

## **Childhood Depression: Familial Causes and Clinical Concerns**

By Jeff Link

### **History**

Today a number of researchers, including Joan Luby, a child psychiatrist at the University of Washington, recommend that children be screened for depression when they enter preschool. The latest research suggests that children may begin to show symptoms of depression as early as three to six years of age, making this time an ideal window for identification and clinical intervention.<sup>1</sup> But can children really be depressed at this age, and, if so, what are the causes? Is depression genetic? Environmental? What importance do maternal depression and life stresses have in mediating the clinical picture? Above all, how do we screen and treat children who exhibit signs of depression?

These questions are not new. Childhood depression, the naïve form of major depressive disorder (MDD), has been described in the psychiatric literature for decades—with much of the early research arising out of the meeting of the fourth Congress of the Union of Pedopsychiatrists in Stockholm in 1970.<sup>2</sup> Since then research has clearly established that children are capable of experiencing depressive states, though the symptoms of these states may not always be similar to those of adults.<sup>3</sup>

Historically, the psychoanalytic view held that children were too developmentally immature to have a fully advanced superego—and as a result, they had no way of directing negative feelings inward toward their own ego.<sup>4</sup> Emotions typically associated with depression appeared masked as “depressive equivalents,” such as conduct problems, somatic complaints, and school problems.<sup>5</sup> Other researchers believed depression occurred in children but assumed different clinical forms than in adults, appearing as “anaclitic” depression, where children separated from caregivers presented symptoms such as a sad, worried facial expression, which advanced through stages, from crying and screaming, to reduced babbling and physical activity, to dejection and withdrawal from the environment.<sup>6</sup>

In the 1980s, consensus emerged regarding the similarities between child and adult major depressive disorder, which is reflected in the DSM-III, DSM-IV, and ICD-9, 10, where no distinction is made between pre-pubertal and adult depression.<sup>7</sup> However newer studies reveal that the developmental nature of childhood depression is particularly important and that to accurately screen and identify children with childhood depression, the symptoms must be appropriately translated to the age of the child. In a recent issue of the *New York Times*,<sup>8</sup> Luby points out how anhedonia (the absence of joy in normally pleasurable activities) may appear in adults as a lack of libido, but will look very different in preschoolers, who may simply show a disinterest in playing with toys.

### **Symptoms**

So what exactly is childhood depression? A major component of clinical diagnosis is the determination of whether a pattern of emotional functioning occurs in severe enough form to result in impaired functioning. For instance, a typical child may throw tantrums with a great deal of anger and distress; however, tantrums in a healthy child progress through a highly structured sequence: symptoms spike quickly in intensity, subside into whining, and relax into the desire for emotional comfort.<sup>9</sup> The tantrums of depressed preschool-age children, on the other hand, are violent and can lead to self-injury, destruction, and verbal assault. They also have a longer recovery time.<sup>10</sup> Clinical and epidemiologic studies show that the average length of an episode is approximately 7 to 9 months; about 90 percent of Major Depressive Disorder episodes recur within 1 to 2 years after onset.<sup>11</sup>

Characteristics of childhood depression vary across the developmental stages, although they tend to be similar to adult depression and grow more similar as children age.<sup>12</sup> For instance a child who exhibits gaze aversion before age 3 may show periods of prolonged unhappiness from ages 6 to 8 followed by the picture of melancholy affect seen in adults. Similarly, infant separation anxiety before age 3 may evolve into school phobias in the elementary years and chronic anxiety in maturity.<sup>13</sup>

Children with depression may show symptoms of insomnia, guilt, brooding, apathy, inconsolable crying, weight and appetite changes, irritability, anhedonia, and deficits in memory and cognitive ability.<sup>14</sup> They are less likely than adults to make suicide attempts, but they are more likely to exhibit symptoms such as tantrums, complaints of stomach aches, and withdrawal from family and friends.<sup>15</sup> In a recent St. Louis study using the Preschool Age Psychiatric Assessment (PAPA) to evaluate the behavior of ethnically diverse 3 to 6 years olds, the markers of guilt and extreme fatigue were found to be highly specific markers for identifying depression in preschoolers.<sup>16</sup>

## **Prevalence**

Although exact prevalence is not known, Major Depressive Disorder is believed to be one of the most common mental health disorders in children. Current estimates show a prevalence of 2.5 percent in early childhood, 4 to 8 percent in adolescence, with at least 28 percent of children experiencing a major depressive disorder by age 19.<sup>17</sup> One meta-analysis found that 61 percent of children of parents with major depressive disorder will develop a psychiatric disorder during childhood or adolescence, and these children were four times more likely than those of healthy parents to develop an affective disorder.<sup>18</sup> Curiously, teens with asthma and diabetes are at a two-fold higher risk for anxiety and depressive disorders,<sup>19</sup> and a low level of respiratory sinus arrhythmia (RSA)—less variation in one's heart rate during a breathing cycle—is associated with increased risk for depression.<sup>20</sup>

