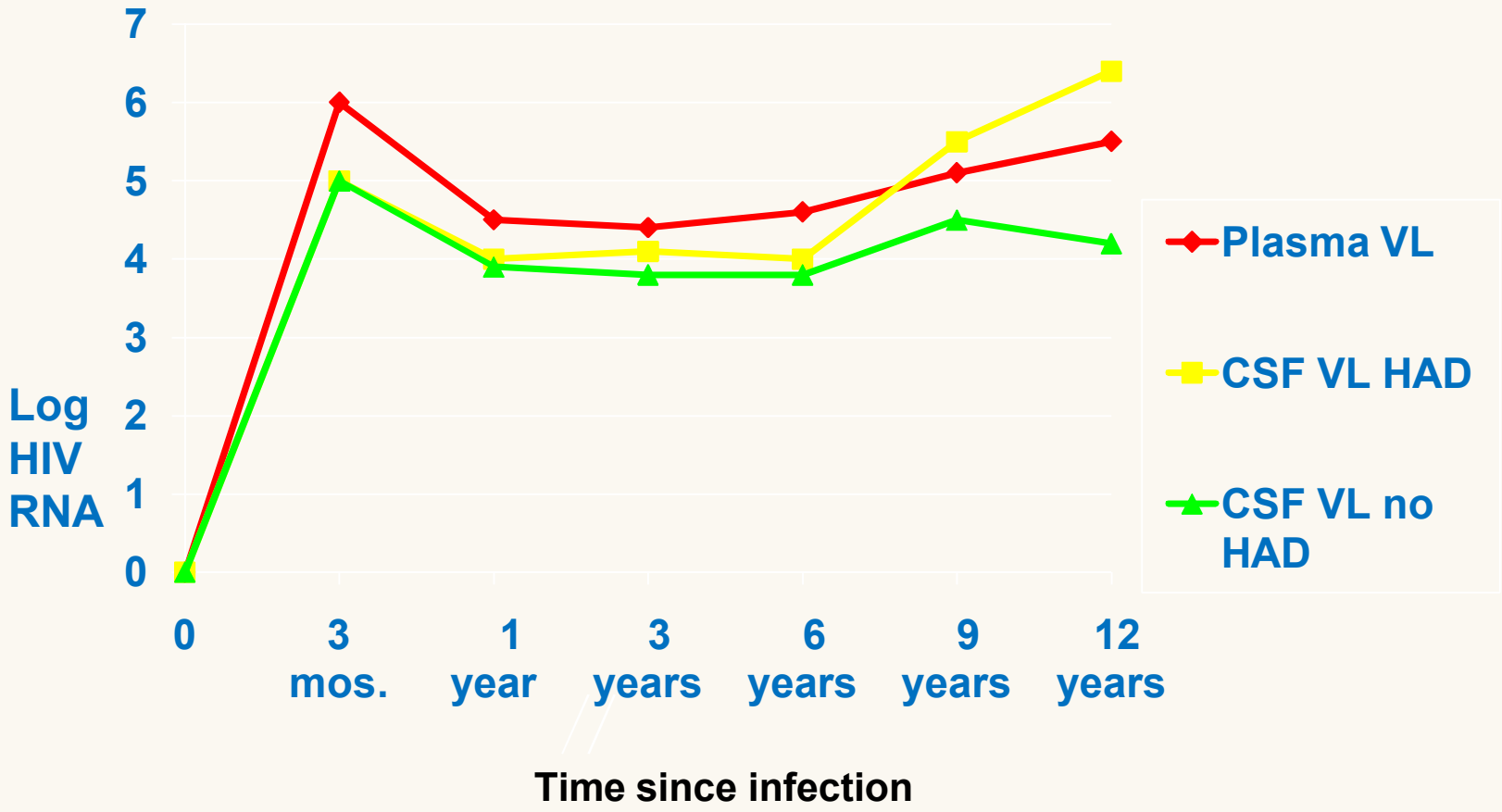
CSF VL reduction

- AZT
- D4T
- Abacavir
- Indinavir
- Efavirenz
- 3TC

Is CSF penetration important?

- Although theoretically sensible, evidence does not yet exist to support the use of brain penetrating agents over non penetrating agents
- Regimen selection should be based on what agents will most effectively reduce systemic viral load based on resistance patterns and adherence & quality of life considerations

Course of Plasma and CSF Viral Load for a Patient With HAD Vs. No HAD



Does CNS penetration profile matter?

- Sacktor N, 2001: no effect on cognitive function
- Cysique L, 2004: effect only in cognitively impaired
- Letendre S., Arch Neurol., 20072007 ~ new index of penetration

	Good 1	Fair 0.5	Poor 0
NRTIs	**Abacavir** **Zidovudine**	Emtricitabine Lamiduvine Stavudine	Didanosine Tenofovir Zalcitabine
NNRTIs	**Delavirdine** **Nevirapine**	Efavirenz	
PIs	**Indinavir** **Lopinavir**	Amprenavir-r Atazanavir Atazanavir-r Darunavir-r	Amprenavir Nelfinavir Ritonavir Saquinavir Saquinavir-r Tipranavir-r
Fusion Inhibitors			Enfuvirtide

Adverse Effects – Short Term Toxicities

- NRTIs
  - ZDV – HA, GI, BM
  - ddI – GI, pancreatitis
  - d4T – PN
  - 3TC – PN
  - Abacavir – HA, GI

