

Psychopathology in the Children of Depressed Parents: Direct Interview Studies

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In 1982, at the American Psychopathological Association's annual meeting, which was devoted to studies of childhood psychopathology and development, Orvaschel (18) presented an excellent scholarly review of the current status of research on parental depression and child psychopathology. She identified six studies of the children of affectively ill parents. Most of the studies included fewer than 40 children. Moreover, these studies showed rates of depression in children that ranged between 7% and 85%. This wide range in rates was attributed to methodologic differences. The studies varied by informant (child about self or parent about child), by diagnostic method (symptom scale or diagnostic interview), by diagnostic criteria (Weinberg, Feighner, or Research Diagnostic Criteria), by methods of calculating rates (the family unit or the number of children affected), and by type of affective illness in the parent (unipolar or bipolar).

In 1983, Beardslee et al. (1) published an independent review of the field which identified a number of additional studies of children of depressed parents using retrospective designs. Both Beardslee et al. (1) and Orvaschel and co-workers (18,22) reached identical conclusions. The methodologic limitations of the studies conducted at that time were considerable. However, the findings all pointed in the same direction. The children of affectively ill parents were at a significant risk for developing psychopathology, particularly depression.

The investigators of these earlier studies should be congratulated, because they conducted their research before structured diagnostic assessments of children's psychopathology were widely available and when the predominant belief of the previous decade was that children were not emotionally or developmentally capable of becoming depressed.

Since the publication of the reviews by Orvaschel (18) and Beardslee et al. (1,2), the field has improved considerably. Several diagnostic scales for children have been tested (21). There is evidence from family and clinical studies that depression does occur in children (15,16,24), that it is common in adolescents (11,14,26,30,34), and that it also does occur in prepubertal children (12,16).

There are now five well-designed studies of children (ages 6 years and older) of depressed parents (3,9,13,19,34). There is also one direct observational study of the infants and toddler offspring of bipolar parents (5). These studies are ongoing and have only recently begun to yield data. Most of the data are still unpublished. All five studies of children aged 6 years and older used structured diagnostic assessment of the parents and of the children. The children have been directly interviewed on the Diagnostic Interview for Children and Adolescents (DICA) (13), Diagnostic Interview Schedule, Children's Version (DISC) (3), or the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Epidemiologic Version (K-SADS-E) (9,19,29).

Over 800 children of depressed or of control parents have been studied. The parent samples have come from treatment clinics as well as the community, so that a range of severity of major depression in the parents is represented. A range of parent control groups has also been included: bipolar or medically ill parents (9); parents with Generalized Anxiety Disorder (GAD) (3); normal controls (3,9,19,29). Many of the studies have also included family history (9,13,19) or direct interview to determine the psychiatric status of the child's first- and second-degree relatives (28).

This chapter will describe our initial findings from a direct interview study of 220 children, ages 6 to 23 years, of parents with major depression as compared to the children of a normal, never psychiatrically ill control group. The findings will be discussed in the context of the emerging data from these most recent high-risk studies of children of affectively ill parents.

DESIGN

The data derive from a high-risk study of offspring which was part of a family case-control design. Information was obtained on the psychiatric status of parents' first-degree relatives, i.e., the first- and second-degree relatives of the offspring (Fig. 1). Since the lifetime risk of illness in relatives is obtained on the basis of the subject's recall of their lifetime course of illness, the study is technically a retrospective cohort design. [See Weissman et al. (31) for discussion of various epidemiologic designs.] The children are also being followed longitudinally over a 2-year period. Thus far, only data on the children from the first wave of interviews are available. Also, data on the other relatives will not be presented here.

Selection of Families

The proband parents derive from the Yale Family Study of Major Depression (28). Ninety-one (87.5%) of the 104 eligible families with children between the ages of 6 and 23 years agreed to participate. The 12.5% of families who refused to participate were equally divided between depressed and normal families. Sixty-

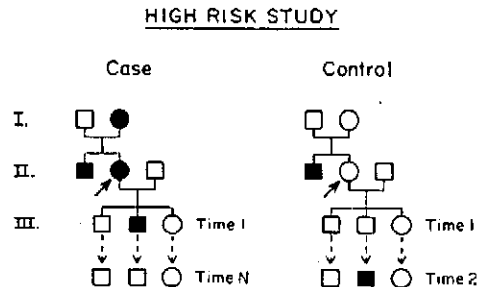


FIG. 1. Design of a case-control, high-risk longitudinal study embedded in a family study.

five couples with 153 children in which either one or both parents had a history of a treated major depression were included. Major depression was defined according to Research Diagnostic Criteria. We also required 4 weeks' duration of symptoms and impairment in a major role. The rates of major depression in children are for these stricter criteria unless indicated. Parents were rarely acutely ill when interviewed for this study, but most had been treated by us at the Depression Research Unit during a past acute depressive episode.