Childhood depression can have serious long-term developmental consequences: poor school performance, more interpersonal conflict, and increased risk for adolescent substance abuse, delinquency, pregnancy, and suicide.<sup>21</sup> In fact, a recent 20-year

prospective study at the Harvard University Medical School found a modest correlation between a child's depressive symptoms at age 8 and age 19.<sup>22</sup> However, despite the severity of the long-term consequences and the apparent link between early and later symptoms, youth depression often goes undetected. Studies of youth suggest that primary care physicians accurately identify only about 20 to 30 percent of cases of anxiety and depressive disorders.<sup>23</sup>

### **Psychological Influences: Family Dynamics and Maternal Depression**

During the first five years of life children are emotionally vulnerable and rely on caregivers for comfort and guidance in coping with stress and conflict.<sup>24</sup> When there is a disorganized pattern of attachment between the mother and child, whether from negligent caregiving, marital conflict, mistreatment, or prolonged periods of parental absence, we often find the emergence of psychopathology.<sup>25</sup> Trouble in this early period is not just “bad” in the abstract sense of making a child unhappy. It may have biologic consequences in the form of functional impairment to neural, cardiovascular, and endocrine processes that affect the child's emotional development.<sup>26</sup>

One of the key factors emerging as a predictor of childhood depression is depression in the child's mother, particularly when onset occurs in the postpartum period.<sup>27</sup> Research suggests that depressed mothers may exhibit difficulty responding to an infant's crying, hostility in interacting with the child, and inability to be responsive to the child's actions—all of which may greatly affect the child's mental health.<sup>28</sup>

Parenting quality is just one of the possible links between maternal and child depression. Other theories explain the transference of depressive risk through genetics, suggesting the heritability of a temperament predisposed to depression, in which the child may show soft signs of depression such as shyness with strangers, sentimentality, and perseverance.<sup>29</sup> Another interesting line of research has to do with a possible epigenetic link—the occurrence in women of the MTHFR C677T genotype. This new research from the University of British Columbia, in Vancouver, shows that the appearance of this gene variant is associated with greater depression in pregnancy, which in turn influences gene-specific DNA methylation patterns in children.<sup>30</sup> In other words, children of mothers who exhibit this genotype are “re-programmed” through a complex set of brain adaptations that occur in the womb and may have lifelong health implications.

Currently, the Illinois Department of Public Aid, Public Health, Human Services, Children and Family Services, Department of Corrections, in collaboration with the Conference of Women's Legislators and the University of Illinois at Chicago Women's Health Program, is working to address perinatal depression with the goal of improving maternal and child outcomes. The program provides reimbursement to health care providers that conduct perinatal screening for depression as well as training workshops for primary care practitioners who wish to learn more about how to identify and treat perinatal depression.<sup>31</sup>

### **Biologic Influences**

We know the brains of depressed children are structurally quite a bit different than the brains of healthy children. For instance, in a retrospective chart review of depressed hospitalized children ages 3 to 17, Steingard and his colleagues found a significantly larger ratio of lateral ventricular volume to total cerebral volume and a smaller ratio of frontal lobe volume to total cerebral volume.<sup>32</sup> Birmaher reviewed literature on the hypothalamic-pituitary axis, the part of the brain that regulates stress, and found that an estimated 50 to 70 percent of depressed children showed elevated levels of corticoid activity.<sup>33</sup> Finally, Nolan et al. studied psychotropic naïve patients aged 9 to 17 with depression and found differences in the size of the prefrontal cortical volume in children who had a family history of depression as compared to those with non-familial major depression.<sup>34</sup>

Over time brain studies may reveal how depression differs from other forms of childhood mental illness. For instance, at least one recent study has identified the amygdala as a site of very different pathophysiologic reactions in children with depression as compared to those with anxiety.<sup>35</sup> In the study, children were given fMRIs while viewing photographs of fearful and neutral facial expressions. Blood oxygen levels were used to measure the amygdala's response in children with major depression as compared to those with anxiety disorders. Interestingly, the researchers discovered that children with depression showed a weakened amygdala response to the distressing photographs, while children with anxiety disorders demonstrated just the opposite reaction.