- NNRTIs
  - Nevaripine – rash, liver
  - Delavirdine – rash
  - Efavirenz – CNS , rash

- PIs
  - Indinavir – stones
  - Ritonavir – GI
  - Nelfinavir – Diarrhea
  - Amprenavir - GI

ART Increase Abeta (1-40) Production in Cultured Cells

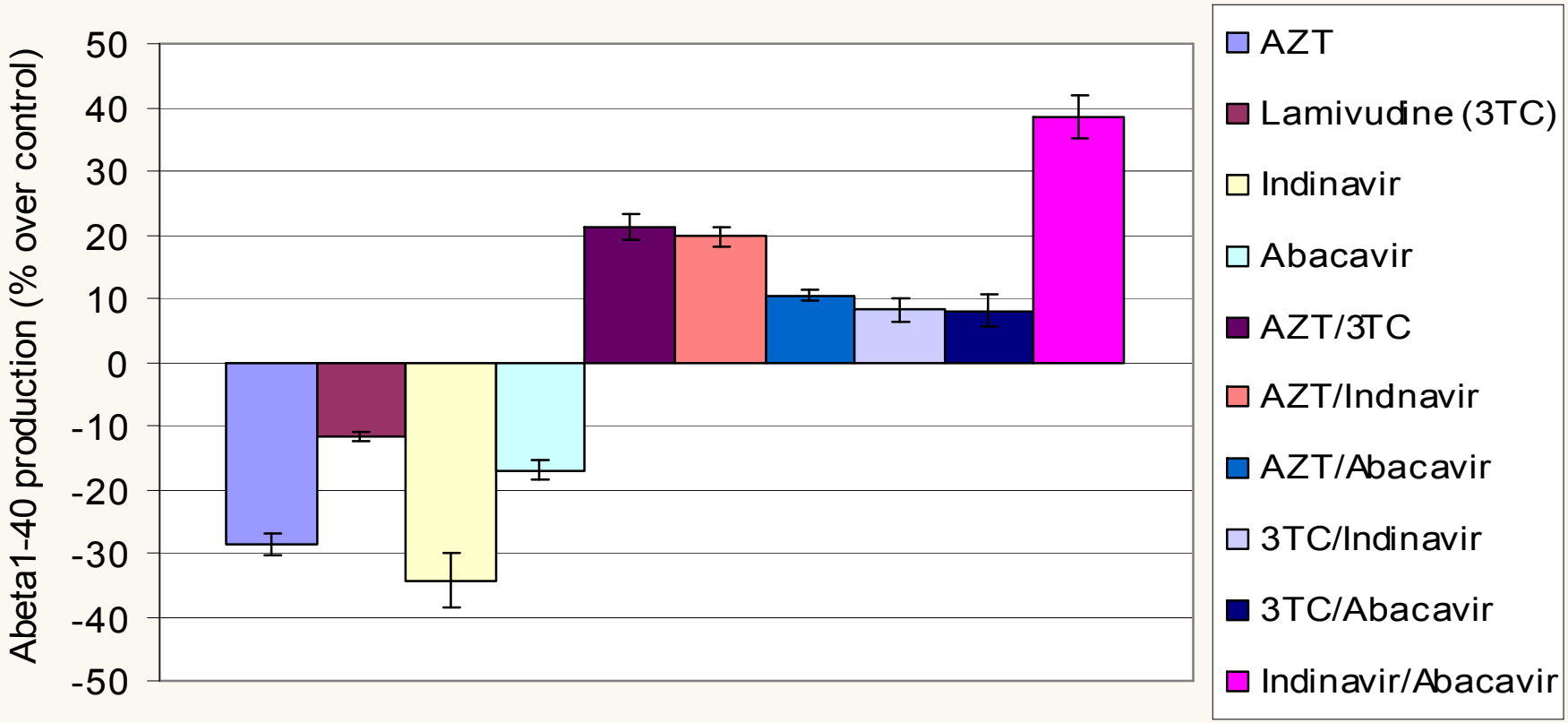
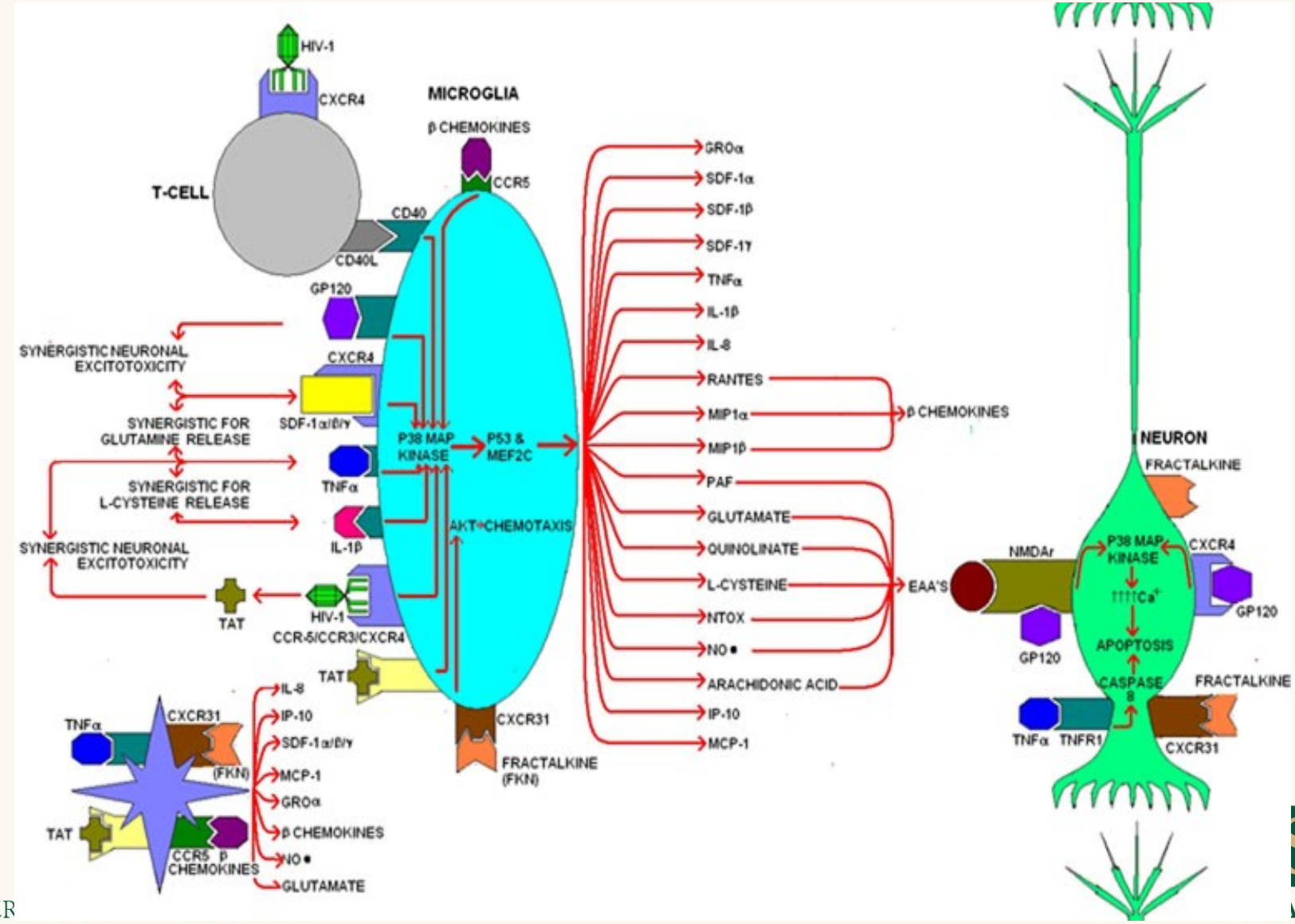


