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Authors
Stuber, M L
Shemesh, E

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Post-traumatic Stress Response to Life-Threatening Illnesses in Children and Their Parents

Margaret L. Stuber, MDa,*, Eyal Shemesh, MDb

Department of Psychiatry & Biobehavioral Sciences, University of California Los Angeles, 760 Westwood Plaza, Los Angeles, CA 90024-1759, USA

Departments of Pediatrics and Psychiatry, Mount Sinai Medical Center, New York, NY, USA

Post-traumatic stress disorder (PTSD) is a constellation of psychological and physiologic symptoms that are persistent in some individuals who have been exposed to a traumatic event. Similar to most psychiatric disorders defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association [1], the diagnosis depends on a combination of specific symptoms, over a set period of time, severe enough to lead to clinical distress or functional impairment. In this case, to qualify for a formal diagnosis of PTSD, a child or adult must display one or more symptoms from each of three clusters: avoidance of reminders of the stressor (eg, a traumatized soldier who does not want to return to the battlefield), re-experiencing of the event (eg, “flashbacks”), and hyperarousal (eg, hypervigilance, persistent heightened level of anxiety). These symptoms need to persist at least 1 month after the event and to be associated with functional impairments or disability to qualify for a diagnosis of PTSD.

In contrast to most diagnoses in DSM, a diagnosis of PTSD also requires that the symptoms be in response to a specific precipitating event, or trauma. According to the definition in the fourth edition of DSM (DSM-IV), a traumatic event must involve “actual or threatened death or serious injury, or a threat to the physical integrity of self or others,” and the...
individual must have experienced “intense fear, helplessness, or horror” at the time it happened [1]. In the early 1990s, the diagnosis or treatment of a life-threatening illness first was considered as a possible precipitating event for PTSD. Field trials done in preparation for DSM-IV evaluated a group of 24 adolescent cancer survivors and their mothers for PTSD [2,3]. The results of this field trial and others provided data that prompted the inclusion of medical illness as a potential precipitating traumatic event for PTSD in the text of DSM-IV and thereafter DSM-IV-TR [4]. Since that time, studies of post-traumatic stress symptoms have been published about a variety of medically ill patient groups, mostly adult but some pediatric studies, including cancer, burns, heart disease, diabetes, human immunodeficiency virus, and organ transplantation. These studies have supported the hypothesis that post-traumatic stress reactions are seen in medically ill children and adults and their families during active treatment and long after in survivors.

There has been little examination of PTSD in the context of palliative care settings, where the aim is to alleviate suffering, rather than offer a cure (see the Preface of this issue for the complexities of this “distinction”). It could be argued that PTSD should be less common for the children and parents in situations at the end of life, in which there are fewer invasive or painful procedures, and the uncertainty about outcome has been resolved. The focus on excellent pain management would be predicted to reduce the likelihood of post-traumatic symptoms [5]. It is also possible, however, that post-traumatic symptoms could give way to hopelessness and grief in the less anxious, but more certain, setting of palliative care. This article provides an overview of the literature on post-traumatic stress responses in children and their parents who are dealing with life-threatening illness, with a special emphasis on issues that may be encountered in palliative care settings.

Epidemiology of post-traumatic stress symptoms in pediatric patients and their parents

Children with cancer are probably the best studied medically ill pediatric population with regard to post-traumatic stress. Studies of children who are undergoing active treatment for cancer indicate evidence of post-traumatic symptoms during and after treatment. In the earliest published research study, nine children undergoing bone marrow transplant for hematologic and malignant disorders were followed longitudinally for evidence of PTSD. Symptoms consistent with PTSD were observed in a clinical interview performed in the hospital immediately before the bone marrow transplant. The children experienced a 4- to 8-week hospitalization in an isolation room, with intensive chemotherapy and radiation. The number and severity of the symptoms were increased from the pretransplant level in interviews held in the children’s homes at the 3-month postdischarge visit after the
transplant. The symptoms decreased at the 6-month and 12-month home inter-
terviews. The number and severity of symptoms did not return to the pre-
transplant level by the 12-month interview, however, despite the fact that
at this point the child’s chance of survival was quite good. Parents were
not assessed formally in this study, but interviews with them about their
children suggested they were distressed, but did not discuss this with their
children [6].