The normal controls were 26 couples with 67 children in which neither parent had a history of major depression or any other psychiatric disorder. This sample, originally identified in a longitudinal community survey in New Haven, Connecticut between 1967 and 1975, had reported no history of psychiatric illness or treatment based on at least five direct interviews over this period (32). The normals were also reinterviewed at the beginning of this study to determine their clinical status. All of the probands were white and were group-matched by age and sex.

Assessments

Direct interviews were obtained from 83% of the eligible children and from a parent for 97% of the children. In all but six cases the parent interviewed was the biological mother. Interviewers were M.D., Ph.D., and master's-level mental health professionals with a minimum of 4 years' experience in child assessment and/or treatment. The interviewer of the child and of the mother about the child was blind to the diagnostic status of the child's parents. Similarly, the interviewer of the parent was blind to the diagnostic status of the child and any previous psychiatric data on the parents. The interviewers received approximately 30 hr of training in research assessments during which diagnostic reliability was achieved using videotaped interviews. Additional checks on interrater reliability were made by the field supervisor during study interviews.

Mothers were asked to provide detailed information, in a structured format, about (a) prenatal, birth, and postnatal events, (b) their own and the child's medical and medication histories, and (c) the child's developmental history, using an interview developed and tested in other studies (7,8,10).

Children were given the Peabody Picture Vocabulary Test, Form M (6), and those who were under 17 years of age also completed the vocabulary and block-design subtests of the Wechsler Intelligence Scale for Children—Revised Version (WISC-R) (27).

The psychiatric diagnostic assessment of the children was made using the K-SADS-E (4,20), which is a widely used research instrument for obtaining lifetime diagnoses in children, according to the American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edition (DSM-III), for most of the major Axis I disorders (8,18).

Child Psychiatrist Best-Estimate Diagnosis

As in the adult sample, a best-estimate diagnostic procedure was employed for making the final diagnosis of the child (17). A child psychiatrist and a psychologist, who had not been involved in the interviewing process, reviewed all sources of information and independently assigned a diagnosis. Discrepancies in diagnoses by the independent evaluators were resolved by arriving at a consensus. The initial level of agreement between the two best-estimators on child diagnosis was 83%.

To further establish the reliability and validity of the best-estimate procedure, a second child psychiatrist reviewed all available information on 38 randomly selected children and made best-estimate diagnoses. Agreement between psychiatrists on child's diagnosis was excellent, with kappas as follows: major depression, 0.89; any attention-deficit disorder, 0.87; any conduct disorder, 0.93; any anxiety, 0.69; any substance abuse, 0.92; and any diagnosis, 1.0.

RESULTS

Age and Sex of Children

Two hundred and twenty children (105 boys and 115 girls) were studied, among whom 35 were 6 to 11 years old, 92 were 12 to 18 years old, and 93 were 19 to 23 years old. The mean age was 17 years. There were no significant differences in the age or sex of children with respect to the clinical status of the parents (Table 1).

Demographic Characteristics of Families

The children of depressed and normal parents were obtained from demographically comparable families. The groups did not differ significantly with respect to the parents' ages, number of marriages, education, current marital status, religion,

TABLE 1. Age and sex of children with respect to clinical status of parents

Age (years) and sex of children	Clinical status of parents		Total
	One or both parents depressed [N (%)]	Neither parent depressed [N (%)]	
Boys			
6-11	17 (11.1)	3 (4.5)	20
12-18	24 (15.7)	15 (22.4)	39
19-23	33 (21.6)	13 (19.4)	46
Girls			
6-11	9 (5.9)	6 (8.9)	15
12-18	37 (24.2)	16 (23.9)	53
19-23	33 (21.6)	14 (20.9)	47
Number of children:	153	67	220
Number of families:	65	26	91

social class, or number of children in the family. More than 30% of the parents came from professional and upper-middle-class families, and over 80% had at least a high school education and were currently married.