Figure 1

Secondary Pharmacotherapy



Secondary Pharmacotherapy

- Tumor Necrosis Factor - promotes demyelination and apoptosis (programmed cell death)
  - Pentoxiphylline (400 mg tid)
    - Decreases whole blood viscosity
      - Demonstrated efficacy in multi-infarct dementia
    - Inhibits production of TNF
  - Thalidomide (300 mg/day)
    - Suppresses expression of TNF

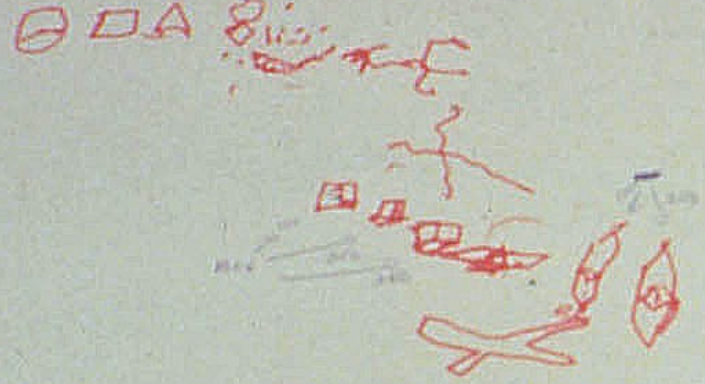
Secondary Pharmacotherapy

- N-Methlyl D-Aspartate (NMDA) receptor blockers
  - Prevent quinolinic acid binding to NMDA
    - Inhibits calcium influx into neuronal cytosol
      - Memantine
        - Antiparkinsonian (10-30 mg/day)
        - Blocks quinolinic acid facilitation of calcium influx
  - Zinc (220 mg bid)
    - Blocks action of NMDA on cortical neurons