### **Screening for depression**

A major reason for the failure to identify young children with depression may be related to the difficulty clinicians have in accurately screening young children. Children may have difficulty recalling information related to their feelings of depression, and holes in memory may require assessment to be done with several different instruments and in conjunction with parents, school teachers, and other adults who can present a more comprehensive picture of the symptoms.<sup>36</sup> Screening is further complicated because face-to-face child psychiatric screening instruments may show weak concordance with international diagnostic systems such as DSM-IV.

The authors of a longitudinal Wisconsin study funded by the MacArthur Foundation and the National Institute of Mental Health suggest that screening at school entry may improve detection of children likely to benefit from early mental health intervention.<sup>37</sup> The researchers point out that the transition to school provides unique accessibility to the population of teachers and parents whose participation is required for initial assessment. Several methods for identification have been found effective in clinical and school settings.

- The Mood and Feelings Questionnaire –Short Form (MFQ-SF) and Childhood Anxiety Sensitivity Index (ASI) are two relatively brief questionnaires that performed well and showed high sensitivity and specificity for screening youth

age 11 to 17 for one or more DSM-IV anxiety or depressive disorders.<sup>38</sup> The MFQ-SF performed better than the ASI for screening major depression. Researchers from the University of Washington School of Medicine conclude that the use of these instruments may increase the accuracy of identification of mental health disorders in youth by primary care physicians.<sup>39</sup>

- The previously mentioned Wisconsin study recommends a short, 15-minute self-administered Teacher and Parent Questionnaire to screen children for mental health problems in kindergarten and elementary school.<sup>40</sup> Researchers found that children with the greatest impairments and physical health problems in grade 5 could be accurately identified by grade 1. With this approach, only the small percentage of children who screen positive are referred to mental health specialists for more intensive evaluations.

### **Assessment of depression in children**

Assessment of children with a positive screen for depression is difficult because clinical interviews with parents and children take a long time (at least 1.5 hours with Children's Interview for Psychiatric Syndromes (CHIPS) and up to four hours for instruments such as the Diagnostic Interview Schedule for Children (DISC) IV or the Interview Schedule for Children and Adolescents (ISCA).<sup>41</sup> Assessment then becomes complicated by the child's fatigue and distractibility as well as the complexity of having to integrate data from multiple instruments into a valid diagnosis. Interestingly, one French study suggests parents tend to better report problems of behavior and school and relational difficulties, while children provide more detailed psychological descriptions of fear, anxiety, obsessions and compulsions.<sup>42</sup> Unfortunately, the complexity of the screening may be a necessary evil to get the most accurate and helpful diagnosis.

Generally, assessment approaches fall into one of three forms: (1) the clinical / developmental interview; (2) the structured interview; and (3) the structured interview.<sup>43</sup>

- The clinical / developmental interview uses open-ended questions to discover the context in which depressive moods occur and to map a clinical narrative of the disorder across social, physical and cognitive domains. This also includes an assessment of cognitive development.
- The structured interview such as the Child and Adolescent Psychiatric Assessment<sup>44</sup> is typically done for research purposes and shows low reliability in younger age groups. An alternative method for assessing psychopathology in children age 10 or less are questionnaires with pictures based on DSM and puppet interviews.
- Self-rating scales are advised for use as follow-up instruments once a diagnosis has been made. Depression scales may show high sensitivity but low specificity.

The Children's Rating Scale and the Hamilton Rating Scale<sup>45</sup> for depression are two examples.

- Diagnostic interview-based instruments that show empirical reliability for younger children include the Preschool Age Psychiatric Assessment (PAPA), for ages 2 to 6,<sup>46</sup> and the Preschool and Early Childhood Functional Assessment Scale (PECFAS), for ages 3 to 7.<sup>47</sup> The Health and Behavior Questionnaire (HBQ) is a valid and reliable tool for assessment of preschooler's functioning as reported by parents, preschools teachers, and daycare staff.<sup>48</sup>

## **Treatment and Prevention**

Treating children with depression leads to a host of difficulties, from the problem of classifying early childhood symptoms into diagnostic categories, to controversy as to the validity of using antidepressants as a method of treatment. There is a wealth of evidence that depression can be successfully treated in adults with antidepressants. However, only one pharmacological agent, the SSRI Fluoxetine, is currently approved in the United States to treat depression in patients under the age of 18.<sup>49</sup>

Kids are not just small adults. David Bylund, a neuroscientist at the University of Nebraska, suggests that the norepinephrine nervous system does not fully develop in humans until adolescence.<sup>50</sup> Thus children's response to tricyclic antidepressants, which target the norepinephrine system, may have harmful side effects and be less effective than SSRIs that act on the serotonergic system. In any case, the use of antidepressants in children remains controversial as both tricyclic antidepressants and SSRIs show a high placebo response rate.