Paranatal Histories of Children

Of the 64 items included in the portion of the self-administered report that mothers completed about prenatal, birth, and postnatal events for each of their children, there were eight significant differences ($p < 0.05$) in the reports of mothers from the depressed and nondepressed families. Mothers from depressed families were younger when their children were born and reported fewer previous miscarriages. They accounted for all 11 reports of medical problems during pregnancy and also reported that they took more medications during pregnancy. Mothers in the depressed families were found not only to have taken more medication during more of their pregnancies than did mothers from the normal families (20.6% vs. 9.2%) but also to have taken a wider variety of medications. In addition to the antiemetics and diuretics reported by both groups of mothers, mothers in the depressed families reported taking sedatives, tranquilizers, thyroid supplement, diethylstilbestrol, other unspecified hormones, and unspecified pills to prevent excessive weight gain.

Mothers from depressed families also reported more adverse perinatal events, including the use of mid- or high forceps ($p < 0.05$), infant's weak or abnormal cry at birth ($p < 0.05$), and the infant's not breathing for 1 min or more at birth ($p < 0.05$). They also reported that their children were less active and strong during the first month ($p < 0.05$).

Developmental Landmarks and Health of Children

The children of depressed parents were described by their mothers as having been significantly delayed in being able to sit without assistance and in completing bowel training as well as both day and night urinary training (Table 2). However, the children of normal controls were described by their mothers as having been more difficult to manage as infants.

Reports of convulsions in 11 children all came from depressed families. Six of these seemed to be febrile convulsions, and three were isolated seizures following accidental head injuries. Two cases of continuing epilepsy requiring medication were reported: One was idiopathic, whereas the other was secondary to an astrocytoma.

Not shown here, nine (5.9%) of the children of depressed parents were said to have suffered a head injury, and three injuries were serious enough to require hospitalization. Only one child (1.5%) from the normal group suffered a head injury, and this was a minor sports accident not requiring hospitalization. Although these differences in rates did not reach statistical significance, they are of interest in relation to the findings regarding seizures.

Children of depressed parents were more frequently hospitalized for a wide variety of major and minor surgical procedures; 54 (35%) children from depressed families versus 14 (21%) children from normal families were hospitalized for surgical procedures. In both groups, the majority of procedures were relatively routine (e.g., tonsillectomies, appendectomies, and grommet insertions).

TABLE 2. Children's developmental landmarks and health history with respect to clinical status of parents

Children's status	Clinical status of parents		p-Value
	One or both parents depressed	Neither parent depressed	
Developmental landmark	Mean age (months)	Mean age (months)	
Sit without assistance	6.2	5.7	$p < 0.05$
Bowel training completed	25.8	21.7	$p < 0.01$
Day urinary training completed	24.9	20.2	$p < 0.001$
Night urinary training completed	32.9	23.9	$p < 0.01$
Health history	Cases (%)	Cases (%)	
Difficult to manage as an infant	2 (1.6)	6 (9.2)	$p < 0.05$
Convulsions, seizures, epilepsy	11 (7.2)	0 (0.0)	$p < 0.01$
Operations requiring hospitalization	54 (35.3)	14 (20.9)	$p < 0.01$

All three cases of major surgery, resulting from "accidents," occurred in the children of the depressed parents. Two of these episodes involved self-inflicted gunshot wounds, whereas the third was a below-the-knee amputation resulting from an automobile accident.

I.Q., School History, and Performance

There were no significant differences between the I.Q.s of the children of depressed and normal parents as measured by the WISC-R vocabulary and block-design subscales (27) or by the Peabody Picture Vocabulary Test (6) (Table 3). Discrepancies between vocabulary and block-design scores for each child were also calculated, and these did not differ between groups.

The children of depressed parents were reported to have entered nursery school or day care at an earlier age ($p < 0.01$). They also had more school problems, including special classes for math ($p < 0.05$) and for attention problems ($p < 0.05$). Although the significance is only marginal ($p < 0.10$), 14 (9.2%) of the children from depressed parents and only two children (3%) from normal parents were described by educational or health professionals as having learning disabilities. Five of the 14 learning problems in the children of the depressed parents were sufficiently severe to require special education. Neither of the two reported learning problems in the children of the normal controls required treatment or special education and were described as reading comprehension problems.

