Psychiatric Hospitalizations Among Children and Youths With Human Immunodeficiency Virus Infection

Denise M. Gaughan, MPH*‡; Michael D. Hughes, PhD‡; James M. Oleske, MD, MPH§; Kathleen Malee, PhD‖; Carol A. Gore¶; and Sharon Nachman, MD#, for the Pediatric AIDS Clinical Trials Group 219C Team

ABSTRACT. *Objective.* **Psychiatric manifestations of pediatric human immunodeficiency virus (HIV) infection have been described. However, data on severe sequelae requiring hospitalization among this population have not been reported.**

Methods. **The Pediatric Acquired Immunodeficiency Syndrome (AIDS) Clinical Trials Group (PACTG) 219C is a prospective cohort study designed to examine long-term outcomes among HIV-infected children and HIV-uninfected infants born to HIV-infected women. Children with HIV infection who have enrolled in PACTG 219C are examined quarterly, with collection of clinical and laboratory data. Hospitalizations and diagnoses for all participants between September 2000 (when enrollment into PACTG 219C was started) and December 2002 were reviewed.**

Results. **Among 1808 HIV-infected participants who were <15 years of age at the last visit date, 25 children had been hospitalized for psychiatric manifestations, 8 before enrollment into PACTG 219C. Seventeen children were hospitalized during 2757 person-years of follow-up monitoring after entry into PACTG 219C, which represents an incidence of 6.17 cases per 1000 person-years (95% confidence interval: 3.59–9.87 cases per 1000 person-years). This was significantly higher than the incidence of 1.70 cases per 1000 person-years (95% confidence interval: 1.67–1.72 cases per 1000 person-years) in the general pediatric population <15 years of age, as reported in the 2000 National Hospital Discharge Survey, yielding a relative rate of 3.62 (95% confidence interval: 2.11–5.80). A total of 32 HIV-infected children, regardless of age, were hospitalized because of psychiatric illnesses. The majority of patients were admitted because of depression (n = 16) or behavioral disorders (n = 8). Fifteen (47%) underwent multiple psychiatric hospitalizations. The median age at the first psychiatric hospitalization was 11 years (range: 4–17 years); all patients had been perinatally infected. Knowledge of HIV seropositivity status and having experienced a significant life event were both significantly associated with an increased risk of psychiatric hospitalization (hazard ratios of 6.13 and 3.04, respectively). No psychiatric hospitalizations were observed among the 1021 HIV-uninfected members of the cohort.**

Conclusions. **Children with HIV/AIDS are at increased risk for psychiatric hospitalizations during childhood and early adolescence, compared with the general pediatric population. Knowledge of HIV seropositivity status and recent significant life events were significantly associated with increased risks of admission in this population.** *Pediatrics* **2004;113:e544–e551. URL: http://www.pediatrics.org/cgi/content/full/113/6/e544; *HIV/AIDS, pediatrics, psychiatric hospitalization, psychologic distress, disclosure, proportional hazards regression.***

ABBREVIATIONS. HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; PACTG, Pediatric AIDS Clinical Trials Group; NHDS, National Hospital Discharge Survey; WITS, Women and Infants Transmission Study.

As the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) epidemic enters its third decade, advances in treatment, most notably combination therapy with a protease inhibitor and improved prophylaxis, have transformed the disease from a rapidly fatal infection into a chronic illness, greatly extending the life expectancy of infected individuals.[1] As children live longer with chronic HIV infection, however, they may be at greater risk of increased incidence and severity of complications, including psychiatric illnesses.