The presence of post-traumatic stress symptoms in childhood cancer sur-
vivors was studied in comparison with other traumatized groups. Pelcovitz
et al [2] compared symptoms of 23 adolescent cancer survivors with 27 ad-
olescents who had been physically abused and 23 healthy, nonabused ado-
lescents. The cancer survivors not only reported more symptoms than the
healthy, nonabused teens, but also more than the physical abuse victims Us-
ing a measure of lifetime symptoms, 35% of cancer patients versus only 7%
of abused adolescents met PTSD criteria. Cancer survivors reported their
families as being significantly more caring than did the victims of abuse.
The low prevalence of PTSD in the physically abused controls is puzzling
and beyond the scope of this article.

Later studies of PTSD prevalence showed mixed outcomes. A large sur-
vey of 309 disease-free childhood cancer survivors, 8 to 20 years old, 6 years
(mean) after the end of cancer treatment represented the following diagno-
sic groups: 38% acute lymphoblastic leukemia, 10% Wilms’ tumor, 9% sar-
coma, 8% acute nonlymphoblastic leukemia, 8% lymphoma, and 6%
Hodgkin’s disease. These pediatric cancer survivors were compared with
219 age-matched healthy control children. Both groups completed the
PTSD Reaction Index, a widely used self-report instrument designed for
children and adolescents. Of the cancer survivors, 2.6% reported severe
PTSD symptoms, and 12.1% reported symptoms in the moderate range.
By contrast, in the comparison group, 3.4% reported severe PTSD symp-
toms, and 12.3% reported symptoms in moderate range [7,8], with no statis-
tically significant difference between pediatric cancer survivors and controls.

This study was followed by investigations of young adult survivors of
childhood cancer, with different results. Of 78 childhood cancer survivors
age 18 to 40 years, 20.5% met DSM-IV criteria for PTSD at some point af-
fter the end of treatment. As a group, participants reported elevated state
and trait anxiety. Subjects meeting criteria for PTSD reported higher per-
ceived current life threat, more intense treatment histories, and higher levels
of psychological distress than subjects who did not have PTSD [9,10]. A sub-
set of 51 of this sample was assessed with a structured clinical interview to
determine PTSD status and given self-report measures of quality of life
(Rand Short-form 36) and psychological distress (Brief Symptom Inven-
tory). On this more rigorous assessment, 20% of the sample met criteria
for PTSD. On all domains, quality-of-life scores were significantly lower (in-
dicating poorer quality of life) for the PTSD group compared with the non-
PTSD group. The survivors with PTSD also reported clinically significant
levels of psychological distress, whereas symptom levels for survivors without PTSD fell well within population norms [11]. Age-specific developmental challenges were hypothesized to account for this higher level of symptoms compared with younger cancer survivors. Young adult survivors faced completion of higher education, career success, search for life partners, and related tasks apt to be affected by cognitive impairment, organ toxicity, infertility, and other late effects of cancer treatment to a greater degree than younger survivors.

Given the findings with PTSD prevalence in these studies of childhood cancer survivors, it might be concluded that post-traumatic stress symptoms are experienced primarily during acute illness at the time of initiation of treatment and after treatment ends by older survivors. Studies of pediatric solid organ transplant recipients suggest, however, that the level of symptoms reported by older cancer survivors in earlier studies may be a better estimate of the overall impact of life-threatening illness on children at all ages. A study of 104 pediatric heart, liver, or kidney transplant recipients, age 12 to 20 years, at least 1 year post-transplant, found that more than 16% of the adolescents reported symptoms meeting criteria for PTSD. An additional 14.4% met two of the three symptom-cluster criteria. Regression analysis indicated no effect of gender, ethnicity, age at interview, organ type, time since transplant, or age at transplant [12].