TABLE 3. I.Q. and school history and performance of children with respect to clinical status of parents

	Clinical status of parents		p-Value
	One or both parents depressed	Neither parent depressed	
I.Q. scores, mean (S.D.)			
Vocabulary, WISC-R ^a :	107.4 (26.8)	111.8 (24.6)	
Block design, WISC-R:	110.2 (24.5)	121.6 (26.3)	
PPVT ^b :	99.0 (14.9)	101.8 (13.5)	
School history and performance			
Age (months) began nursery or day care:	37.6 (10.0)	46.2 (11.6)	$p < 0.01$
Special class for math problem [cases (%)]:	9 (7.0)	0 (0.0)	$p < 0.05$
Special class for attention problem [cases (%)]:	7 (5.7)	0 (0.0)	$p < 0.01$
Described as having learning disability [cases (%)]:	14 (9.2)	2 (3.0)	$p < 0.10$

^a WISC-R, Wechsler Intelligence Scale for Children—Revised.

^b PPVT, Peabody Picture Vocabulary Test.

Rates of DSM-III Disorders and Suicide Attempts in Children

Table 4 shows the rates of psychiatric disorders in children based on the child psychiatrist's best estimate of all available information on the child. The children of depressed parents were at significantly higher risk than were the children of normal parents for major depression, anxiety disorder, substance abuse, or any disorder, as well as mean number of diagnoses per child. The relative risks for these disorders, which differed significantly in children with respect to proband group, were 2.1, 2.2, 1.6, and 1.3, respectively. Adjusting the relative risk for age and sex of child did not change the risk, since the children did not differ significantly with respect to age and sex and proband group.

The children of depressed parents, when compared with the children of normal controls, reported a history of more suicidal gestures or attempts (i.e., 8.6% and 3.3%, respectively; $p < 0.05$).

Treatment

The children of depressed parents received treatment for psychiatric or behavioral problems significantly more frequently than did the children of normal controls (39.2% versus 17.9%; $p < 0.05$). Two children of depressed parents had been placed in a residential treatment facility for behavior problems. In both cases the children had multiple diagnoses, including major depression. Four of the 153 children of depressed parents and none of the 67 children of normal controls were hospitalized for psychiatric disorders. Three of the four hospitalizations were

TABLE 4. Lifetime prevalence of DSM-III diagnosis in children based on child psychiatrist's best estimate with respect to proband parent group

DMS-III diagnosis in children	Proband parent group		Relative risk and p -value
	One or both parents depressed (rates/100)	Neither parent depressed (rates/100)	
Major depression	28.1	13.4	2.1, $p < 0.05$
Dysthymia	20.9	14.9	
Attention-deficit disorder	6.5	4.5	
Conduct disorder	22.9	13.4	
Anxiety disorder	39.9	17.9	2.2, $p < 0.05$
Substance abuse	14.4	8.9	1.6, $p < 0.10$
Any diagnosis	75.8	56.7	1.3, $p < 0.05$
Mean number of diagnoses	2.4 (2.5)*	1.5 (1.9)*	1.6, $p < 0.01$

* Numbers in parentheses represent the S.D.

for serious suicide attempts. In all four cases, the children met criteria for multiple diagnoses, including major depression and anxiety disorders.

Onset of Major Depression with Respect to Sex of Child and Proband Group

Figure 2 shows the age-specific incidence rates of major depression with respect to (a) sex of child and (b) proband group. These rates can be interpreted as the conditional probability of onset of major depression in a specific age interval, given that an individual has been free of the disorder prior to entering this interval. The peak age of onset of major depression in the children of normal proband parents is after age 15 years for both boys and girls. However, in the offspring of depressed proband parents the onset occurs earlier, around age 12 years for both boys and girls. The age-specific rates for the age interval 20–23 years have not been presented because of the small numbers of children remaining at risk beyond age 20 years (numbers range from 6 to 13 years).

Table 5 shows that age of onset of major depression, using the stricter criteria of 4 weeks' duration and social role impairment, is lower in both boys and girls of depressed parents (overall mean age of onset, 12.8 years) as compared to normal proband parents (overall mean age of onset, 15.7 years).

When the less strict DSM-III criteria for major depression, i.e., 2 weeks' duration and no requirement of social role impairment, were used, the results were similar.

