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## Psychotropic Medication Use in HIV-Infected Youth Receiving Treatment at a Single Institution

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### Abstract

A cross sectional study designed to document the use of psychotropic medication in a population of HIV-infected children and adolescents (N = 64) found 45% of the sample had been prescribed at least one psychotropic medication over a 4-year period. The most common medication category prescribed was antidepressants (30%) followed by stimulant type medications (25%). This study suggests that psychotropic medications are commonly prescribed to HIV-infected children and adolescents. Close partnership with mental health professionals to develop treatment approaches for psychiatric disorders in youth living with HIV is recommended.

### 1 Introduction

The HIV/AIDS epidemic, now well into the third decade, has been altered from a rapidly fatal infection into a chronic illness. Consequently, most perinatally HIV-infected children are surviving into their adolescent and young adult years (Gortmaker et al. 2001). Unfortunately, data suggest that in this population of survivors there is a high rate of psychiatric symptoms (Havens et al. 1994; Battles and Wiener 2002; New et al. 2003; Mellins et al. 2003; Misdrahi et al. 2004; Wiener and Battles, in press) and psychiatric hospitalizations (Gaughan et al. 2004) compared with the general pediatric population (Lewinsohn et al. 1993; Reinherz et al. 1993; Shaffer et al. 1996; Olfson et al. 2005). Little is known about psychotropic medication use among a cohort of adolescent survivors receiving long-term HIV treatment.

Since early in the epidemic, considerable attention has been given to the significant neurological and neuropsychological effects of pediatric HIV/AIDS, although few studies report formal psychiatric diagnoses. Psychological distress has been documented among HIV-infected youth in several studies, with depression, anxiety, behavioral, and social problems ranging from 12% to 44% (Mellins et al. 2003). Attention-deficit/hyperactivity disorder (ADHD) has been reported to be the most common psychiatric diagnosis among perinatally infected youths, ages 5–12 (Havens et al. 1994), a finding later confirmed in a study conducted by the Women and Infant Transmission Study Group (Mellins et al. 2003). More recently, depression and attentional disorders have been reported to be a common psychiatric

manifestation in HIV-infected youth ages 6–15 with a possible association between depression and the presence of HIV encephalopathy (Misdrahi et al. 2004).

Each of these studies provide substantial evidence of psychiatric distress among HIV-positive youth suggesting that this is a subgroup for whom psychotropic medication use may be fairly common, yet few studies have addressed this issue. Rather, investigations have focused on factors found to be associated with adverse psychological and behavioral outcomes such as encephalopathy and worsening immune function (Misdrahi et al. 2004), negative life events (Bose et al. 1994), maternal loss, limited social support (Battles and Wiener 2002), disclosure, (Wiener and Battles, in press; Gaughan et al. 2004; Lester et al. 2002) or other environmental factors (Mellins et al. 2003).

The prevalence and pattern of use of psychotropic medications has been described in HIV+ adults (Vitiello et al. 2003), however, limited information exists regarding use of psychotropic medication in youth with HIV. Gaughan et al. (2004) reported 9% of 2757 HIV-infected youth on the PACTG 219C (median age of 10 years) were prescribed a psychotropic medication compared to < 1% of 1,021 HIV-negative sibling controls. Within this cohort, 32 children were hospitalized because of psychiatric illness during an observation period (2000–2002) and 10 of these patients (31%) had been treated with a psychotropic medication prior to the hospitalization. Outside of this report, the use of psychotropic medications in HIV+ youth remains empiric with a few case reports summarized in Donenberg and Pao (2005). Trials to determine appropriate dosing of psychostimulants in HIV+ children with ADHD are underway.

Due to the dearth of information on the use of psychotropic medications in this evolving population, a naturalistic, retrospective study was designed to better understand the use of psychotropic medication among children and adolescents seen in an HIV clinic. With the high rate of parental loss in this cohort of youth, we also wanted to explore whether an association exists between psychotropic medication use and the loss of a biological parent with whom they resided.