According to a recent review article published in the *Indian Journal of Medicine Research*,<sup>51</sup> psychotherapy in the form of play therapy, behavioral therapy, family therapy and cognitive behavioral therapy has been found useful in the management of mild to moderate depression. For any form of psychotherapy, the child's cognitive and emotional development should be an important concern. Play therapy and parental training, for example, are more appropriate for preschool-age children and cognitive behavioral therapy is more useful for older children and adolescents.

One of the best treatment strategies, interestingly enough, may be to provide educational services to parents whose depression puts their children at elevated risk. The Preventive Intervention Project at the Judge Baker Children's Center in Boston found that family-based cognitive therapy in school and clinical settings was effective when children were reaching adolescence.<sup>52</sup> The 2½-year study is the first and only longitudinal analysis of healthy children at high risk for developing depression attributable to their parent's mood disorder. Children played only a small part in the clinician intervention, but they demonstrated increased understanding of the illness and self-reported a decrease in internalizing symptoms. On the basis of these results, researchers conclude that the onset of depression in children can be deterred through clinical approaches that help children to

understand their parent's disorder, acquire resiliency, and come to view themselves as autonomous individuals separate from their parent's mental illness.

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<sup>1</sup> Luby, J., et al. (Jan 2009). The clinical significance of preschool depression: Impairment in functioning and clinical markers of the disorder. *J Affect Disord*, 112(1-3):111-119; Essex, M., et al. (May 2009). Screening for Childhood Mental Health Problems: Outcomes and Early Identification. *J Child Psychol Psychiatry*, 50(5):562-570.

<sup>2</sup> Malhotra, S. & Das, P. (Feb. 2007). Understanding childhood depression. *Indian Med. Res*, 125: 115-12

<sup>3</sup> Birmaher, B., et al. (1996). Childhood and adolescent depression: A review of the past 10 years. Part 1. *Am Acad Child Adolescent Psychiatry*, 35:1427-39; Bureau, J., Easterbrook M. & Lyons-Ruth, K. (2009). Maternal depressive symptoms in infancy: Unique contribution to children's depressive symptoms in childhood and adolescence. *Dev Psychopathol*, 21(2): 519-537; Malhotra, S. & Das, P. (Feb. 2007). Understanding childhood depression. *Indian Med. Res*, 125: 115-12; Nolan, C., et al. (2002). Prefrontal cortical volume in childhood-onset depression. *Arch Gen Psychiatry*, 59:73-9; Nolen-Hoeksema, S. et al. (1992). Predictors and consequences of childhood depressive symptoms a 5-yr longitudinal study. *J Abnormal Psychol*, 101:405-22; Steingard, R., et al. (1996); Structural abnormalities in brain magnetic resonance images of depressed children. *Am Acad Child Adolescent Psychiatry*, 35:307-11; Thomas, K., et al. (2001). Amygdala responses to fearful faces in anxious and depressed children. *Arch Gen Psychiatry*, 58: 1057-63.

<sup>4</sup> See note 2.

<sup>5</sup> Puig-Antich, J, et al. (1978). Pre-pubertal major depressive disorder. Pilot Study. *J Am Acad Child Adolescent Psychiatry*, 17:695-707. See note 3; Malhotra S.

<sup>6</sup> Ibid.

<sup>7</sup> See note 2.

<sup>8</sup> Pamela Paul, Can Prechoolers Be Depressed? *The New York Times*, Aug. 25, 2010.

<sup>9</sup> Luby, J., Cole, P. & Sullivan, M. (Dec 2008). Emotions and the Development of Childhood Depression: Bridging the Gap. *Child Dev Perspect*, 2(3):141-148.

<sup>10</sup> Ibid.

<sup>11</sup> McCauley, E., et al. (1999). Depression in young people. Initial presentation and clinical course. *J Am Acad Child Adolescent Psychiatry*, 31:600-6; Kovacs, M., et al. (1984). Depressive disorders in childhood. A longitudinal study of characteristics and recovery. *Arch Gen Psychiatry*, 41:643-9

<sup>12</sup> See note 2; See note 9.

<sup>13</sup> Ibid.

<sup>14</sup> See note 11, McCauley, E., et al.

<sup>15</sup> See note 2.

<sup>16</sup> See note 1.

<sup>17</sup> Lewinsohn P., Rhode P. (1998). Major Depressive disorder in older adolescents: prevalence, risk factors, and clinical implications. *Clin Psychol Rev*, 18:765-94. See note 9, Kovacs, M.