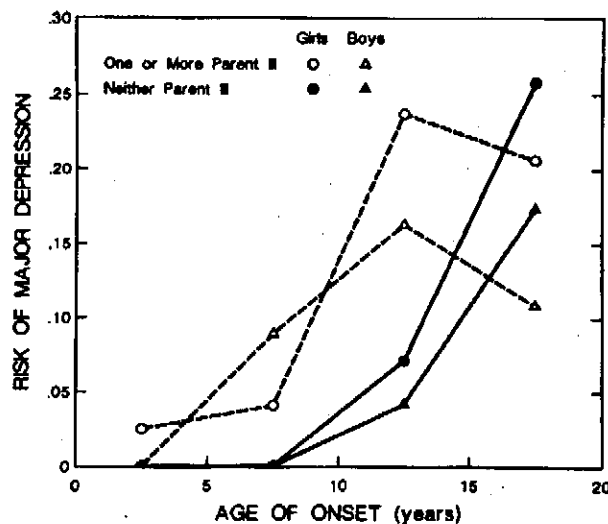


FIG. 2. Age-specific incidence rates of major depressive disorder with respect to sex of child and number of parents with major depressive disorder.

TABLE 5. Mean age of onset of major depression in children with respect to proband parent group

Sex of child	Proband parent group	
	One or both parents depressed [mean age (S.D.)]	Neither parent depressed [mean age (S.D.)]
Girls	12.4 (3.9)	15.8 (2.7)*
Boys	13.4 (4.3)	15.3 (3.1)
Mean:	12.8 (4.1)	15.7 (2.6)*

* $p < 0.05$.

The Nature of Depression in Children

The symptom profiles for 21 symptoms of depression in the children were compared with respect to proband group, age of onset of depression, and sex of child. For the comparison by proband group, only one significant difference was found. The children of depressed proband parents reported significantly more loss of pleasure when depressed. However, there were no differences in sleep and appetite disturbance, guilt, etc. Only three differences in symptom profile with respect to age of onset (onset age < 15 years versus onset ages ≥ 15 years) were found. The children with later onset of depression significantly more often reported weight loss, initial insomnia, and boredom than did those with earlier onset of depression. There was only one significant difference between boys and girls in terms of symptoms reported. The girls significantly more often reported feeling worse in the morning.

Comorbidity of other psychiatric disorders in the depressed children of depressed and normal proband parents was also examined. There were no significant differences in the type of additional disorders among the children of either proband group. In both groups of depressed children, the most frequent additional diagnoses were (in decreasing frequency) anxiety disorder (42%), dysthymia (34%), conduct disorder (27%), and substance abuse (20%).

DISCUSSION

The major findings of this study are an increased prevalence of major depression as well as a variety of other medical problems, including increased head injuries, seizures, and accidents in the children of depressed as compared to normal proband parents. There is a low frequency and an equal sex ratio of major depression before age 10 years. Overall, there is a marked increase in the incidence of major depression around age 15 years in girls. The age of onset of major depression is

significantly earlier in both the boys and girls of the depressed (mean age 12.8 years), as compared to those of the normal (mean age 15.7 years), proband parents.

Children of depressed parents, as compared to children of normal ones, are at significantly increased risk for major depression, substance abuse, and multiple diagnoses. They have poorer overall functioning, more school problems, and more psychiatric treatment, including hospitalization for serious suicide attempts.

Recent Studies of Children of Depressed Parents

Table 6 describes four current studies that will form the basis of information on children of depressed parents. A fifth study by Breslau et al. (3) was not designed specifically to estimate familial aggregation of psychiatric disorders but, rather, was designed to determine child disability and its effect on families. This study will also provide some information on relative risk of psychiatric illness in children of depressed mothers. However, because only annual, and not lifetime, prevalence is reported in the Breslau et al. (3) study, rates are not directly comparable with the other studies.

More than 350 offspring of depressed parents and 450 offspring of controls have been studied. A variety of control groups have been included, most commonly the children of never psychiatrically ill parents. However, children of bipolar parents, parents with an anxiety disorder, and medically ill parents have also been studied. All these studies have included (a) a structured diagnostic interview of children (K-SADS, DISC, DICA) and of at least one parent, (b) diagnoses of children made blindly to their parents' clinical status, (c) DSM-III criteria for children, and (d) consensus diagnosis of child made on all available data.

In all but the Breslau et al. (3) and Hammen et al. (9) studies, family history is available on the child's first- and second-degree relatives, and attention has been paid to the spouse's diagnosis. Three of the studies include a follow-up assessment.