## Methods

Clinic charts of all patients who received continuous treatment in a pediatric HIV clinic during the period between January 2000 through December 2003 (N = 64) were reviewed. Any documented use of psychotropic medications was recorded for each patient for each study year. The study was approved by the NIH Office of Human Subjects Research. Chart reviews were blinded and all identifying information was stripped from the database prior to analysis. Demographic information (age, race, gender, mode of HIV acquisition, parental loss), psychiatric diagnosis, and psychiatric hospitalizations were recorded for each study year. All prescribed psychotropic medications during this period of time were recorded (Table 1). Simple frequencies were run to describe prevalence of the use of each type of psychotropic medication, and Pearson chi-square analysis was conducted to compare incidence of parental loss to prevalence of psychotropic medication use, psychiatric diagnoses and psychiatric hospitalizations.

## Results

Sixty-four patient charts were queried. A summary of demographic information and psychotropic medication use in the patient population are presented in Table 2. Less than half of the patients were living with a biologic parent (45%) at the start of the study but all participants remained in the same home during the study period. The majority of patients (94%) were on highly active antiretroviral therapy (HAART) for their HIV infection throughout the study period. The remaining 6 % received modified HIV treatment throughout this period.

Forty-five percent of patients (n = 29) had been prescribed a psychotropic medication with 13% (n = 8) of the patients taking more than one psychotropic medication concurrently at some point during the study period. Single year prevalence of any psychotropic medication ranged from 23% (n = 15) to 31% (n = 20). There were no differences found in psychotropic medication use for those who acquired their HIV infection perinatally versus those who acquired their infection through a transfusion early in life.

A formal psychiatric diagnosis was found in the charts of 44% (n = 28) of the sample and for 90% of those prescribed psychotropic medication. Diagnoses included depression (n = 10), ADHD (n = 7), psychosis (n = 1), anxiety disorder (n = 1) and personality disorder (n = 1) with the remaining having comorbid diagnoses, including ADHD and depression (n = 5), ADHD and mood disorder (not otherwise specified) (n = 1), ADHD and psychosis (n = 1), and ADHD and Asperger's (n = 1). Eleven percent (n = 4 of 36) of patients with no recorded psychiatric diagnosis had been prescribed psychotropic medication during the study period and 5% (n = 3) of those who were not prescribed psychotropic medication had a psychiatric diagnosis of depression noted in their chart. In these cases, counseling was initiated and medication was not prescribed during the study period.

The most commonly prescribed medications (Table 2) were antidepressants (30%, n = 19), with sertraline (12%, n = 7) as the most prescribed agent in this class. Twenty-five percent of patients (n=16) were prescribed stimulants and other medications to treat ADHD. The next most common drug class was atypical antipsychotics (16%, n = 10), followed by anxiolytic medications (3%, n = 2), and other types of medication for psychiatric symptoms (6%, n = 4). Sixteen percent of the sample (n = 10) had been hospitalized due to psychiatric manifestations during this period.

Thirty-one percent (n = 20) of patients had lost a biological parent while living with them during their lifetime. Of these, 18 had lost their mother, one lost their father, and one lost both their mother and father. Those youth who had lost a parent were more likely to have been prescribed antidepressants (50%) than those who had not (21%) ( $X^2 = 5.8, p < .05$ ), and were slightly more likely to be hospitalized though this did not reach statistical significance (25% vs. 11%, respectively) ( $X^2 = 1.9, p = .16$ ).