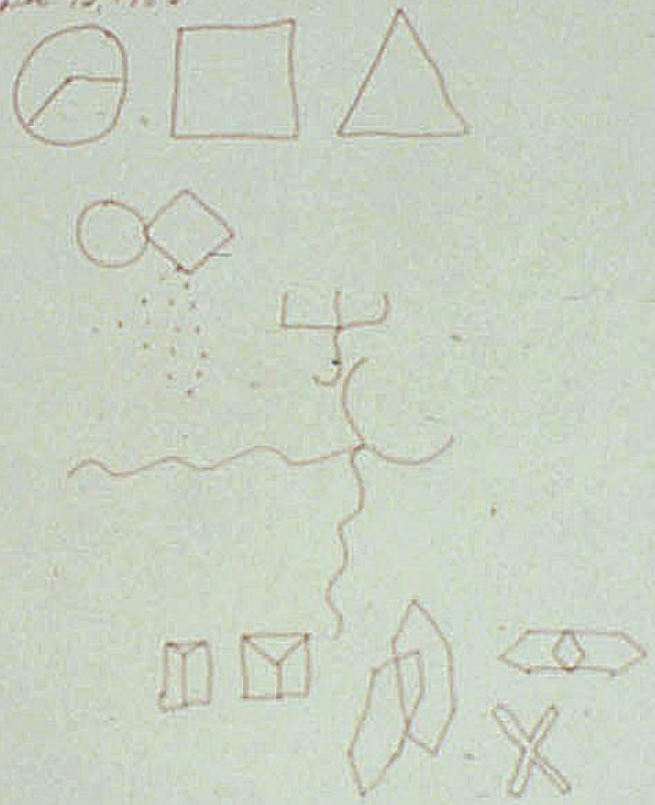
Palliative Therapy

- Psychostimulants (e.g., d-amphetamine, methylphenidate)
- Dopamine precursors (e.g., carbidopa)
- MAO type B inhibitors (e.g., selegiline)
- SNRIs

Vera M. Klatt
Oct. 20, 1983



Vera M. Klatt
Dec 13, 1983



Vera Klatt - 12-5-83

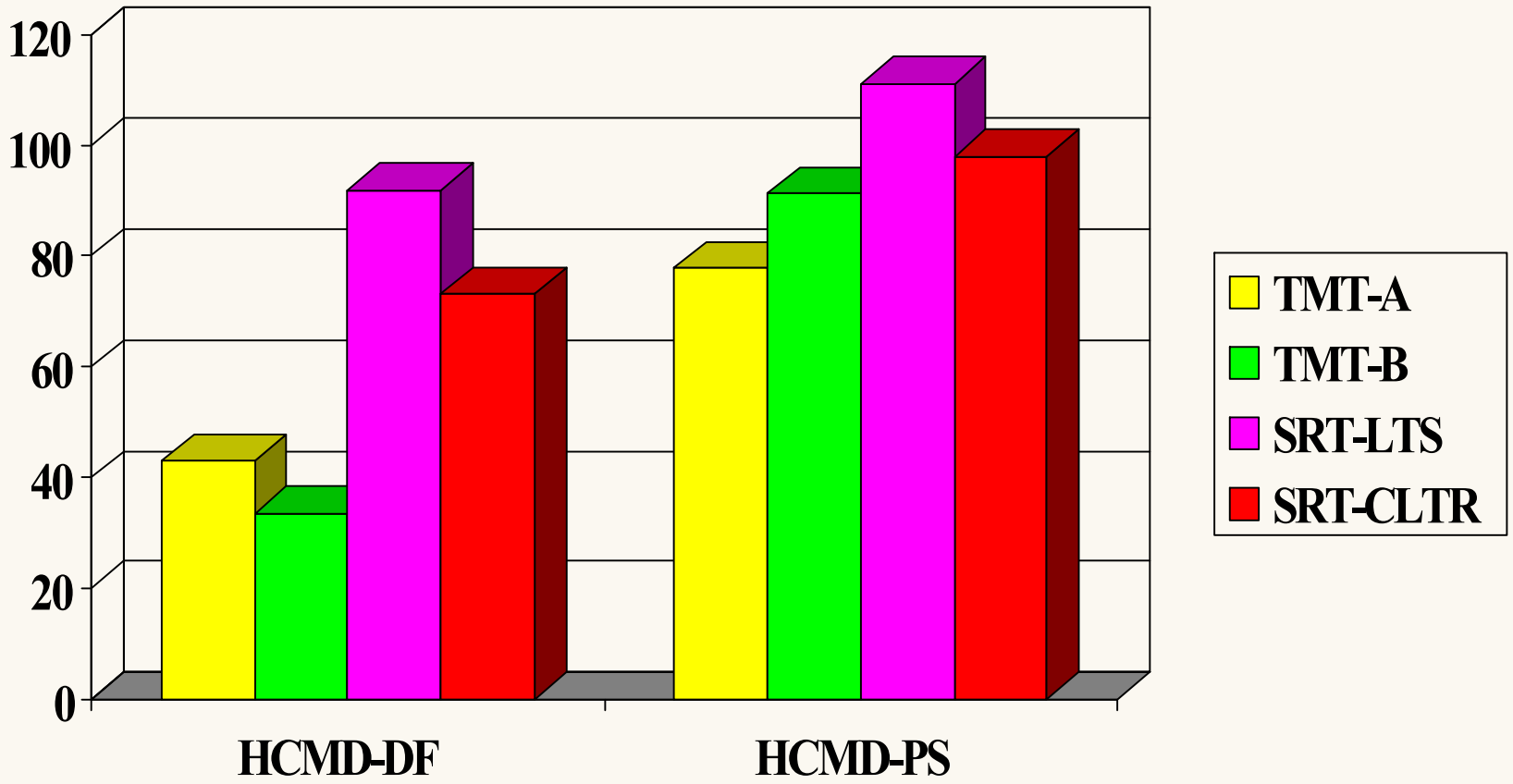
PsychostimulantsPsychostimulants

- Methylphenidate
  - Dopamine agonist
    - 5-10 mg daily
    - Move to tid dosing (7 am, 10 am, and 1 pm)
    - Usual dose range 30-60 mg/daily
    - Beware of potential for abuse
      - Infrequently seen
    - Beware in patients with history of seizures
      - May exacerbate any disposition to seizures/movement disorders
    - Watch for appetite suppression