Psychologic manifestations among children with life-limiting or chronic illnesses have been reported.[2–7] Conflicting findings suggest a multifactorial relationship defined by the disease, the degree of social support, and the quality of and access to medical care. Bennett[8] reviewed 60 studies of depressive symptoms among children and adolescents with chronic medical problems and concluded that chronically ill children were at slightly elevated risk for depressive symptoms but not clinical depression. He reported that the risk may depend on the disorder, ie, children with asthma, recurrent abdominal pain, or sickle cell anemia are possibly at greater risk than children with other chronic disorders such as cancer, cystic fibrosis, or diabetes mellitus.[8] A recent case-control study found no significant differences in depression, anxiety, or loneliness ratings among 76

From the *National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, West Virginia; ‡Center for Biostatistics in AIDS Research, Harvard School of Public Health, Boston, Massachusetts; §Department of Pediatrics, University of Medicine and Dentistry of New Jersey, Newark, New Jersey; ‖Departments of Infectious Diseases and Child and Adolescent Psychiatry, Children's Memorial Hospital, Chicago, Illinois; ¶Community Constituency Group, Conroe, Texas; and #Department of Pediatric Infectious Disease, State University of New York, Health Science Center, Stony Brook, New York.

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Address correspondence to Sharon Nachman, MD, Department of Pediatric Infectious Disease, State University of New York, Health Science Center, T11-060, Stony Brook, NY 11794-8111. E-mail: sharon.nachman@stonybrook.edu

children with cancer, compared with school-age peer control subjects.[9]

Children with HIV infection have additional risk factors for mental illness, including poverty, a disrupted home life, a family history of mental illness, psychiatric disorders, and/or substance abuse, and inadequate social support. Other possible risk factors that are more specific for HIV infection include forced disclosure of HIV status to others, fear of progression to AIDS, and body image concerns resulting from delayed development, chronic dermatologic conditions, or lipodystrophy/lipoatrophy.[10] Psychologic problems among children and youths with HIV infection have been documented.[11–18] In a convenience sample of 34 HIV-positive adolescents, Pao et al[19] reported a prevalence rate of 44% for ongoing depressive disorders and a 68% lifetime risk of an affective disorder. The study also reported phobias and anxiety disorders, as well as a 59% prevalence rate of substance abuse.

Recent data from the Women and Infants Transmission Study (WITS) indicated high rates of emotional and behavioral problems among HIV-infected children between the ages of 3 and 7 years. The association ceased to be significant, however, in multivariate analyses comparing the HIV-infected children with HIV-exposed, uninfected, control subjects, which led the authors to conclude that the relationship between these disorders and HIV may be attributable to psychosocial factors, as opposed to the disease itself.[20]

In the general pediatric population, stressful life events often precede depression or suicide attempts.[21,22] In a longitudinal study of 24 HIV-infected children assessed at baseline and 2 years later, Moss et al[23] reported an association between negative life events and adverse psychologic and behavioral outcomes. In the adult HIV literature, mental disorders (specifically acute stress reactions) are reported to be most common immediately after notification of HIV seropositivity, occurring for up to 90% of subjects.[24]

Lester et al[25] examined factors related to emotional distress among 51 children with perinatal HIV infection. In cross-sectional univariate analyses, HIV disclosure and major life events were associated with increased parent-rated anxiety. However, after adjustment for age, major life events, and medication dose, HIV disclosure ceased to be significant. The authors acknowledged that the study was limited by the small sample size.

The incidence of psychiatric hospitalization in the pediatric HIV-infected population has not been investigated extensively. Hein et al[12] reported increased numbers of psychiatric hospitalizations among 72 HIV-infected adolescents, compared with 1142 uninfected control subjects receiving care in an urban adolescent clinical care unit. The purpose of this analysis of the Pediatric AIDS Clinical Trials Group (PACTG) 219C database was to determine the incidence of psychiatric hospitalizations among members of the cohort with HIV infection and to examine predictors of first psychiatric hospitalization.

METHODS

Study Design

The PACTG Late Outcomes Study (PACTG 219C) is a prospective cohort study designed to examine the long-term effects of in utero and/or postnatal exposure to HIV and antiretroviral therapies. PACTG 219C opened to enrollment on September 15, 2000, and continues to enroll patients at 45 sites in the mainland United States and Puerto Rico. The institutional review board at each site approved the study, and informed consent was obtained from each child's parent or guardian before study entry.