## Discussion

The rate of psychotropic medication use seen in our HIV+ cohort is higher than the rates of psychotropic medication use seen in other medically ill adolescents such as those with cancer where at least one study has reported a prevalence rate of 14% (Pao et al. in press), but not as high as those reported for youth ages 2–17 years in routine psychiatric treatment (Duffy et al. 2005) where 84% of pediatric psychiatric patients received one or more psychopharmacologic agents. While early studies of children living with HIV suggest attentional problems and hyperactivity are clinical concerns in younger children, our data suggest that depression is an increasingly important clinical issue in older HIV+ youth. A recent case report suggests that as older adolescents with HIV/AIDS survive longer, they may progress, as adults do, into dementia and delirium requiring increasing treatment with antipsychotic medications as well (Scharko et al. 2006). The rise in use of antipsychotics found in this study (3% in 2000 to 11% in 2003) supports this finding. Clinicians are seeing and responding to a range of clinically significant psychiatric symptoms in children and adolescents with HIV/AIDS, which is reflected in the growing number of published case reports. The unknown long-term effects and the complexity of drug-drug interactions of HAART suggest that careful longitudinal studies taking into account the use of all these medications and their interactions on a developing brain is imperative.

It is not surprising that our cohort had a high rate of antidepressant prescriptions given the number of risk factors for depression they experience. Known factors that increase the risk of psychological distress include a high exposure to family/friend deaths, family disruption, discrimination, prolonged chronic illness, medical trauma (to self and others) and the uncertain nature of their illness (Grubman et al. 1995; Mellins et al. 2003). In addition, biological factors such as a genetic predisposition to depression and immune status may play a role in the etiology of depression in those youth living with chronic HIV infection (Rausch and Stover, 2001). Our data found a higher rate of antidepressant prescriptions among youth who had lost a biological parent they had lived with compared to those who had not. For children or adolescents living with HIV/AIDS mourning is often complicated by such factors as stigma, secrecy, previous losses, substance use, lack of environmental stability, and/or previous neglect (Siegel and Gorey 1994). Almost all of the documented losses in this study were maternal. Loss of the mother, often the single parent caring for the child or the parent to whom the child was more intensely attached, makes mourning more difficult, especially when one considers that the child is living with the same disease that caused their parent's illness and death. The term "disenfranchised grief" has been coined to describe grief that persons experience when they incur a loss that is not or cannot be openly acknowledged or socially supported (Doka 1989). Such grief can exacerbate bereavement by intensifying strong emotional reactions typically associated with bereavement, such as anger, guilt, and depression. Shame, isolation, secrecy, survivor guilt, economic deprivation, and cultural factors often stand as barriers to critically needed mental health services leaving youngsters more vulnerable to negative psychiatric sequelae. Ideally, mental health professionals can help support adaptive coping strategies and prepare the family to facilitate an adolescent's mastery of adaptive tasks posed by the terminal phase of the parent's illness, the death, and its aftermath (Christ et al. 2002). At a minimum, bereavement counseling should be provided to facilitate constructive mourning followed by monitoring of the child's mental health over time.

Several limitations need to be noted. Children and adolescents in our study comprise a select population of families within a single institution that were motivated to be enrolled in clinical trials and therefore, may not be representative of, or generalizable to, perinatally HIV-infected youth in the larger U.S. population. This study did not track the psychotropic medication use prior to 2000. It is possible that some of the children may have received treatments for prolonged periods prior to the data collection period. Others may have had several trials and discontinued medication prior to 2000, which would lead us to consider that the prevalence rate found is an underestimate of actual exposure to psychotropic medication. Conversely, additional children who warranted treatment based on a psychiatric diagnosis may not have been prescribed treatment due to a reluctance to add additional medications to an already complicated HAART regimen. Additionally, the clinical context in which these medications were prescribed (whether an actual diagnosis was made, specialty of prescribing physician, events at time of prescription) was not consistently documented and makes a determination of why specific agents were or were not prescribed difficult. The retrospective design of our study limits results to the documentation process of practitioners in an HIV clinic.