MPD: Cognitive Effects

- MPD normalizes performance
  - Reaction Time
  - Continuous Performance Task
  - Selective Reminding Test
    - Long Term Retrieval
    - Continuous Long Term Retrieval

HMCMD Response to Methylphenidate



DF = Drug Free, PS = Psychostimulant (MPD = 30 mg/day). Raw scores age-corrected, z-transformed and converted to SS (mean=100, SD=15). All tests significant improvement on PS ($p < 0.05$). Fernandez et. al., Psychosomatics 29 (1) 38-46, 1988

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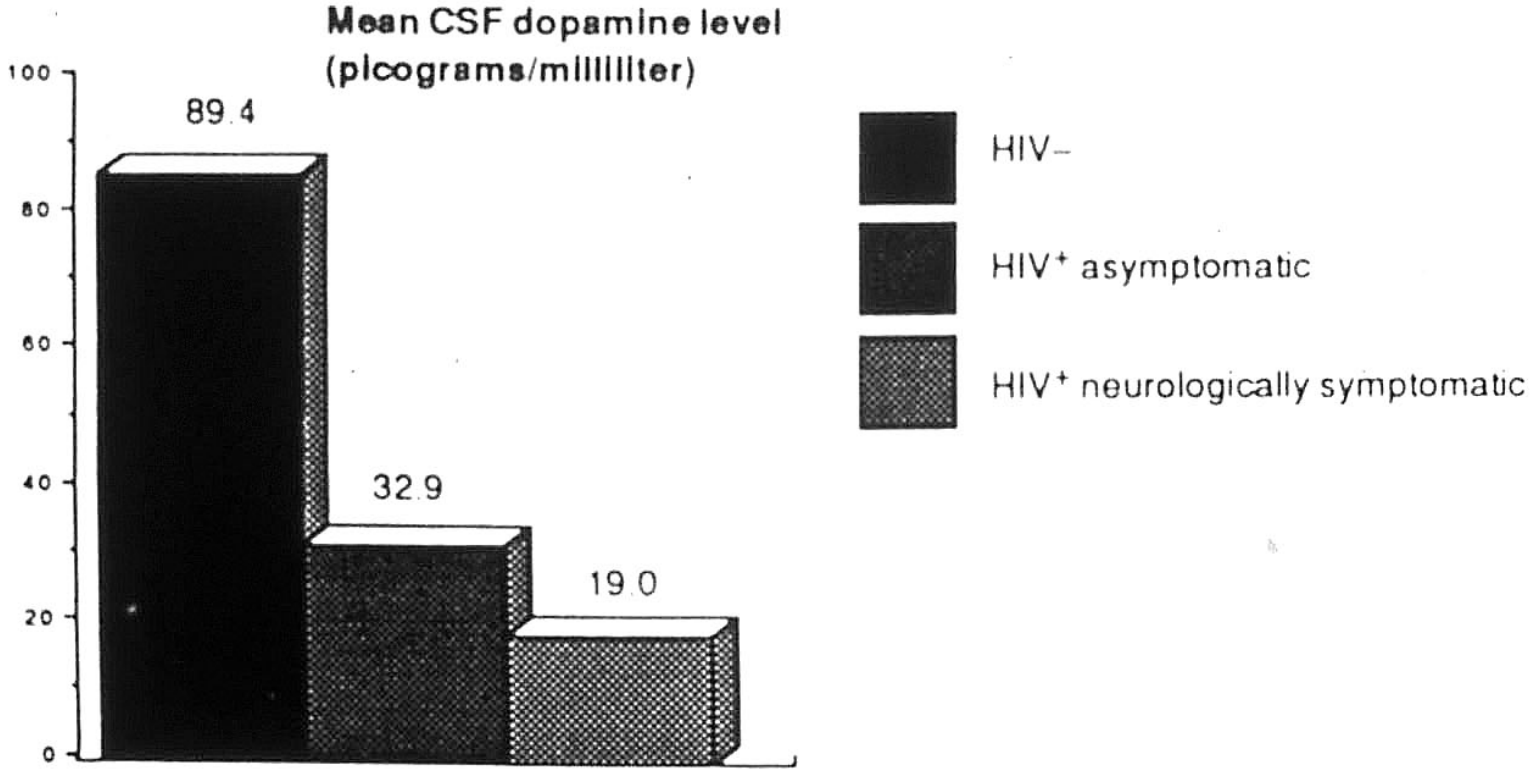
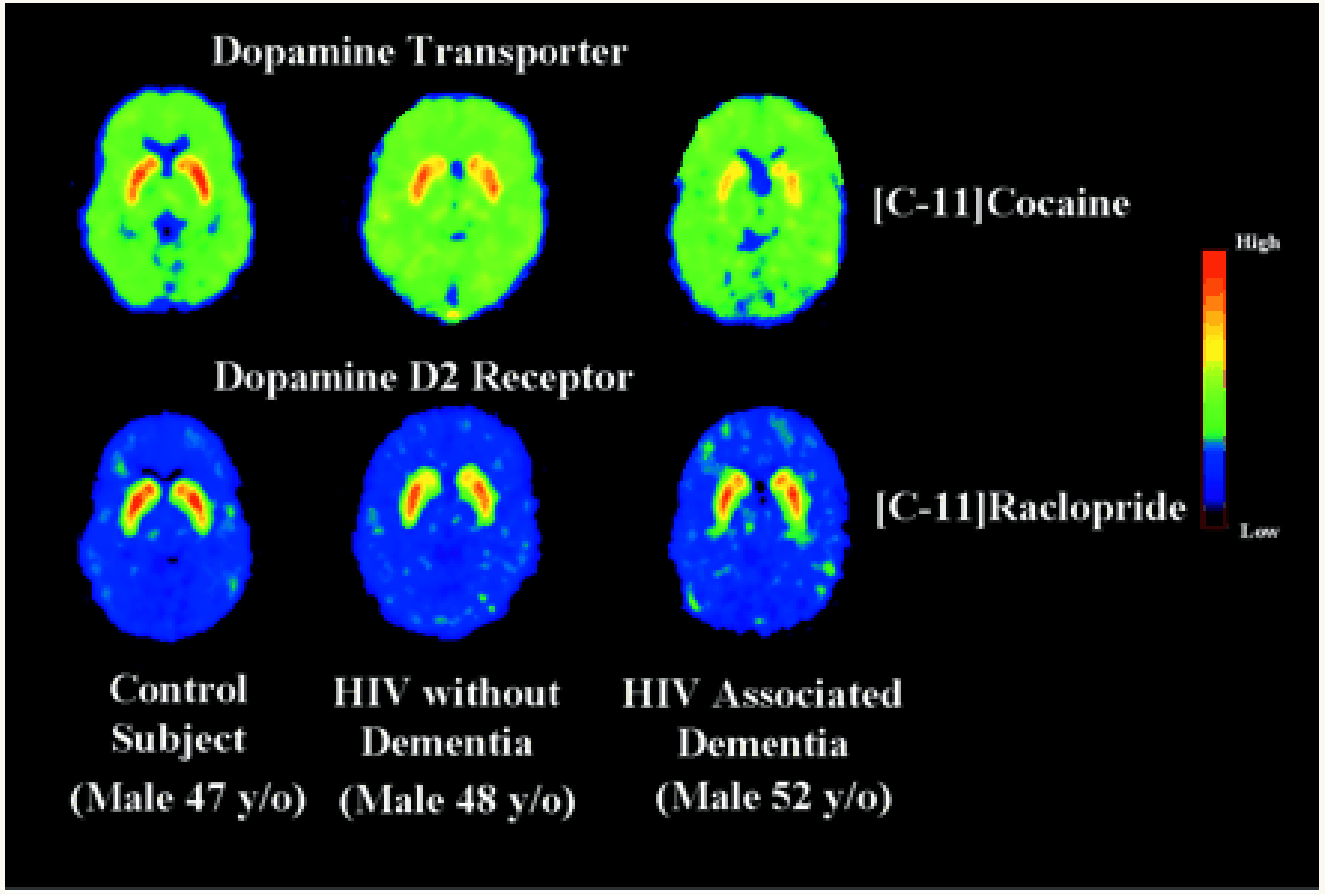
CSF Dopamine Levels in HIV Disease