Eligible subjects for PACTG 219C include all perinatally HIV-exposed (infected, undetermined status, or uninfected) infants, children, and adolescents and children with postperinatally acquired HIV infection being monitored at a PACTG site. Infected children enrolled in PACTG 219C are examined quarterly, with routine clinical and laboratory evaluations. The PACTG 219C database was reviewed for psychiatric hospitalizations among perinatally HIV-infected and perinatally HIV-exposed, uninfected participants (children and adolescents) between September 2000 (when enrollment in PACTG 219C was initiated) and December 2002. An incident case was defined as a psychiatric hospitalization after the individual's PACTG 219C study enrollment date. A prevalent case was defined as a psychiatric hospitalization before the individual's study enrollment date. Prevalent cases were excluded from the incidence analyses to avoid ascertainment bias.

Knowledge of HIV seropositivity status and significant life events are assessed quarterly in PACTG 219C with the General Health Assessment for Children.[26] This age-specific questionnaire, which is modular in design, documents whether the individual has been informed of his or her HIV seropositivity status and includes some or all of the following domains: general health perceptions, physical resilience, physical function, psychologic function, social and role function, health care utilization, and disease-related symptoms. The General Health Assessment for Children has been demonstrated to have good psychometric properties.[27] A significant life event was defined as a positive response regarding any of the following 18 points on the General Health Assessment for Children: parent lost job, family member left home, loss of housing or had to move, loss of entitlement, loss of health insurance, family member hospitalized, family member very sick, change of caregiver, separation of parents, divorce of parents, jail sentence of parent, marriage of parent, birth of a sibling, mother starting to work, beginning school or moving to a new school, change in financial status of parents, loss of a close friend (to child), or death in the family.

The incidence of psychiatric hospitalizations in the general pediatric population was obtained from the National Hospital Discharge Survey (NHDS).[28] The NHDS is an annual, national, probability survey detailing characteristics of inpatients discharged from nonfederal, short-stay hospitals in the United States. The NHDS collects data from a sample of ~270 000 inpatient records acquired from a national sample of ~500 hospitals. Only hospitals with an average length of stay of <30 days for all patients, general hospitals, and children's general hospitals are included in the survey.

Statistical Methods

The relative risks and 95% exact confidence intervals were calculated using maximum likelihood estimation of the Poisson rate parameters of the incidence of psychiatric hospitalizations among HIV-infected PACTG 219C participants <15 years of age. This age restriction was necessary to enable comparisons with the incidence for the general pediatric population reported in the 2000 NHDS. Observation times were calculated in person-years for both populations. The 2 rates then were compared for homogeneity.

Because age-specific rates of hospitalization are not available in the NHDS, indirect age standardization was used to allow for the possibility that the age distribution for children in the PACTG 219C cohort was different from that observed in the general pediatric population. This standardization involved applying the rate of hospitalization observed in PACTG 219C for infected children in each year of age to the number of children in the United States having that age, to provide a predicted number of hospitalizations in the pediatric population in the United States. This then was compared with the number in the NHDS to yield an

age-adjusted relative risk. It was not possible to estimate the standard error of this relative risk, however, because of the small numbers (sometimes zero) of hospitalizations for some ages in PACTG 219C.

Cox proportional hazards regression techniques[29] were used to examine predictors of first psychiatric hospitalization for all incident cases regardless of age. Demographic and clinical variables including age, gender, race/ethnicity (non-Hispanic white, non-Hispanic black, or Hispanic), caregiver status (biologic parent versus other), time-varying values for knowledge of HIV status, recent significant life events, CD4 percentage, HIV-1 RNA viral load (<400 copies per mL vs ≥400 copies per mL), and antiretroviral medications (specifically nonnucleoside reverse transcriptase inhibitors and protease inhibitors) were examined with respect to their associations with first psychiatric hospitalization.

RESULTS

A total of 2298 HIV-infected and 1021 HIV-exposed, uninfected infants, children, and adolescents were enrolled in PACTG 219C between September 15, 2000, and December 31, 2002. Population characteristics are detailed in Table 1.