This study highlights the need for careful psychiatric assessment at regular intervals in children and adolescents with HIV/AIDS who develop behavioral or psychiatric symptoms. It also underscores the importance of documenting clinical diagnoses and significant target symptoms of treatment in the medical chart in order to communicate critical information between practitioners of different disciplines. Many psychotropic medications are prescribed for a variety of conditions and it is important for practitioners to document their rationale, e.g. whether a tricyclic antidepressant is used for pain, sleep, or depression or some combination.

In summary, this is the first cross-sectional report to describe the pattern of use of psychotropic medications in a population of HIV-infected children and adolescents. Youth growing up with

HIV face significant challenges and may be at higher risk for depression of multiple etiologies or other psychiatric illnesses as they get older. Higher levels of depression have also been significantly associated with decreased adherence in HIV-infected adolescents (Murphy 2001). Considering that nonadherence to antiretroviral therapy may be one of the greatest public health challenges associated with the management of HIV/AIDS, an urgent need exists for better assessment of the mental health needs of adolescents with HIV.

An ideal treatment model for children and adolescents living with HIV would be an integrated system of primary care, social services, and mental health services in the community. Some researchers have advocated for the presence of a psychiatric team within the medical HIV clinic in order to promote routine and systematic mental health screening, evaluation and treatment (Lyketsos et al. 1994). This team would promote clearer diagnoses, treatment plans and hopefully, the rational use of psychotropic medication in medically complicated youth. In addition, mental health clinicians are in a position to employ mental health treatments and techniques to work with youth and their families to manage the myriad psychosocial stressors they experience and to decrease additional adolescent risk behaviors (Donenberg and Pao, 2005). Multidisciplinary programs that offer comprehensive and practical health delivery systems for youth with HIV have been intensive and mostly available only through experimental programs; the most successful programs have had aggressive case management and active peer components (Huba and Melchoir, 1998). Additional treatment recommendations for psychiatric disorders in children and adolescents living with HIV that include combined psychological and pharmacologic interventions to guide comprehensive care for these youth and families need to be developed.

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#### References

- Battles HB, Wiener LS. From adolescence through young adulthood: Psychosocial adjustment associated with long-term survival of HIV. *J Adolesc Health* 2002;30(3):161–168. [PubMed: 11869922]
- Bose S, Moss HA, Brouwers P, Pizzo P, Lorion R. Psychologic adjustment of human immunodeficiency virus-infected school-age children. *J Dev Behav Pediatr* 1994;15(3 Suppl):S26–33. [PubMed: 8063915]
- Christ GH, Siegel K, Christ AE. Adolescent Grief. *JAMA* 2002;288(10):1269–1278. [PubMed: 12215135]
- Doka, K. Disenfranchised grief. In: Doka, KL., editor. *Disenfranchised Grief: Recognizing Hidden Sorrow*. Lexington, MA: Lexington Books; 1989. p. 3-11.
- Donenberg GR, Pao M. Youth and HIV/AIDS: Psychiatry's role in a changing epidemic. *J Am Acad Child Adolesc Psychiatry* 2005;44(8):728–747. [PubMed: 16034275]
- Duffy FF, Narrow WE, Rae DS, West JC, Zarin DA, Rubio-Stipec M, Pincus HA, Regier DA. Concomitant pharmacotherapy among youths treated in routine psychiatric practice. *J Child Adolesc Psychopharmacol* 2005;15(1):12–25. [PubMed: 15741782]
- Gaughan DM, Hughes MD, Oleske JM, et al. Psychiatric hospitalizations among children and youths with human immunodeficiency virus infection. *Pediatrics* 2004;113(6):e544–e551. [PubMed: 15173535]
- Gortmaker SL, Hughes M, Cervia J, Brady M, Johnson GM, Seage GR 3rd, Song LY, Dankner WM, Oleske JM. Pediatric AIDS Clinical Trials Group Protocol 219 Team: Effect of combination therapy including protease inhibitors on mortality among children and adolescents infected with HIV-1. *N Engl J Med* 2001;345:1522–1528. [PubMed: 11794218]

