

Psychiatric Aspects of Pediatric Cancer

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KEYWORDS

- Cancer • Psychosocial issues • Psychiatry
- Pediatric • Coping

The diagnosis and treatment of children and adolescents with cancer has a tremendous and lasting effect on the patients, their families, and other individuals in their social network. It carries a host of psychological and behavioral ramifications, from questions of mortality to changes in levels of functioning in multiple domains. This review looks at the psychosocial and treatment-related issues that arise in children with cancer.

OVERVIEW OF CHILDHOOD CANCERS

Cancers of any kind during childhood are rare. Childhood cancer accounts for less than 2% of all cancers diagnosed each year. About 150 to 160 per 1,000,000 children, or around 12,000 children in total, will be diagnosed in any given year.^{1,2} By comparison, asthma, the most common chronic illness of childhood, is prevalent in 8.5% of the child population (6.2 million children), and juvenile diabetes has an annual incidence rate 1.5 to 2 times greater than cancer (about 240 per 1,000,000).^{3,4} The most common forms of childhood cancer are leukemias (28%), specifically acute lymphocytic leukemia (ALL)

A version of this article was previously published in the *Child and Adolescent Psychiatric Clinics of North America*, 19:2.

Please note that this review includes reference to investigations into uses of medications for indications other than those which have received FDA approval (such as use of antipsychotics to treat severe mood symptoms secondary to corticosteroid treatment and antidepressants to treat depressive symptoms occurring in the context of cancer or interferon treatment). Careful clinical judgment is encouraged when using medications for indications other than those approved by the FDA.

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Pediatr Clin N Am 58 (2011) 1003–1023

doi:10.1016/j.pcl.2011.06.009

pediatric.theclinics.com

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(21%), and central nervous system (CNS) tumors (18%), which together account for almost half of all malignancies. Other tumor types include germ cell tumors (7%), Hodgkin lymphoma (7%), non-Hodgkin lymphoma (6%), neuroblastoma (5%), acute myeloid leukemia (5%), Wilms tumor (4%), osteosarcoma (3%), rhabdomyosarcoma (3%), thyroid carcinoma (3%), melanoma (3%), retinoblastoma (2%), and Ewing sarcoma (1%).⁵ Childhood cancer remains the leading cause of illness-related death in childhood, but significant advances in survival have been made in the past 35 years.² The overall 5-year survival rate for 0- to 19-year-olds diagnosed between 1975 and 1979 was 62.9%, compared with 81.5% in 2001.¹

Much of this progress has come from the collaboration of pediatric oncology researchers and clinicians. The Children's Oncology Group (COG), supported by the National Cancer Institute, creates standardized treatment protocols for pediatric cancers and then analyzes the responses to care and disseminates this information to all pediatric cancer providers.⁶

To appreciate the experience of a child who has cancer it is helpful to have an understanding of the treatments involved. Treatment of pediatric cancer may involve chemotherapy, radiation, surgery, or stem cell/bone marrow transplant, or some combination of these modalities. In children with ALL, the most common type of childhood cancer, children receive chemotherapy for 2 to 3 years depending on their risk stratification. The stages of treatment of ALL are divided into induction, CNS-directed treatment and intensification, reinduction, and maintenance. Children initially receive chemotherapy treatment in an inpatient pediatric unit, and subsequently receive chemotherapy treatment in the outpatient setting.^{7,8} In contrast, children with primary CNS malignancies, the second most common cancer of childhood, may have surgery only (eg, children with a pilocytic astrocytoma) or have surgery, radiation, and intensive chemotherapy (eg, children with medulloblastoma).^{9,10}

PSYCHOLOGICAL ADJUSTMENT

As with any severe stressor, the way in which a child is affected by cancer and responds psychologically varies with age. It is useful to view adjustment to a cancer diagnosis and the subsequent treatments through a developmental lens, keeping in mind key markers for each age group.¹¹ Ultimately, some children with cancer may develop problems with mood or anxiety.

Preschool Age

During the preschool years (ages 2–6 years), children are egocentric (a perspective of being at the center of everything) and use associative logic, which means that any 2 unrelated things can be understood in terms of 1 causing the other. The combination of egocentricity and associative logic results in magical thinking and interweaving of reality and fantasy. The use of magical thinking may lead a child to believe that his cancer is a punishment for a bad thought or deed. An example of this might be a 4 year-old boy who thinks he has leukemia because he took his sister's toy or he ate too many cookies. As a result procedures and treatment side effects may feel like punishments, especially if the child is unable to localize the medical illness to a particular body part, as is the case in leukemia. These feelings are consistent with a perception of whole body vulnerability, that "my whole body is sick," even though only 1 organ system is involved. Whole body vulnerability is made more real for the child with cancer who endures intravenous lines, hair loss, and nausea and vomiting. For children with leukemia this vulnerability is heightened, as it is difficult to grasp the concept of a hematologic malignancy.