Among the 1808 HIV-infected participants who were <15 years of age at their last visits, 25 children were hospitalized because of psychiatric manifestations, 8 before enrollment in PACTG 219C. Seventeen children were therefore hospitalized during 2757 person-years of follow-up monitoring, representing an incidence of 6.17 cases per 1000 person-years (95% confidence interval: 3.59–9.87 cases per 1000 person-years). This was significantly higher than the general pediatric incidence of 1.70 cases per 1000 person-years (95% confidence interval: 1.67–1.72 cases per 1000 person-years) reported in the 2000 NHDS, yielding an incidence ratio of 3.62 (95% confidence interval: 2.11–5.80). On the basis of age-specific rates in the PACTG 219C cohort, 262 217 psychiatric hospitalizations would be expected in the general pediatric population, whereas 103 000 events were reported in the NHDS, yielding an age-standardized incidence ratio of 2.55 for the PACTG 219C cohort. No psychiatric hospitalizations were observed among the 1021 HIV-negative members of the cohort.

Proportional hazards univariate regression models revealed that knowledge of HIV seropositivity status and significant life events were associated with increased risks of psychiatric hospitalization (Table 2). In a multivariate analysis that included these 2 variables, participants who were aware of their HIV seropositivity status were 6 times more likely to be hospitalized because of psychiatric illnesses, compared with participants who were unaware of their HIV status (hazard ratio: 6.13). Participants who reported a significant life event were 3 times more likely to be hospitalized because of psychiatric illnesses, compared with participants who did not report such an event (hazard ratio: 3.04). Race/ethnicity, gender, age, caregiver status, immunologic and virologic markers, and nonnucleoside reverse transcriptase inhibitor and protease inhibitor antiretroviral medications were not significantly associated with first psychiatric hospitalizations.

A total of 32 children (regardless of age) were hospitalized because of psychiatric illnesses during the observation period. The majority were admitted because of depression ($n = 16$), behavioral disorders ($n = 8$), or suicidal ideation/attempts ($n = 6$) (Table 3). Fifteen participants (47%) experienced multiple psychiatric hospitalizations; 10 were hospitalized twice and 5 were hospitalized ≥3 times. At the first psychiatric hospitalization, the median age was 11 years (range: 4–17 years), 20 patients were male (63%), 28 patients (88%) were aware of their HIV seropositivity status, 14 patients (44%) had a previous psychiatric diagnosis, and 10 patients (31%) had been treated with a psychotropic medication previously. All patients had been exposed to a nucleoside reverse transcriptase inhibitor before their first psychiatric hospitalizations, 26 patients (81%) had been exposed to a protease inhibitor, and 15 patients (47%) had been exposed to a nonnucleoside reverse transcriptase inhibitor. The median length of stay for all psychiatric hospitalizations was 7 days (range: 1–252 days). During the 2757 person-years of observation, 276 person-days of psychiatric hospitalization occurred. This is equivalent to 100 person-days of hos-

TABLE 1. Baseline Characteristics of the PACTG 219C Population Enrolled Between September 2000 and December 2002

Variable	Infected ($n = 2,298$)	Uninfected ($n = 1,021$)
Person-years of follow-up monitoring	2757	937
Median age, y (10th and 90th percentiles)	10 (4, 16)	1 (<1, 6)
Gender, female, %	51	51
Race/ethnicity, %		
White, non-Hispanic	14	11
Black, non-Hispanic	57	56
Hispanic	27	32
Other	2	1
Median CD4 percentage (10th and 90th percentiles)	30 (14, 43)	42 (32, 53)
Median CD4 T-lymphocyte count, cells/mm^3 (10th and 90th percentiles)	739 (239, 1560)	2,085 (853, 3898)
Median HIV-1 RNA level, copies/mL (10th and 90th percentiles)	1432 (50, 64, 382)	N/A
HIV seropositivity status known by subject, %	48	N/A
Primary caregiver biologic parent, %	43	90
Antiretroviral exposure, %		
Nucleoside reverse transcriptase inhibitor	98	89
Nonnucleoside reverse transcriptase inhibitor	57	<1
Protease inhibitor	81	2
Psychotropic medication (%)	9	<1

N/A indicates not applicable.