- Grubman S, Gross E, Lerner-Wiess N, Hernandez M, McSherry GD, Hoyt LG, Boland M, Oleske J. Older children and adolescents living with perinatally acquired human immunodeficiency virus infection. *Pediatrics* 1995;95(5):657–663. [PubMed: 7724299]
- Havens JF, Whitaker AH, Feldman JF, Ehrhardt AA. Psychiatric morbidity in school-age children with congenital human immunodeficiency virus infection: A pilot study. *J Dev Behav Pediatr* 1994;15(3 Suppl):S18–25. [PubMed: 7520454]
- Huba GJ, Melchior LA. A model for adolescent-targeted HIV/AIDS services. *J Adolesc Health* 1998;23S: 11–27. [PubMed: 9712250]
- Lester P, Chesney M, Cooke M, Weiss R, Whalley P, Perez B, Glidden D, Petru A, Dorenbaum A, Wara D. When the time comes to talk about HIV: Factors associated with diagnostic disclosure and emotional distress in HIV-infected children. *J Acquir Immune Defic Syndr* 2002;31(3):309–317.
- Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology: Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *J Abnorm Psychol* 1993;102(1):133–144. [PubMed: 8436689]Erratum in: *J Abnorm Psychol* 1993
- Lyketsos CG, Hanson A, Fishman M, McHugh PR, Treisman GJ. Screening for psychiatric morbidity in a medical outpatient clinic for HIV infection: the need for a psychiatric presence. *Int J Psychiatry Med* 1994;24(2):103–113. [PubMed: 7960418]
- Mellins CA, Smith R, O'Driscoll P, Magder LS, Brouwers P, Chase C, Blasini I, Hittleman J, Llorente A, Matzen E. NIH NIAID/NICHD/NIDA-Sponsored Women and Infant Transmission Study Group. High rates of behavioral problems in perinatally HIV-infected children are not linked to HIV disease. *Pediatrics* 2003;111(2):384–393. [PubMed: 12563068]
- Misdrahi D, Vila G, Funk-Brentano I, Tardieu M, Blanche S, Mouren-Simeoni MC. DSM-IV mental disorders and neurological complications in children and adolescents with human immunodeficiency virus type 1 infection (HIV-1). *Eur Psychiatry* 2004;19(3):182–184. [PubMed: 15158930]
- Murphy DA, Wilson CM, Durako SJ, Muenz LR, Belzer M. Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort. *AIDS Care* 2001;13:27–40. [PubMed: 11177463]
- New, M.; Lee, S.; Pao, M. Prevalence of mental health in pediatric HIV: A family perspective. Presented at the NIMH Conference on the Role of Families in Preventing and Adapting to HIV/AIDS; Washington, DC. 2003.
- Olfson M, Gameroff MJ, Marcus SC, Greenberg T, Shaffer D. National trends in hospitalization of youth with intentional self-inflicted injuries. *Am J Psychiatry* 2005;162(7):1328–1335. [PubMed: 15994716]
- Pao, M.; Ballard, ED.; Rosenstein, DL.; Wiener, L.; Wayne, AS. Archives of Pediatrics and Adolescent Medicine. Psychotropic Medication Use in Pediatric Oncology Patients. in press
- Rausch DM, Stover ES. Neuroscience research in AIDS. *Prog Neuro-Psychopharmacol & Biol Psychiat* 2001;25:231–257.
- Reinherz HZ, Giaconia RM, Lefkowitz ES, Pakiz B, Frost AK. Prevalence of psychiatric disorders in a community population of older adolescents. *J Am Acad Child Adolesc Psychiatry* 1993;32(2):369–377. [PubMed: 8444767]
- Scharko AM, Baker EH, Kothari P, Khattak H, Lancaster D. Case Study: Delirium in an adolescent girl with human immunodeficiency virus-associated dementia. *J Am Acad Child Adolesc* 2006;45(1): 104–108.
- Shaffer D, Fisher P, Dulcan MK, Davies M, Piacentini J, Schwab-Stone ME, Lahey BB, Bourdon K, Jensen PS, Bird HR, Canino G, Regier DA. The NIMH Diagnostic Interview Schedule for Children Version 2.3 (DISC-2.3): Description, acceptability, prevalence rates, and performance in the MECA Study. *Methods for the Epidemiology of Child and Adolescent Mental Disorders Study. J Am Acad Child Adolesc Psychiatry* 1996;35(7):865–877. [PubMed: 8768346]
- Siegel K, Gorey E. Childhood bereavement due to parental death from acquired immunodeficiency syndrome. *Journal of Developmental and Behavioral Pediatrics* 1994;15(3):S66–S70. [PubMed: 8063923]
- Vitiello B, Burnam MA, Bing EG, Beckman R, Shaprio MF. Use of Psychotropic Medications Among HIV-Infected Patients in the United States. *Am J Psychiatry* 2003;160:547–554. [PubMed: 12611837]