Comparable prevalence is found in other pediatric studies. A group of 35 children, and their parents, who had been hospitalized in a pediatric ICU were compared with 33 children/parent pairs who had been hospitalized on general pediatric wards; 21% of pediatric ICU–discharged children developed PTSD compared with none of the ward admissions. Pediatric ICU children had significantly more PTSD features of irritability and persistent avoidance of reminders of the admission [13]. In another study, 22% of 143 children 7 to 15 years old who experienced motor vehicle injury met criteria for PTSD. There were no associations for presence or absence of PTSD with age, gender, race, injury, or cause of injury [14].

Parents of children with serious medical illness

The largest study of post-traumatic stress symptoms in parents of children with life-threatening illness compared 309 mothers and 213 fathers of childhood cancer survivors with 211 mothers and 114 fathers of a healthy control group. Of the survivors’ mothers, 10.1% reported severe levels of current post-traumatic stress symptoms, and 27% reported moderate levels of symptoms. The mothers in the comparison group reported 3% severe and 18.2% moderate levels of symptoms ($P = .001$). Of the fathers, 7.1% reported severe and 28.3% reported moderate symptoms of PTSD compared with 0% severe and 17.3% moderate in the fathers in the comparison group ($P < .001$) [7].

Another large but uncontrolled study of parents included 170 caregivers (mostly mothers) of pediatric transplant recipients 10 to 38 months after
their child’s most recent transplant. Although the parents did not report elevated levels of depression or anxiety, they did report elevated levels of post-traumatic stress symptoms, with 27.1% of the parents meeting diagnostic criteria for PTSD. The rate of post-traumatic stress symptoms did not vary by type of transplant or by ethnic group [15].

A similar prevalence is found in populations of parents dealing with a more acute life threat to their children. A study of 272 parents of children in the pediatric ICU for more than 48 hours found that 32% met symptom criteria for acute stress disorder. At follow-up 2 months later with 161 of the parents, 21% met symptom criteria for PTSD [16]. A British study found that parents of children hospitalized in the ICU were more likely to screen positive for PTSD (27%) compared with parents of children admitted to the ward (7%) [13]. In another study of mothers of children experiencing acute life-threatening illness, 111 mothers of children who survived hematopoietic stem cell transplantation completed self-report measures of psychological functioning at the time of hematopoietic stem cell transplantation and self-report measures and a structured psychiatric interview 18 months later. Approximately 20% of mothers had clinically significant PTSD spectrum symptoms. This prevalence increased to nearly one third when subthreshold PTSD was included [17].

Predictors for the development of post-traumatic stress disorder in medically ill children and their parents

Children

Studies examining predictors of post-traumatic stress symptoms in children with life-threatening illness have found consistent factors similar to those found for other types of traumatic exposure. In a report from the largest study to date of childhood cancer survivors, 186 survivors age 8 through 20 years, off treatment for more than 1 year, significant, independent predictors of persistent post-traumatic stress symptoms included (1) the survivor’s retrospective subjective appraisal of life threat at the time of treatment, and the degree to which the survivor experienced the treatment as “hard” or “scary”; (2) the child’s level of trait anxiety; (3) history of other stressful experiences; (4) time since the termination of treatment (negative association); (5) female gender; and (6) family and social support (negative association). The survivor’s anxiety and current appraisal of life threat, but not post-traumatic stress symptoms, were related to the mother’s perception of stress of treatment and current life threat. The assessment of prognosis and treatment intensity made by the oncologist was not significantly related to the appraisals of life threat or treatment intensity by the survivor and did not predict post-traumatic stress symptoms in the survivor [18].

Even injuries that are not life-threatening seem to result in post-traumatic stress symptoms in some cases. In one study, 400 pediatric orthopedic
trauma patients with an average age of 11 years were assessed an average of 36 days after injury. Of the children, 33% reported high levels of post-traumatic stress symptoms. Levels of symptoms were not related to the mean Injury Severity Score or summed Extremity Abbreviated Injury Score. The only identified predictor was that patients admitted to the hospital after injuries were significantly more likely to develop high levels of post-traumatic stress symptoms compared with patients not admitted [19].

