

## HIV-RELATED MOOD DISORDERS

# FAST FACTS

- ◆ **Depressive Symptoms:** (SIGECAPS criteria may change with HIV disease progression). **Affective sx's:** depressed mood, loss of interest, guilt, hopelessness, suicidality. **Somatic sx's:** appetite/weight loss, sleep disturbance, agitation/retardation, fatigue, poor concentration. **Risk factors:** past h/o prior mood d/o, ETOHism, substance use (SU), anxiety, suicide attempts, poor social supports, non-disclosure of sero-status, disease junctures, tx failure. **Manic symptoms:** elevated/expansive mood, increased activity, pressured speech, flight of ideas, grandiosity; distractibility, impaired judgment, possible psychosis. **Suicide issues:** since HAART, suicide rates have decreased to levels comparable to other chronic, serious medical illnesses. Ideation remains elevated throughout disease trajectory with higher risk at key junctures (after sero-positive notification, at mid-stage, at end-stage). Desire for assisted suicide correlated with untreated/undertreated depression and/or pain syndromes. AIDS pts have less suicidal ideation than asymptomatic HIV+ pts. **Suicide risk factors:** current depression, personality d/o, delirium/dementia, social isolation, SU, prior attempts, unremitting pain, hopelessness, multiple (AIDS) losses, unsettled sexual identity, stage of disease.
- ◆ **DSM Differential:** major depression, dysthymia, adjustment d/o, bipolar disorder (manic, hypomanic, depressed, mixed), cyclothymia, schizoaffective d/o, anxiety d/o, SU, personality d/o.
- ◆ **Medical differential: Always r/o organic etiologies! (1) Depression:** Mood d/o due to medical condition (e.g., PCP), HIV cognitive d/o's (MCMD, HAD), CNS OI's (toxoplasmosis, cryptococcal meningitis, PML, brain lymphoma/cancers), other (anemia, malnourishment), endocrinopathies (hypogonadism, Addison's, hypothyroidism). **Medications:** steroids, efavirenz (Sustiva®), AZT, interferon-alpha, ribavirin, interleukin-2 (IL-2), vinblastine, vincristine, trimethoprim-sulfa, INH. **(2) Mania:** AD, OI's, steroids, AZT, ganciclovir, hyperthyroidism, neurosyphilis and cryptococcal meningitis.
- ◆ **General Treatment Principles:** decide between inpatient care (suicide risk, inability to care for self, need for controlled environment, medically frail) vs outpatient care. Decide type of psychotherapy & pharmacotherapy. HIV pt.'s extremely sensitive to med side effects (SE's). Start *lower* - go *slower*. Titrate to lower therapeutic serum levels. Avoid very anticholinergic meds if possible. Seek meds with shorter half-lives & fewer drug interactions (important to monitor for potential drug-drug interactions in context of polypharmacy regimens). If psychosis also present, "atypical" neuroleptics usually preferred to "typical". Why? *Low-potency "typicals"* are too anticholinergic (leading to worsening cognition). *High potency "typicals"* may cause EPS/NMS. *Mid-potency "typicals"* may be considered (loxitane, trilafon, molindone), if necessary. (See *Psychotic Disorders*.)
- ◆ **Pharmacokinetic Issues:** absorption, distribution, metabolism, clearance. Due to shared CYP450 metabolism, consider drug interactions and induction/inhibition of enzymes that affect substrate serum levels. Co-administered inhibitors of 2D6, or 3A4 can *decrease* substrate clearance, resulting in potentially fatal *increase* in serum levels.
- ◆ **Pharmacokinetic Issues:** drug interactions may lead to toxicity, e.g., MAOI + SSRI = fatal serotonin syndrome. HIV med regimen may: change absorption; compete for protein binding; affect free drug; induce/inhibit cytochromes. Know pt.'s prescribed & OTC meds. Check PDR/pharmacy for latest data/dosing/drug interactions.
- ◆ **Non-Pharmacologic Interventions:** Psychotherapy (individual, group, couples). Screen for bereavement treatment needs. Most patients do better with *both* psychotherapy and pharmacotherapy. Pharmacotherapy *allows* pt. to benefit from counseling. *Common themes* include: losses, anger, control, death & dying, rejection, dementia, pain, relationships, sexuality, regret, stigma, suicide. ECT may be useful in: severely suicidal pts; those too medically ill to tolerate meds; those psychotic or treatment resistant.