TABLE 2. Proportional Hazards Regression of Time to First Incident Psychiatric Hospitalization ($n = 21$)

Variable	Unadjusted Hazard Ratio (95% Confidence Interval)
Age*	1.08 (0.99–1.19)
Gender	
Female	0.49 (0.20–1.22)
Male	1.0
Race/ethnicity	
Black, non-Hispanic	1.32 (0.38–4.58)
Hispanic	0.73 (0.16–3.27)
White, non-Hispanic	1.0
CD4 percentage†‡	1.01 (0.97–1.05)
HIV-1 RNA†	
<400 copies/mL	0.31 (0.07–1.35)
≥400 copies/mL	1.0
HIV seropositivity status known by subject?†§	
Yes	6.32 (1.86–21.5)
No	1.0
Significant life event?†‖	
Yes	3.07 (1.18–7.96)
No	1.0
Caregiver biologic parent?	
Yes	0.66 (0.27–1.63)
No	1.0
Nonnucleoside reverse transcriptase inhibitor?†	
Yes	0.82 (0.32–2.11)
No	1.0
Protease inhibitor?†	
Yes	1.28 (0.50–3.31)
No	1.0

* Per 1-year increase.
† Time-dependent observation.
‡ Per 1% increase.
§ Multivariate hazard ratio = 6.13 (95% confidence interval: 1.80–20.8).
‖ Multivariate hazard ratio = 3.04 (95% confidence interval: 1.17–7.87).

pitalization per 1000 person-years of follow-up monitoring.

DISCUSSION

Data from the PACTG 219C cohort indicate that children with HIV/AIDS are at increased risk for psychiatric hospitalizations, compared with the general pediatric population. The reported incidence of psychiatric hospitalizations in the general pediatric population is 1.70 cases per 1000 person-years. This contrasts with an incidence of 6.17 cases per 1000 person-years among PACTG 219C participants infected with HIV, a >3-fold increase in the rate of hospitalizations. Psychiatric hospitalizations occurred exclusively among children with HIV infection, with no hospitalizations among HIV-exposed, uninfected children monitored in PACTG 219C. The main reason why the uninfected children were younger than the infected children was the fact that a requirement for entry into PACTG 219 was previous enrollment in another PACTG study. For uninfected children, this would have been a perinatal transmission study; for infected children, however, it could have been either a perinatal transmission study or a treatment study, including treatment studies that enrolled older children. Similarly, PACTG 219C permitted entry of any infected children but restricted entry of uninfected children who were not continuing from PACTG 219 to those <1 year of age. This explains the difference in age distributions between the uninfected and infected cohorts in PACTG 219C. Because no uninfected child was hospitalized, it is not possible to estimate the relative risks of hospitalization in a comparison of infected and uninfected children, without or with adjustment for the age differences. However, given the age discrepancy between the infected and uninfected PACTG 219C cohorts, comparisons that may clarify the specific effects of HIV infection and other chronic risk factors are limited.

In a multivariate analysis, individuals aware of their HIV seropositivity status were 6 times more likely to be hospitalized for psychiatric illness compared with those unaware of their HIV status. Also, those reporting a significant life event were 3 times more likely to be hospitalized for psychiatric illness compared with those not reporting such an event. Because of insufficient statistical power, we were unable to examine associations between psychiatric hospitalization and the 18 individual significant life events. It is possible that that there are varying degrees of predictability among these events. Clinicians should be aware that these occurrences might precipitate a psychiatric crisis, particularly in the context of a preexisting psychiatric disorder or mental health issue.

Data from the WITS found no significant difference in emotional and behavioral problems in HIV-infected children compared to HIV-exposed, uninfected controls and concluded that the relationship between these disorders and HIV may be attributed to psychosocial factors rather than HIV. However,

TABLE 3. Information on Participants Hospitalized Because of Psychiatric Illnesses (n = 32)