Levels of the neurotransmitter dopamine differ significantly between 17 HIV-infected and 6 uninfected individuals, and are lowest in HIV-positive patients with neurological involvement. (Based on a study of 17 HIV-infected subjects conducted by Bonnie Levin and colleagues, University of Miami School of Medicine, Florida.)



Novel Measures for HAD: DA-PET Data



Chang et al, Brain 2004

Mood Disorders → Depression

Major Depressive Disorder
Depressed Mood or Anehdonia
Modified – Hopelessness
(Sleep, Interest, Guilt, Energy, Concentration, Appetite, Psychomotor, Suicide)
SIG: E-CAPSCAPS

- Depression due to general medical condtion
- Substance induced mood disorder (iatrogenic)
- Adjustment disorder with depressed mood

DSM IV Depressive Disorders

- Dysthymia
- Bipolar depression
- Major depression
  - Can include psychotic features
- Substance induced mood disorders
- Mood disorder
  - Due to general medical condition

DepressionDepression

- Common non-pathologic processes
  - Grief
  - Sadness
  - Demoralization
  - Disillusionment
  - Despondency

How Often Do Patient's With HIV Infection Get Depressed?

- Depression common clinical problem
  - Point prevalence of 8-67%
  - Prevalence in community based HIV+ cohort studies
    - 4-14% men and non-drug using women
  - Can be even higher in medically ill patients
    - 18 months prior to AIDS diagnosis
    - Advanced illness
    - Injection drug use

Is Depression "Appropriate" In HIV-1 Infection?

- Patients with HIV infection are under extreme duress
  - Illness no different than other marked stressors
  - Stress is often a precipitant
  - Stress is associated with diminished immune parameters
- Severe life stress increased the odds of developing HIV disease progression nearly fourfold
- Depression in HIV is never understandable or appropriate reaction
  - Warrants treatment

HIV Mood Disorders: Completed Suicide

Study	Subjects	Findings
Marzuk 1992	AIDS vs others	36-66 x increase w/ AIDS
Kizer 1992	AIDS vs others	17 x increase w/ AIDS
Cote 1992	US suicides	7.4 x increase w/ AIDS
Marzuk 1997	HIV+ vs others	2-3x increase w/ HIV

Suicide Risk Factors

- Prior attempt
- African American, Hispanic Men
- Ages 25-54
- Personal/Family history of SAs
- Psychiatric disorder
- Drug/Alcohol abuse or dependence
- Higher levels of distress, hopelessness

Suicide Risk Factors, continued

- More reported HIV symptoms
- Multiple losses
- Unsettled sexual identity
- Poorly controlled pain
- Psychosocial stressors
- Stage of HIV disease
- Cognitive dysfunction

Can Depression Be Reliably Diagnosed in HIV Disease?