The subjective appraisal of the traumatic event, rather than an objective measure of actual risk or exposure, is particularly significant for the palliative care setting. Although it could be argued that the prognosis is grim for all of the children in a palliative care setting, not all experience it as traumatic, and not all children receiving palliative care services die (see Preface). There are many stressful events in the course of a serious illness, however, which may have been experienced as traumatic by a child or parent. This appraisal is highly individual and is shaped significantly by developmental level and by the parent’s, usually the mother’s, appraisal of risk. Younger children are less likely to interpret the diagnosis or life threat as the most traumatic aspect of the illness because they are less likely to understand fully the potential implications. Younger children are more likely than older children and parents to find separation from friends and family to be a major traumatic event, however [20]. Exposure to traumatic events at different developmental stages is likely to result in different psychological outcomes and disorder profiles, but interpretation of studies published to date are limited by failure to stratify by age or stage of development. Studies are needed with the sample sizes necessary to examine this question by age and developmental level stratification.

Often the intrusive or painful medical procedures and treatments, such as transplantation and chemotherapy, are cited later as traumatic events by children of all ages who report medically related post-traumatic stress symptoms. Medical professionals may be perceived as “inflictors” of trauma, with parents as collaborators. Clinical experience suggests some children may experience medical treatment as akin to interpersonal violence, despite sensitive, well-intentioned caregivers. Studies of children exposed to repeated, interpersonal traumatic events suggest these events are more likely to lead to blunting and dissociation, whereas an acute, noninterpersonal event, such as a natural disaster, are more likely to lead to hypervigilance and avoidance of reminders. Although this distinction has not been firmly established for medically related traumatic stress responses, it should be considered for seriously ill children in intensive medical settings whose withdrawal and “depression” may reflect traumatic dissociation, rather than a mood disorder.

Parents

Predictors for post-traumatic stress responses in parents resemble the predictors seen in childhood cancer survivors. Mothers and fathers of 331
survivors of childhood cancer age 8 to 20 years were surveyed using the Posttraumatic Stress Disorder Reaction Index, a validated instrument used for self-report of traumatic stress symptoms in adults and adolescents. Trait anxiety as reported at 5 years after the end of treatment was the strongest predictor of post-traumatic stress symptoms for mothers and for fathers. Other significant contributors were the parent’s perception of the life threat to the child, the parent’s perception of the intensity of the child’s treatment, and the parent’s social support. Similar to the children, the oncologist’s rating of life threat and treatment intensity did not contribute to post-traumatic stress symptoms in the parent. In contrast to the child survivors, there was a small but statistically significant correlation between the parent’s and oncologist’s rating of life threat and treatment intensity [21].

Similar predictors were found in the pediatric ICU study previously cited. Symptoms of PTSD and acute stress disorder at 2-month follow-up were associated with the parents’ perception of life threat rather than actual life threat as measured by the Pediatric Risk of Mortality Scale. Other predictors of PTSD at 2 months were the symptoms of acute stress disorder assessed in the pediatric ICU, an unexpected admission, and the occurrence of another hospital admission or other traumatic event after the index admission [16].

The relationship between post-traumatic stress symptoms in children and their parents was studied in 209 children, age 6.5 to 14.5 years, interviewed 5 to 6 weeks after an accident or a new diagnosis of cancer or diabetes mellitus type 1. Of the children, 11.5% reported post-traumatic stress symptom levels in the clinical range of PTSD; 16% of the 175 fathers and 23.9% of the 180 mothers met full DSM-IV diagnostic criteria for current PTSD. Predictors of the development of PTSD in the children included accident-related injury (rather than cancer or diabetes) and the functional status of the child. The development of PTSD in the parents was associated with the diagnosis of cancer in their child (more commonly than injury). PTSD symptom scores of mothers and fathers were significantly correlated with each other. The children’s PTSD symptoms were not significantly related to the symptoms of the mothers and fathers, however [22].