Identification	Incident or Prevalent	Diagnosis	Age at Hospitalization, y	Time in Hospital,[d]	HIV Status Known? (Age, y)	Significant Life Event Before First Hospitalization?	Psychiatric Diagnosis Before First Hospitalization?	Psychotropic Medication Before First Hospitalization?
1a	P	Behavior disorder	16	7	Y (9)	Y	Y	N
1b*	P	Mood disorder, adjustment disorder, ODD	16	252				
2a	P	Eating disorder	11	4	Y (9)	N	N	N
2b*	P	Eating disorder	11	3				
3a	I	ADHD	8	2	Y (7)	Y	Y	Y
4a	P	Depression	10	7	N	N	Y	N
5a	P	Depression	16	18	Y (10)	N	N	N
6a	I	Suicidal gesture	9	10	Y (7)	Y	N	N
7a	I	Major depressive disorder	13	4	Y (8)	Y	N	N
8a	P	Psychotic episode	11	5	Y (11)	N	Y	Y
8b*	P	Psychotic behavior	11	2				
8c*	P	Major depression with psychosis	13	16				
8d*	P	Bit case manager	13	UNK				
8e*	P	Psychosis	13	19				
9a	P	Depression	11	7	Y (9)	N	N	N
9b*	P	Depression, adjustment disorder, polysubstance abuse	14	4				
9c*	P	Depression	14	6				
9d*	P	Depression	14	5				
10a	I	Depression	12	UNK	UNK	Y	N	N
11a	P	Adjustment disorder	11	31	Y (8)	N	N	N
11b*	P	Depression	12	25				
11c*	P	ODD	12	5				
11d*	P	ODD	13	UNK				
12a	I	Suicide attempt	17	2	Y (12)	Y	N	N
13a	P	Bipolar disorder, depression, ODD	17	15	Y (13)	N	Y	N
14a	I	Depression	15	7	Y (8)	N	N	N
14b*	I	Suicide attempt	15	1				
15a	I	ODD	13	8	Y (11)	Y	N	N
15b*	I	ODD	14	3				
16a	P	ADHD, ODD	14	154	Y (8)	N	Y	Y
17a	I	ODD, ADHD	11	5	Y (11)	Y	N	N
18a	I	Major depressive disorder	15	7	Y (12)	Y	Y	N
18b*	I	Major depressive disorder	15	9				
19a	I	Homicidal ideation	11	12	Y (4)	Y	Y	Y
20a	I	Bipolar disorder	11	10	Y (7)	Y	N	N
21a	I	Trichotillomania/trichophagia	11	5	Y (5)	N	N	N
22a	I	Suicidal ideation	11	7	Y (9)	Y	N	Y
23a	I	Depressive disorder, ADHD	9	23	Y (8)	Y	Y	Y
23b*	I	Affective psychosis	9	UNK				
24a	I	Adjustment reaction	8	2	N	Y	Y	N
24b*	I	Conversion disorder	8	2				
25a	P	Behavior problems	4	3	N	N	N	N
25b*	P	Potential suicide attempt	9	4				
26a	I	Depression	15	UNK	Y (12)	Y	N	Y
27a	I	Bipolar disorder	13	4	Y (9)	Y	N	N
28a	I	Depression	10	7	Y (7)	N	Y	Y
28b*	I	Depression	10	7				
29a	I	Clinical depression	9	31	Y (9)	N	Y	Y
29b*	I	Clinical depression	9	UNK				
29c*	I	ODD	10	39				
30a	I	Depression, generalized anxiety disorder	12	10	Y (12)	N	N	N
30b*	I	Depression	12	7				
30c*	I	Suicide attempt	12	9				
31a	P	Depression	9	15	Y (8)	N	Y	N
32a	I	Depression	14	40	Y (9)	Y	Y	Y
32b*	I	Depression	14	3				

UNK indicates unknown; ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional defiant disorder.
* Duplicate responses for fixed values for subjects with multiple admissions.

the WITS population was restricted to children <7 years old. In the PACTG 219C sample, the marginally significant age effect in the unadjusted analysis disappears when age is included in a multivariate analysis that also includes knowledge of HIV seropositivity status. A likely explanation is that the older a child is, the more likely they are to know their HIV seropositivity status. This may explain the discrepancy in the findings between the PACTG 219C sample and the WITS population. It is important to note, however, that there were significant differences in design between the 2 populations with PACTG 219C focusing on psychiatric hospitalizations as opposed to emotional/behavioral problems.