- Approach to diagnosis of depression
  - Exclusive
    - Exclude symptoms of depression that overlap with disease process
  - Substitutive
    - Substitute psychological symptoms for somatic symptoms of depression
  - Modified
    - Qualifying affective symptoms include hopelessness
    - Associated symptoms must coincide or intensify with the onset of the qualifying affected symptoms
  - Inclusive

Medical Differential Diagnosis of HIV Related Depressive Illness

- CNS HIV cognitive disorders(MCMD & HAD)
- CNS opportunistic illnesses and cancers
- Substance abuse
- Medication effects
- Endocrine abnormalities (hypogonadism, adrenal insufficiency)

HIV-Related Medications that may Induce Mood Disorder Symptoms

- Steroids: mania or depression
- Interferon: neurasthenia fatigue syndrome, depression
- Interleukin-2: depression, disorientation, confusion and coma
- Zidovudine - mania, depression
- Vinblastine - depression, cognitive impairment
- Efavirenz: decreased concentration, depression, nervousness, nightmares

How Is Depression Treated in Patients With HIV Disease?

- Optimal management includes psychopharmacological and psychological interventions
- Pharmacotherapy is mainstay – all Rx's are equally effective

FDA Public Health Advisory
March 22, 2004
Subject: WORSENING DEPRESSION AND SUICIDALITY IN PATIENTS BEING TREATED WITH ANTIDEPRESSANT MEDICATIONS

Today the Food and Drug Administration (FDA) asked manufacturers of the following antidepressant drugs to include in their labeling a Warning statement that recommends close observation of adult and pediatric patients treated with these agents for worsening depression or the emergence of suicidality.
The drugs that are the focus of this new Warning are:

Prozac (fluoxetine); Zoloft (sertraline); Paxil (paroxetine); Luvo x (fluvoxamine); Celexa (citalopram); Lexapro (escitalopram); Wellbutrin (bupropion); Effexor (venlafaxine); Serzone (nefazodone); and Remeron (mirtazapine).

Treatment of Depression In HIV Disease

- Psychological interventions
  - Decrease high risk behaviors
  - Increase compliance
  - Enhance quality of life
  - Improve coping
  - Decrease utilization of health care services
  - Lengthen survival time (?)

Treatment of Depression in HIV Disease

- Cognitive-behavioral therapy
- Interpersonal therapy
- Behavioral therapy
- Brief psychotherapy
- Short-term dynamic psychotherapy
- Supportive psychotherapy
- Group psychotherapy

Pharmacological Treatment of Depression In HIV Disease

- All ADs are equally effective
  - Previous personal or family history of response
  - Target symptoms
  - Side-effects (exacerbate the medical illness)
  - Pharmacodynamic interactions - by direct effect on receptors or by modulating effect of other substances at receptors
    - Serotonin syndrome - SSRIs & amphotericin, ZDV
    - Potentiation - alcohol/benzodiazepines and narcotics
    - Enhancement - co-administration of benzodiazepines and TCAs, neuroleptics, isoniazid, protease inhibitors

Somatic Therapies for Depression In HIV Disease

- TCAs
- SSRIs
  - Fluoxetine, Paroxetine, Sertraline, Citalopram, Escitalopram
- SSRI-SNRIs
  - Venlafaxine
  - Nefazodone
- Atypicals
  - Bupropion
  - Mirtazapine
- MAOIs
- Psychostimulants
- [IV-Antidepressants]
- ECT
- Vagal nerve stimulation
- rTMS

HIV Mood Disorders: CHOOSING MEDICATIONS

- Adverse effects
- Elimination via liver or kidney or both
- Time to expected *onset* of action
- Expected *duration* of action
- *"Less is better"*
- Interactions with other medications/drugs

Psychomotor Stimulants in HIV-1 Infection and AIDS

- “Failure to thrive”
- Apathy
- “Low level” depression
- Demoralization & disillusionment
- Pain
- Cognitive impairment

Psychomotor Stimulants in HIV-1 Infection and AIDS

- Dextroamphetamine
- Pemoline
- Modafinil
- Methylphenidate

Hypogonadism and Depression

- **When evaluating depressive disorders** (Major Depressive D/o, Dsythymic D/o, Depressive D/o NOS, Adjustment D/o w/depressed mood) **in HIV+ men, check testosterone levels, r/o hypogonadism**
- HIV+ men have a greater risk of hypotestosteronism than the general population
- Tx of hypotestosteronism consists of testosterone replacement (Androderm®, Androgel®, Depo-Testosterone®), in addition to tx for depression