These studies will provide the basis of our understanding of the familial aggregation of illness in the offspring of depressed parents over the next few years. All of the studies confirm earlier reports that offspring of depressed patients are at increased risk of major depression as well as of a variety of other disorders.

A range of diagnoses in children is represented in Table 7. The rates of any diagnosis in children are quite high and range from 50.0 to 75.8/100. The most common diagnoses in children, in addition to major depression, are anxiety disorder and substance abuse, suggesting that major depression may not be specific to children of depressed parents. However, these studies have not yet examined assortative mating, cross-mating, or comorbidity in parents.

Between studies, the range of rates of major depression in children is still wide (15/100 to 41/100), although these variations are not nearly as great as in previous studies. The lowest rates in children are obtained from the Orvaschel et al. (19) study. In the Breslau et al. (3) study, only annual rates of illness in the

TABLE 6. Characteristics of recent studies of children of parents with major depression

Study (reference)	Cases (N children)	Controls (N children)	Age of children (years)	Diagnostic instrument	Consensus diagnoses	Family information	Follow-up
Orvaschel et al. (19)	One or both parents with MDD* (N = 61)	Neither parent ill (N = 45)	6-17	K-SADS-E	Yes	History of child's first- and second-degree relatives	18 months
Keller et al. (13)	One or both parents with MDD (N = 72)	Neither parent ill (N = 24)	6-19	DICA	Yes	History and interview of child's first- and second-degree relatives	No
Hammen et al. (9)	One or both parents with MDD (N = 19)	One or both parents with BP (N = 12) One or both parents with chronic medical illness (N = 18) Neither parent ill (N = 35)	8-16	K-SADS	Yes	Interview of both parents	Every 6 months for 3 years
Breslau et al. (3)	Mother with MDD (N = 56)	Mother with anxiety disorder (N = 101) Mother not ill (N = 174)	8-23	DISC	No	Interview of mother	No
This study	One or more parents with MDD (153)	Neither parent ill (N = 67)	6-23	K-SADS-E	Yes	History and interview of child's first- and second-degree relatives	2 years

* MDD, major depressive disorder.

TABLE 7. Comparison of rates of illness in children in recent studies of children of parents with major depression

Study (reference)	Rates/100 in children ^a				
	Major depression	Attention- deficit disorder	Any anxiety disorder	Any substance abuse	Any disorder
Keller et al. (13)	24.0	10.0	16.0	13.0	65.0
Orvaschel et al. (19)	15.0 (21.0) ^b	20.0	20.0	—	41.0
Hammen et al. (9)	41.0	10.0	21.0	26.0	74.0
Breslau et al. (3)	16.0	—	21.0	—	—
This study	28.1 ^c	4.8	39.9	14.4	75.8

^a All rates are lifetime prevalence, except for the Breslau et al. study, which included only 1-year prevalence rates.

^b Rates for any affective disorder.

^c Rates for major depressive disorder was based on stricter criteria of 4 weeks of symptoms and social role impairment. If criteria of 2 weeks of symptoms are used, the rates are 35/100.

children are reported, and the parents are mildly ill subjects drawn from a community sample. The highest rates are from the Hammen et al. (9) study, which included only 19 children whose mothers had chronic and recurrent depression. Keller et al. (13) showed that chronicity of depression in parents increased the risk of disorder in children.

CONCLUSION

The designs of the studies do not allow us to determine if genetic factors are involved in the transmission of psychiatric disorders between parents and children, nor do they permit us to examine the specificity of the findings with regard to major depression. The problems we found could be a reflection of stress in ill families or inadequate parenting among ill mothers and may not be specific to major depression. We do not yet understand the significance of the paratal and the developmental problems in the children of depressed parents found in our study. Although there were significant differences between groups, some of the differences, such as reported time for day and night urinary training and for bowel training, may not have clinical significance. Reporting bias may account for some of the problems reported by the mothers. It should be noted, however, that the mothers' clinical status may not account for overreporting. Although information was obtained from the mothers, in about 40% of the cases the depressed parent was the father. Moreover, the parents were rarely in an episode of depression when they were being interviewed, and information was also obtained from the children directly.