Hein et al[12] reported increased psychiatric hospitalization rates among HIV-infected adolescents, compared with uninfected control subjects. The majority of infected participants in the sample had acquired HIV infection through high-risk behaviors, as opposed to perinatal exposure. It is possible that psychiatric manifestations may differ for these 2 populations, because the acute and chronic effects of HIV infection during neurodevelopment may predispose children with perinatally acquired HIV infection to specific mental illnesses. The association between HIV acquisition and psychiatric illness should be investigated more thoroughly.

Depression and behavioral disorders were the 2 most common reasons for psychiatric hospitalizations for the PACTG 219C cohort. The prevalence of mood disorders in the general pediatric population (specifically major depressive disorder, dysthymia, and cyclothymia or bipolar disorder) has been estimated at 2% for prepubertal children and 5% for adolescents.[30] Before puberty, similar rates of depression are observed for male and female subjects. However, adolescent and adult female subjects are more than twice as likely as male subjects to be affected.[31,32] With respect to behavioral disorders, prevalence estimates for attention-deficit/hyperactivity disorder vary from 3%–5% to 8%–17% for community samples to 30%–50% for child psychiatric outpatients and 40%–70% for child psychiatric inpatients. The rates for male and female subjects differ by a 4:1 ratio.[31,32] The rates of oppositional defiant disorder are higher among prepubescent male subjects. However, the rates for male and female subjects are equal after puberty.[33]

Evidence suggests that affective and behavioral disorders may be precursors to more severe psychopathologic conditions, eg, bipolar disorder and suicide. Weissman et al[34] reported that, in a 10- to 15-year follow-up study of adolescents diagnosed with major depression, 7% committed suicide some time later. The depressed adolescents were also 5 times more likely to have attempted suicide in the follow-up period, compared with age-adjusted control subjects without depression.[34] Controlled studies of suicide suggest similar risk factors for both genders.[35] Shaffer et al[35] reported a 12-fold increased risk of suicide among adolescent female and male subjects with a diagnosis of major depressive disorder. Disruptive behavior disorders increased the suicide rate for male subjects 2-fold.

In 2000, suicide was the third leading cause of death for subjects 10 to 24 years of age.[36] Between 1980 and 1997, the rate of suicide among persons 15 to 19 years of age increased 11%. Among non-Hispanic, black, male subjects, the rate increased 105% during this period. Among persons 10 to 14 years of age, the rate increased 109%.[37] Therefore, the higher rate of depression found for our cohort of children and adolescents infected with HIV suggests that clinicians should be alert for potential increased risks of suicide in this population.

Of the 32 children with psychiatric hospitalizations in the PACTG 219C cohort, 15 (47%) experienced multiple admissions. The phenomenon of multiple hospitalizations has been observed in the general population. Studies found that 20% to 40% of children with depression experienced relapse within 2 years and 70% experienced relapse by adulthood.[38–40]

Disease status, as measured by CD4 percentage and viral load, was not significantly associated with first psychiatric hospitalizations. Zorrilla et al[41] reviewed 19 studies examining the relationship between depressive symptoms and HIV progression and failed to find a relationship except for an increase in the reports of disease symptoms. The HIV-infected children in PACTG 219C experienced substantial exposure to all 3 classes of antiretroviral drugs before their first psychiatric hospitalizations. All had been exposed to a nucleoside reverse transcriptase inhibitor, 81% had been exposed to a protease inhibitor, and 47% had been exposed to a nonnucleoside reverse transcriptase inhibitor. These percentages are comparable with the percentages of patients in the overall cohort who have received each class of drug. For protease inhibitors and nonnucleoside reverse transcriptase inhibitors, we found no significant association between use of the drugs and the risk of psychiatric hospitalization. Because all subjects had received a nucleoside reverse transcriptase inhibitor, it was not possible to evaluate an association with that class of drugs.

The median time spent in the hospital for the PACTG 219C participants was 7 days. This was less than the mean length of stay in the general pediatric population, which averaged 12.4 days for mental disorders. There may be multiple complex reasons for this observation of a shorter length of stay for psychiatric admissions among children with HIV infection. Children with HIV may be released earlier because of the comprehensive care programs provided at PACTG sites and support systems developed by the pediatric care team, which allow early discharge to home care. Alternatively, complications of the HIV illness and the cost of treatment may discourage lengthy hospitalizations. Whether early release contributes to the recidivism rate of nearly 50% is unclear. Associations between the length of stay and rehospitalization should be investigated more thoroughly.