<sup>18</sup> Lovie, R. & Hodgins, S. (1994). Mental disorders among children with one parent with a lifetime diagnosis of major depression. In Hodgkins, S. et al. *A Critical Review of the Literature on Children at Risk for Major Affective Disorders*. Ottawa, Canada: Strategic Fund for Mental Health; 37-82.

<sup>19</sup> Shannon K., et al. (2007). Familial and temperamental predictors of resilience in children at risk for conduct disorders and depression. *Dev Psychopathol*, 19(3): 701-27.

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- <sup>20</sup> Katon, W., et al. (2004). The relationship of asthma and anxiety disorders. *Psychosom Med.*, 66:349-55.
- <sup>21</sup> Elgar, F. et al. (2004). Mutual influences on maternal depression and child adjustment problems. *Clinical Psychology Review*, 24:441-59; See note 3, Nolen-Hoeksema, S., et al.
- <sup>22</sup> See note 3, Bureau, J., Easterbrook M. & Lyons-Ruth, K.
- <sup>23</sup> Horwitz S., et al. (1992). Identification and management of psychosocial and developmental problems in community-based, primary care pediatric practices. *Pediatrics*, 89:480-85
- <sup>24</sup> Cole, P., Luby, J. & Sullivan, M. (2008) Emotions and the Development of Childhood Depression: Bridging the Gap. *Child Dev Perspect*, 2(3):141-48
- <sup>25</sup> Ibid.
- <sup>26</sup> Gunnar, M. (2007). The Neurobiology of stress and development. *Annual Review of Psychology*, 58:145-7; Pollak, S. (2005). Early adversity and mechanisms of plasticity: Integrating affective neuroscience with developmental approaches to psychopathology. *Development and Psychopathology*, 17:735-52.
- <sup>27</sup> See note 24, Cole, P., Luby, J. & Sullivan, M.
- <sup>28</sup> See note 3, Thomas, K., et al.
- <sup>29</sup> Elovainio, M., et al. (2004). Temperament and depressive symptoms: a population based longitudinal study on Cloninger's psychobiological temperamental model. *J Affective Disorder*, 83:227-34
- <sup>30</sup> Devlin, A. (2010). Prenatal Exposure to Maternal Depressed Mood and the MTHFR C677T Variant Affect SLC6A4 Methylation in Infants at Birth. [forthcoming]
- <sup>31</sup> Onunaku, N. (2005). *Improving Maternal and Infant Mental Health: Focus on Maternal Depression*. Los Angeles, CA: National Center for Infant and Early Childhood health Policy at UCLA.
- <sup>32</sup> See note 3, Steingard, R., et al.
- <sup>33</sup> See note 3, Birmaher, B., et al.
- <sup>34</sup> See note 3, Nolan, C., et al.
- <sup>35</sup> See note 3, Thomas, K., et al.
- <sup>36</sup> See note 2.
- <sup>37</sup> See note 1, Essex, M., et al.
- <sup>38</sup> Nolen-Hoeksema, S. et al. (1992). Predictors and consequences of childhood depressive symptoms a 5-yr longitudinal study. *J Abnormal Psychol*, 101:405-22;
- <sup>39</sup> Ibid.
- <sup>40</sup> See note 1, Essex, M., et al.
- <sup>41</sup> Hergueta R. et al. (2004). Diagnostic structured interviews in child and adolescent's psychiatry. *Encephale*, 30(2):122-34
- <sup>42</sup> Ibid.
- <sup>43</sup> See note 2.
- <sup>44</sup> Ibid.
- <sup>45</sup> Ibid.
- <sup>46</sup> Egger, H., et al., (2006). Test-retest reliability of the Preschool Age Psychiatric Assessment (PAPA). *J Am Acad Child Adolesc Psych*, 41:588-603.
- <sup>47</sup> Murphy et al. (1999). Validation of the preschool and early childhood functional assessment. *J Child Fam Stud*, 8:343-356.
- <sup>48</sup> Essex, M., et al. (2002). The confluence of mental, physical, social, and academic difficulties in middle childhood II: developing the MacArthur Health and Behavior Questionnaire. *J Am Acad Child Adolesc Psych*, 41:588-603
- <sup>49</sup> Bylund, D. & Reed, A. (2007). Childhood and Adolescent Depression: Why do Children and Adults Respond Differently to antidepressant Drugs? *Neurochem Int*, 51(5):246-53



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<sup>50</sup> Ibid.

<sup>51</sup> See note 2.

<sup>52</sup> Beardslee, W. et al. (2003). A Family-Based Approach to the Prevention of Depressive Symptoms in Children at Risk: Evidence of Parental and Child Change. *Pediatrics*, 112(2):119-21.