Implications for care

Children

Given the focus on quality of life and comfort care in a palliative care setting, what are the implications of PTSD in this setting? The study of Meeske et al [11] of 51 young adult survivors of childhood cancer, 20% of whom met symptom criteria for PTSD, lends support to PTSD as an indicator of distress, finding that the summative score for psychological distress was in the upper 97th percentile compared with a normative population. Of importance
to children in palliative care, in this study subjects with moderate and severe “late effects” of treatment (eg, cardiovascular or pulmonary complications) were more likely to have PTSD. This finding suggests that a more severe medical outcome might act to sustain chronic symptoms of PTSD and be an indicator of more traumatic exposure over time [11]. In the pediatric oncology setting and by implication with other life-limiting illnesses, a substantial proportion of children sick enough to reach the point of palliative care are likely to have experienced multiple risk factors for PTSD and associated distress. These patients also are likely to experience functional impairment and reduced quality of life, which may be improved if PTSD symptoms are addressed.

Post-traumatic stress symptoms also seem to be related to nonadherence to treatment. A study of 19 pediatric liver transplant recipients found that 6 reported symptoms consistent with a diagnosis of PTSD. Three of these, and none of the others, had been rated as significantly nonadherent by their medical care team. The children with PTSD had significant fluctuations in their blood levels of immunosuppressive drugs. In this study, no significant differences were found in perception of disease threat or demographic variables between the subjects reporting PTSD and the subjects who did not. Most importantly, the three children who had been nonadherent became adherent to their medications when they were treated successfully for PTSD, using a cognitive-behavioral therapy (CBT) approach with an imaginal exposure component. Nonadherence to medications seemed to be related to the avoidance dimension of PTSD (patients avoid taking the medication because it is a traumatic reminder of the illness), as the avoidance dimension of PTSD accounted for much of the association with nonadherence [25].

Parents

The impact of post-traumatic stress on the parents is at least as serious a problem, given the higher prevalence of post-traumatic stress symptoms in parents than in their ill children and the added impact of grief and loss if the child dies. A small study found potentially adverse physiologic correlates of chronic PTSD in mothers of childhood cancer patients, even when the child survived. Participants included 21 mothers of pediatric cancer survivors with \( n = 14 \) and without \( n = 7 \) PTSD and control mothers of healthy children \( n = 8 \). The PTSD group showed higher total urinary cortisol and a trend for higher total urinary norepinephrine than the non-PTSD group, who were no different from controls. This finding is consistent with findings in other populations of PTSD patients and suggests these mothers have a chronic stress response [26]. These findings are of even greater concern with the speculation that the parent’s PTSD symptoms may affect the child’s perception of threat and influence his or her risk for PTSD and other psychological symptoms. Parental functioning is unquestionably
important for medically ill children, who might be dependent on their parents to administer medical treatments, make and transport to medical appointments, and perform related essential practical and psychological support functions.

Interventions

In the palliative care setting, some of the known contributors to psychological trauma and PTSD already have been reduced or eliminated, including painful medical interventions and the side effects of curative chemotherapy. Life threat is, by definition, always present. As noted elsewhere in this issue, adequate pain management, psychopharmacotherapy, CBT, and psychodynamic psychotherapy, with varying and emerging evidence bases, are cornerstones in the treatment of children with life-limiting illness. PTSD and acute stress disorder can be conceptualized as major symptom clusters with which children with life-limiting illness may present. Although controlled clinical intervention trials of PTSD treatment options in the unique setting of life-limiting pediatric illness have not been performed, other pediatric (and adult) research offers guidance until more definitive studies are conducted. The only rigorously investigated approach for the treatment of PTSD in children to date [27] used a manual to deliver an imaginal exposure–based CBT treatment in nonmedical PTSD. This was a randomized, multicenter, controlled trial of 229 children, age 8 to 14 years, all of whom had a history of sexual abuse. The trauma-focused CBT was superior to a form of “child-centered therapy” on all outcome measures, including depression, PTSD, and behavior. No other forms of treatment have been evaluated in large randomized trials. In adults, the best studied approaches include trauma-focused CBT (see later) and selective serotonin reuptake inhibitors (SSRIs). Paroxetine and sertraline are approved by the US Food and Drug Administration (FDA) for the treatment of PTSD in adults. A cautionary note is that for children, the use of SSRIs, as described in the FDA’s “black box” warning, may be associated with an increase in suicidal ideation. An open trial [28] suggested the safety and efficacy of the SSRI fluvoxamine when given to children with cancer; fluvoxamine is the only SSRI studied in depressed children with cancer. At present, trauma-specific CBT techniques and, in selected cases, SSRIs are the best justified interventions for medically ill children who experience significant distress or impairment related to PTSD based on a growing, if incomplete, evidence base and with appropriate FDA-mandated precautions.