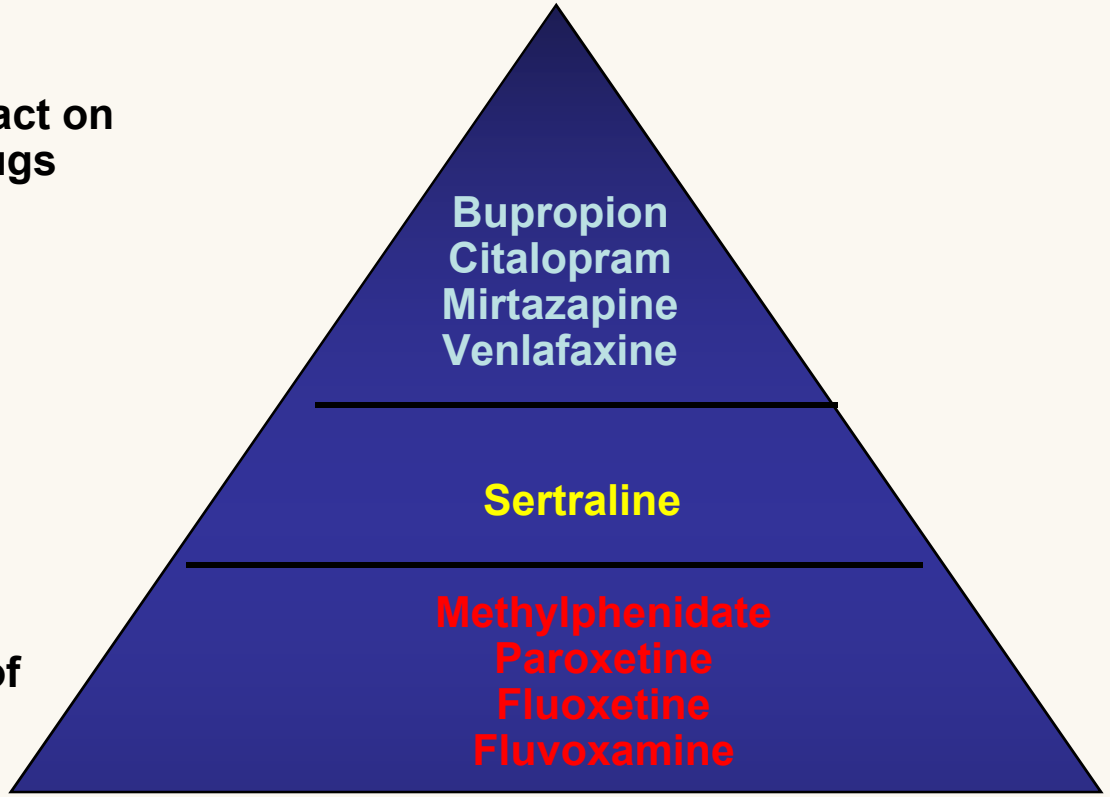
Cytochrome P450 & Drug Interactions

- All Protease Inhibitors (PIs) & Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) are substrates of cytochrome P450
- Therapeutic concerns: some psychotropic medications (i.e. TCAs) and antiretrovirals (ARVs) may have narrow therapeutic indices (including PIs & NNRTIs)
- Drug interactions b/n psychotropic medications & ARVs may lead to resistance to not just the specific ARV, but all within the same drug class

Selecting an Antidepressant: Potential for Drug-Drug Interactions

Low P450 blockers:
Likely to have little impact on metabolism of other drugs

Potent P450 blockers:
Potential for strong impact on metabolism of other drugs



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Issues For Caregivers

- Define boundaries of care giving role
- Be good to YOU
  - Vacation, exercise, nutrition
- Share feelings with others
  - Countertransference
- Spread out the care with others
- Be aware of burn out
  - Depressed mood, fatigue, irritability, decreased productivity, lack of emotional investment in work
- Encourage others to assume a care giving role
- Focus on quality of care and not outcome alone
- Limit HIV related activities in free time
- Utilize available professional support services
  - Consultation with colleagues, national and local organizations
- Staff or professional support groups
  - Use experienced facilitator who is external to the working group
- Initiate journal club

Substance Abuse

- Naltrexone (both the oral and injectable formulations) is FDA approved for treating alcoholism, although more recent studies suggest that certain types of alcoholic may experience the greatest therapeutic benefit.
- Evidence for acamprosate's efficacy in treating alcoholism has come from European studies. Although the U.S. studies have been negative, acamprosate is FDA approved for treating alcoholism.
- Topiramate is an exciting and promising new compound for treating alcohol dependence.
- Ondansetron is a promising agent for treating EOA (Type B-like alcoholics).
- SSRIs might be useful in treating type A-like alcoholics.

Substance Abuse

- Preliminary work suggests that ondansetron's efficacy in treating EOA appears to be enhanced synergistically by adding naltrexone; ongoing studies are attempting to establish these exciting results.
- It has not been established that the combination of acamprosate and naltrexone is more efficacious than either alone in treating alcohol dependence.
- Other ongoing studies are testing the efficacy of other medication combinations for treating alcoholism.
- Mechanistically driven clinical studies of putative therapeutic medications, both alone and together, hold the key to advancing the alcoholism treatment field.
- Future developments in the field include use of genetic and molecular biomarkers to predict and monitor treatment success in clinical trials.

SummarySummary

- HIV infection affects the CNS in various ways
  - Cognitive impairment of sufficient severity to cause dementia
    - Presentation may masquerade as functional psychiatric symptoms
    - Careful medical and neurobehavioral evaluation is required to rule out primary treatable CNS disease
  - Depression and psychosis are common complications
- Effective treatment strategies are available for the primary and secondary manifestations of HIV disease
- The neuropsychiatric complications of the disease deserve the same aggressive approach as that of the systemic aspects of the disease

Questions ?