CLINICAL  
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- ◆ **Pharmacologic Interventions: AD's:** 5 classes: SSRI's, TCA's/Heterocyclics, Atypicals, MAOI's (not used in HIV/AIDS), psychostimulants. (Hormonal tx may also be useful.) **SSRI's** preferred due to fewer side effects, often once a day dosing, lower lethality in overdose. **SE's:** HA, sexual dysfunction, GI, anxiety, agitation, akathisia. Drug sensitivity increases with advancing disease stage. Keep doses as low as possible. **TCA's** are anticholinergic, but *may* help some w/diarrhea, weight, insomnia, nausea, neuropathic pain, delirium; but fatal in OD. Use very cautiously. Some AD's commonly used:

(Side effects: 0-6 (none, very low, low, moderate, high, very high). Inhibition scale: min., low, moderate, high.)

SSRI's	dose range/day	t <sub>1/2</sub> parent/met.	met'd by:	potential inhibition	an-ch.	sed.	ortho.	agit.
sertraline	25-200mg/d	<1day/negligible	3A4/2D6	3A4:low; 2D6:low	0	1	0	4
paroxetine	10-60mg/d	1day/negligible	2D6	3A4:low; 2D6:high	2	2	0	2
fluoxetine	10-60mg/d	2-4d/7-15d	2D6	3A4:mod; 2D6:high	0	0	0	6
citalopram	20-60mg/d	1.5d/negligible	3A4/2C19	3A4:min; 2D6:low	0	1	0	1

TCA's	dose range/day	t <sub>1/2</sub> parent/met.	met'd by:	potential inhibition	an-ch.	sed.	ortho.	Agit
desipramine	25-300mg/d	~1day	2D6	3A4:mod; 2D6:mod	3	3	3	1
nortriptyline	25-150mg/d	~1.5d/4.5days	2D6	3A4:mod; 2D6:mod	3	3	3	0

Atypicals	dose range/day	t <sub>1/2</sub> parent/met.	met'd by:	potential inhibition	an-ch.	sed.	ortho.	agit.
*bupropion	75-150mgBID/TID	~12hrs	2B6	3A4:?: 2D6: mod	0	0	0	6

[\*give 6 hrs apart; do not exceed 150mg per dose; avoid in pt's with late disease, HAD, seizure disorders.]

~nefazodone	50-300mgBID	~2-4hrs	3A4	3A4:high; 2D6:low	0	5	2	1
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[~Black Box Warning: potential life-threatening hepatic failure; contraindication if receiving drugs which inhibit CYP4503A4. Clinically significant, dangerous drug interactions with alprazolam, triazolam, ketoconazole.]

venlafaxine	75-150mgBID	~5hrs~12hrs	2D6/3A4	3A4:low;2D6:low	0	2	1	4
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[may cause hepatic dysfunction; monitor LFTs; avoid in liver disease. High rates of nausea, anorexia. Not a 1<sup>st</sup> choice.]

methylphenidate	5-10mgBID/TID	2-4hrs		[psychostimulant; do not give after 6pm; useful in refractory, or cognitive dysfunction depressions; <b>avoid</b> in pt's with h/o seizures, hypertension, mania, or psychosis]				
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(trazodone) avoid as AD; better used as *sleep adjunct*, 25-100mg hs prn insomnia (inform of priapism risk); recent FDA warning of potential interactions with ritonavir, indinavir, and ketoconazole (due to CYP 3A4 inhibition) – monitor for possible sx indicating increased trazodone levels, including increased sedation, dizziness, hypotension, syncope.

(mirtazapine) although rare, may cause agranulocytosis

#### Mood Stabilizers (see also "Psychotic Disorders" for use of Atypical Neuroleptic Medications):

Agent	dose range/day	comments:
valproic acid	500-1500mg/d, divided	[serum therapeutic levels between 50-100 microg/ml. Monitor LFT's, plt. count, serum level, amylase. Beware potential drug interactions, hepatotoxicity, pancreatitis. Increases AZT levels.]
olanzepine	5-20mg/d	[an atypical neuroleptic with <i>mood stabilizing</i> efficacy. Monitor LFT's; may induce orthostatic hypotension; low EPS; inform pt. of weight gain risk, risk for diabetes, dyslipidemia.]
lithium carbonate	<u>see the PDR for important information</u>	[in this population, often poorly tolerated, depending on stage of disease and other comorbid variables. Neurologic and GI toxicities more common. Li+ levels may suddenly increase due to intercurrent infections, dehydration, diarrhea, poor fluid intake. As HIV progresses, toxicity more likely.]
(clonazepam)	2-8mg/d, divided	[rarely used as monotherapy; 3A4 inhibitor; beware sedation/disinhibition.]
(gabapentin)	100-900mgBID	[best for post-herpetic neuralgia, neuropathy. No significant efficacy as mood stabilizer in studies.]
(carbamazepine)	<u>see the PDR for important information</u>	[may cause pancytopenia; not 1 <sup>st</sup> choice. Requires weekly CBC if co-administered with AZT. Increased toxicity if co-administered with INH, erythromycin. The "great inducer" of 3A4 - use with caution with antiretrovirals (ARVs) – may lead to decrease ARV serum levels.]