A different set of interventions may hold promise for PTSD prevention in medically ill children by addressing presymptomatic risk factors. Interventions can be made to decrease the fear and helplessness associated with illness and treatment. Although there has been limited formal study of family interventions in such settings [29], principles of humane family-centered care
mandate psychosocial child and family support in pediatric palliative care, as exemplified by novel multidisciplinary team approaches such as the Helping Hands Service at the Cleveland Clinic Children’s Hospital.

The following guidelines are offered to help clinicians develop a sensible approach to intervention for children in palliative care and their parents as a broader base of empirical evidence is awaited:

1. Given that perceptions of life threat and treatment intensity are a major contributor to symptoms, and that these perceptions vary greatly among child, parent, and physician, open and careful communication among the child, parents, and medical team about the child’s medical condition is essential. This is not primarily to ensure the child has “the truth” so much as for the parents and medical care team to understand the child’s perspective. It is often difficult for the medical team to comprehend that treatments that are aimed at palliation of symptoms (eg, placement of an intravenous catheter for administration of opiate analgesics) could be perceived as traumatic by the pediatric patient and his or her family, as reminders of past traumatic events.

2. When it is clear which specific reminders or treatments are distressing to a given child, interventions can be designed to help minimize this distress. Such an intervention may be improved pain control, but more often it is a matter of decreasing a sense of helplessness. Interventions often can be set up that restore more control and choice for the child or parents even with seriously or terminally ill children. Not every medical intervention can be eliminated or postponed, but some can, and such small changes as moments of privacy for child and family unencumbered by medical intervention can make a great difference.

3. Pretreatment with medications that decrease pain without causing confusion or perceived loss of control may be helpful in decreasing trauma symptoms. Pain and anxiety seem to amplify the imprinting of traumatic reminders and the conditioning of specific reactions. Increasing the morphine given to a burn-injured child while in the hospital diminishes the risk of PTSD 6 months after discharge [5]. As discussed elsewhere in this issue, desensitizing interventions, based on established behavioral principles, also can be useful.

4. Identification of traumatic reminders can help minimize avoidance by directly addressing the symptoms associated with re-experiencing. The child, family, and medical team can be helped by the psychiatric consultant to recognize traumatic reminders and develop ways of dealing with and minimizing these.

The staff can be trained to recognize and help with symptoms of PTSD. A toolkit has been created by the National Child Traumatic Stress Network (NCTSN), with support from the Substance Abuse and Mental Health Services Administration of the National Institute of Mental Health. These materials were designed to be useful for hospital-based health care providers,
including physicians, nurses, and emergency care providers, and for parents.

The toolkit includes the following:

1. An introduction to traumatic stress as it relates to children facing illness, injury, and other medical events.
2. Practical tips and tools for health care providers.
3. Handouts that can be given to parents with evidence-based tips for helping their child cope.

These materials can be downloaded free of charge from the NCTSN website, www.nctsnet.org.

Summary

Symptoms of PTSD have been reported in response to a variety of life-threatening medical illnesses and injuries in adults and children. Emerging data suggest that children often experience medical treatment and hospitalization as traumatic, putting caregivers and medical personnel in the role of the unintended accomplice. Adequate pain control by pharmacologic and behavioral means; child and family psychological support using evidence-based CBT, dynamic psychotherapy, and other techniques; and meticulous attention to communication via a team-based approach are the cornerstones of pediatric palliative care in general and PTSD prevention and treatment in particular. Emerging evidence suggests that PTSD in life-limiting pediatric illness can be ameliorated, if not prevented, and treated when it occurs, contributing materially to the quality of life of a child and family. A landmark finding of PTSD research with medically ill children and their families is that parents are at least as symptomatic, or more so, as their children, underlining the importance of a family-directed approach addressing every family member. Pediatric caregivers increasingly recognize their therapeutic role when curative therapy is no longer possible is as pivotal as in the setting of acute illness.

References