As with any observational study, there is a degree of confounding by severity, insofar as the children with the most severe mental disorders may not be able to meet the demands of the study, ie, neuropsy-

chologic testing and other lengthy clinical assessments, and thus may not be enrolled in PACTG 219C or, if enrolled, may be lost to follow-up monitoring. These reported rates are specific to the PACTG 219C cohort and may underestimate rates in the broader HIV-infected pediatric population.

As these children live longer with chronic HIV infection, the incidences of psychiatric hospitalizations and major psychiatric illness may increase. Screening for warning signs of psychiatric illness should be provided within the context of comprehensive primary care, particularly at important points of transition in a child's life. Parent- and self-report instruments can be used to identify and monitor emotional and behavioral problems. Referrals for mental health services should be provided when psychiatric issues become apparent, and risk factors for treatment failure, such as an unsafe family/home environment and a family history of mental illness, should be recognized. Additional research is needed to adequately characterize the complex etiologic factors for severe psychiatric symptoms associated with HIV infection among children and adolescents, so that the quality of life matches the marked gains observed in survival times.

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Hayes; Johns Hopkins University: N. Hutton and S. Marvin; University of Maryland: P. Vink and K. Fore; Baylor College of Medicine/Texas Children's Hospital: W. Shearer and K. Owl; Chicago Children's Memorial Hospital: R.Yogev and D. Fonken-Cloutier; Cook County Hospital: K. Boyer and E. Gliwa; University of Chicago Children's Hospital: J. Englund and P. Lofton; Women and Children's HIV Program: D. Johnson and B. Wolfe; Columbia Presbyterian Medical Center: A. Gershon and M. Donahue; Incarnation Children's Center: A. Gershon and P. Miller; Cornell University-New York Presbyterian Hospital: A. Gershon and A. Monroe; University of Miami: G. Scott and P. Bryan; Jackson Memorial Hospital: M.J. O'Sullivan and P. Bryan; New York University-Bellevue Hospital: W. Borkowsky and N. Deygoo; University of California, San Francisco-Moffitt Hospital: D. Wara and D. Trevithick; San Francisco General Hospital: D. Wara and M. Shannon; Children's Hospital of Oakland: A. Petru and T. 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Mrus and N. Boosveld; State University of New York-Brooklyn: E. Handelsman and D. Swindell; North Shore University Hospital: S. Pahwa and L. Rodriquez; St. Christopher's Hospital: M. Bagarazzi and R. Buie; Oregon Health Sciences University: P. Lewis and R. Croteau; Bronx Lebanon Hospital Center: S. Bakshi and C. Nubel; St. Luke's/Roosevelt Hospital Center: S. Arpadi and R. Warford; Cornell University: R. Johan-Liang and K. O'Keefe; University of Illinois: K. Rich and J. Camacho; Emory University Hospital: S. Nesheim and R. Dennis; San Juan City Hospital: E. Jimenez and M. Thurin; Children's Hospital of the King's Daughters: T. Rubio and D. Sandifer; University of Medicine and Dentistry of New Jersey-Robert Wood Johnson: S. Gaur and L. Cerrachio; Ramon Ruiz Arnau University Hospital: W. Figueroa and E. Reyes; Medical College of Georgia: W. Foshee and S. Cobb; University of South Alabama: M. Mancao and J. Bebawy; The Medical Center: R. Stauffer and D. 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Salbenblatt; North Broward Hospital District: A. Puga and D. Cruz; University of Florida-Gainesville: J. Sleasman and C. Delaney; Palm Beach County Health Department: G. Stiebel-Chin and P. Vann; Vanderbilt University Medical Center: G. Wilson and P. Bender; Earl K. Long Early Intervention Clinic: R. VanDyke and M. Cowie; Sacred Heart Children's Hospital/Children's Medical Services of Florida; St. Louis Children's Hospital: G. Storch and L. Stiffler; Robert Wood Johnson AIDS Program: S. Gaur and L. Cerrachio; and University of South Florida: P. Emmanuel and C. Graisbery.

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