Wiener L, Battles H. Untangling the web: A close look at diagnosis disclosure among HIV-infected adolescents. *J Adolesc Health* 2006 March;38(3):307–10. [PubMed: 16488835]

**Table 1****Drug Classifications of Psychotropic Medications Prescribed to an HIV+ Youth Cohort**

<b>Drug Category</b>	<b>Drug</b>
Antidepressants	Amitriptyline bupropion citalopram escitalopram fluoxetine mirtazapine paroxetine sertraline venlafaxine
Stimulants, norepinephrine reuptake inhibitor, alpha-adrenergic agonist	dextroamphetamine methylphenidate pemoline atomoxetine clonidine
Atypical Antipsychotics	aripiprazole olanzapine quetiapine risperidone
Anxiolytics	Bupirone clonazepam
Other	Divalproex sodium fish oils melatonin



**Table 2**  
Demographic Characteristics and Psychotropic Medication Use in the Sample ( $N = 64$ )

Variable	n (%)
Gender	
Male	32 (50%)
Female	32 (50%)
Age at end of study period: mean (range)	15.3 years (8–24)
Race	
African American/Black	28 (44%)
Caucasian/White	25 (39%)
Hispanic/Latino	4 (6%)
Other	7 (11%)
Mode of transmission	
Vertical/perinatal	54 (84%)
Transfusion	10 (16%)
Prescribed any psychotropic medication	29 (45%)
Number of psychotropic medications per patient prescribed during study period	
0	35 (54.7%)
1	10 (15.6%)
2	9 (14.1%)
3	3 (4.7%)
4	4 (6.2%)
5+	3 (4.7%)
Type of psychotropic medication prescribed (not mutually exclusive)	
Antidepressants	19 (30%)
Stimulants*	16 (25%)
Atypical Antipsychotics	10 (16%)
Anxiolytics	2 (3%)
Other	4 (6%)
Hospitalizations due to psychiatric manifestations (during study period)	10 (16%)

\*Includes atomoxetine and clonidine

**Table 3**

Use of Psychotropic Medication in a Cohort of HIV+ Youth (n = 64) by Year

	2000 n (%)	2001 n (%)	2002 n (%)	2003 n (%)
Prescribed any psychotropic medication	18 (28%)	16 (25%)	15 (23%)	20 (31%)
Antidepressants	6 (9%)	7 (11%)	7 (11%)	13 (20%)
Stimulants*	14 (22%)	10 (16%)	6 (9%)	6 (9%)
Atypical Antipsychotics	2 (3%)	2 (3%)	6 (9%)	7 (11%)
Anxiolytics	2 (3%)	0 (0%)	1 (2%)	0 (0%)
Prescribed >1 medication concurrently	8 (12%)	5 (8%)	5 (8%)	8 (12%)

\* Includes atomoxetine and clonidine