Whatever the mechanism, it seems reasonably well established that the offspring of depressed parents are at increased risk for major depression as well as for a host of other health problems. These findings clearly have implications for secondary prevention in children. They suggest that detailed inquiry into the psychiatric and health status of the offspring of depressed parents should be made by professionals treating the depressed parents. Although information on the efficacy of treatment of depressed young children is not extensive, attention by mental health professionals and family members to potential health problems in these children may lead to early case-finding. Alternately, a child presenting with depression and/or multiple school problems, social problems, and/or accidents may be the child of a depressed parent. Treatment of the parent's depression may have an impact on the health of the child.

Our findings highlight the importance of parental depression as a risk factor for a variety of health problems in children. Major depression is a highly prevalent disorder in women, and, although somewhat less so in men, it may be increasing (25,33). There are many treatments now available, both pharmacotherapy and psychotherapy, the efficacy of which has been established through well-designed clinical trials. Direct inquiry into the past and current psychiatric status of parents, as well as children, may be a first step toward preventive intervention. The nature of the children's illness and their continuity into adulthood require longitudinal follow-up of the children. The studies that are under way will provide the information.

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DISCUSSION

Dr. Taylor: Michael Taylor from the Chicago Medical School. I was struck by your data on the antecedents of illness, i.e., the gestational, perinatal, and other problems of the group. You had comparisons between offspring of depressives and offspring of normal probands. Do you have any information regarding the offspring of depressives who did or did not become ill. Is there a particular relationship between the antecedents of illness and the expression of depression or anxiety in those high-risk offspring?

The other question relates to the large prevalence of illness you report in the offspring of normal probands. As that figure is likely to be used as a normal proband group prevalence for genetic studies, how do you think that is going to affect our understanding of those studies?

Dr. Weissman: Well, in regard to the first question, what you are really, I think, asking about is main effects and interactions in a risk analysis. Priya Wickramaratne, Ph.D., a biostatistician with my group, is in the process of trying to examine these issues.

In regard to the high frequency of depression reported in the children of normals, it raises serious questions about the accuracy of reporting here. The longitudinal data will be useful to tell us about the stability, recall, and continuity of the depressions reported by the children.

Dr. Hirschfeld: Robert Hirschfeld from NIMH. Myrna, I was struck by the high prevalence. I think it was over 50%, of any psychiatric disorder in the children of parents without any psychiatric illness; I am impressed that you have done everything possible to ensure objectivity and replicability. I believe the data, and I am concerned about their implications. For example, if somebody has a psychiatric disorder, they presumably should be treated. Does that mean that over half of our children have a psychiatric disorder and should be treated, or is having a psychiatric disorder analogous to having a cold, a disorder 100% of our children have from time to time? I am wondering about your thoughts about that.

Dr. Weissman: Many of the depressions reported by the children are more like common colds. No. They probably shouldn't be treated, especially since we don't have good treatments.

Dr. Kramer: Morton Kramer from Baltimore. Will you determine the person years of life the child lived in the family of origin? For a child whose parents were divorced and who is in the custody of the mother, will you determine the years the child lived with mother alone and, if the mother remarried, the years the child lived in a family with a stepfather?

Dr. Weissman: Yes. We did find that divorce has a main effect for both the children of depressed and children of normals. It doesn't have a stronger effect in the children of depressed.

Dr. O'Connell: Ralph A. O'Connell from New York City. Myrna, I was particularly interested in your paper. We have been following a group of bipolar patients at St. Vincent's for 15 years. Drs. Mayo and Abright, and other colleagues are looking at them again. We have been impressed that the children who have early affective symptoms are the ones who also had developmental lags that you described, the late milestones, the hospitalizations for psychiatric and medical illnesses, poorer functioning in school, and drug abuse problems. So it seems that with the bipolar disorders, this comorbidity of medical and psychiatric disorders may also be present.

One other comment. We have found that, in trying to identify other factors which may be risk factors for affective disorders, there is a complexity and difficulty of separating out the cause and effect, as Dr. Dunner spoke of.

One particular finding which impressed us was that the children of our bipolars who were more symptomatic were the ones whose parents had had more hospitalizations during their earlier years. At first sight, this seems to be a contradiction of the usual assumption. However, in thinking about it, it seems that families who are better structured and able to have the parent hospitalized may actually represent the more stable families. So factors like hospitalization and treatment in a family may actually turn out to be positive signs of family health and structure and indicate reduced exposure to a nontreated episode. These complexities are very difficult and interesting.

The other problem that we are beginning to have is that the proband children who are now in their early twenties are very difficult to find in a long-term follow-up study.