The concept of time develops gradually in this age range. Although parents may be focused on the seriousness of a diagnosis, the expected course of treatment, and probabilities of survival, the child will likely only comprehend what will affect him or her in the moment.

The dominant social sphere of the preschool child, and the area most affected by the illness, is family life. Children aged 3 to 6 years spend most of their time with their immediate family, and their contacts outside the home are usually limited to preschool and day care. Separations from family members and care providers can be anxiety provoking and challenging during the course of treatment.

School Age

School age is characterized by mastery of skills. There is the emergence of logical thinking (causal logic) and more appreciation for another's point of view. School and peer groups play an increasing role in a child's life. Therefore, disrupted functioning in school performance and peer relationships are common social sequelae, either from direct effects of cancer (time missed from school and friends) or a regressive loss of coping skills. Offering school tutors and age-appropriate activities (such as board games, video games, computers, puzzles, and arts and crafts) can help children to function closer to their premorbid level and may serve as a counterweight to the regressive pull of dependency, helplessness, and loss of control that often accompanies intensive medical treatment.

When school-age children are diagnosed with cancer, they are able to understand the simple functional explanations of their illness and often pride themselves in mastering the names or procedures and treatments they have received. Innovative programs targeting this developmental level include "My Story in Beads"¹² which allows children to mark off each procedure and treatment with a special bead on a string (Elyse Levin-Russman, MSW, LICSW, personal communication, January 2010). Children create a narrative about how their cancer was diagnosed and the treatment they are receiving, allowing them to be active participants in their care. Rules provide predictability in this age group, but a cancer diagnosis disrupts this way of thinking because there are no identifiable causes for most childhood cancers, unlike some adult cancers (eg, smoking leading to lung cancer). It can be frustrating to a child who plays by the rules and follows the doctors' orders to then face setbacks in treatment despite their best efforts. Helping this age group feel competent in the midst of medical complications can be challenging.

Adolescence

During normal adolescence, areas of growth include identity and independence, sexual development, and peer group involvement. Cognitively, adolescents are able to think abstractly and can understand the complexity of a chronic illness in the same way as adults. They can appreciate the meaning of a life-threatening or chronic illness, but often are not prepared to manage the changes in their lifestyle and activities that the treatment requires.¹³

The multiple demands of living with cancer (including enduring the diagnosis and treatments, physical discomfort, limitations, pain, effect on appearance, and fears about the present and future) threaten the adolescent's ability to exercise newly acquired independence. These demands occurs at the same time as the adolescent is striving to individuate from parents and trying to establish an independent identity. An adolescent's identity usually relies on the peer group to determine what is "in" and what is "out," and attractiveness within this group plays a significant role in determining one's self-esteem. Time away from school and other activities may strain

friendships and create feelings of isolation at a time when feeling connected to peers is of utmost importance to the development of identity. Often the illness occurs at a time when other tensions between the adolescent and parent make relying on the parents uncomfortable or unacceptable. Logistical and emotional reasons thwart individuation; parents may need to bring the adolescent to appointments or stay at the bedside during a hospitalization, or may experience longing for closeness with the adolescent when faced with the issues of mortality raised by cancer. In the setting of this emotionally complex dilemma, some teens become sullen, aggressive, nonadherent, or withdrawn, whereas others are able to negotiate the discomfort of returning to a more dependent supportive relationship with parents.

A recent study examined the rates and types of distress experienced by teenagers 4 to 8 weeks after they were diagnosed with cancer.¹⁴ The main areas included physical concerns (eg, mucositis), personal changes (eg, hair loss, fatigue, and weight changes) and treatment-related worries (eg, missing school and missing leisure activities).

Body image and sexuality are tremendously affected by cancer. In adolescence, an extraordinary amount of time is spent on one's appearance and presentation because it often determines one's self-esteem. For the adolescent with cancer, physical attractiveness takes on new meaning. Competence and interest in developing interpersonal and intimate relationships depend on having a positive sense of self and body image. Both of these are challenged during treatment because of feelings of being different and physical appearance changes such as hair loss caused by chemotherapy or weight gain caused by corticosteroids. As a result of low self-esteem and body image concerns expressed by adolescents with cancer, they avoid or are less likely to establish intimate relationships.¹⁵ Future fertility, threatened by cancer treatment, is also a prominent issue. Semen cryopreservation is available for boys but there are no definitive preservation methods available for girls.¹⁶

Mood

One might assume that a severe stressor such as a diagnosis of cancer during childhood would overwhelm an individual's ability to cope emotionally and most if not all children would experience emotional difficulties. However, studies suggest that most children with cancer do not exhibit significant levels of depression or anxiety, although a significant minority do experience marked levels of psychological distress.¹⁷⁻²⁰ Some clinical observations have indicated that a subset of patients exhibit more problems, such as greater difficulty coping.¹⁹ Other studies show the emotional well-being of children with cancer currently receiving chemotherapy to be remarkably similar to case-control classroom peers,²¹ and initial studies of cancer survivors similarly failed to find increases in social and emotional problems in children with cancer,²² although new data on survivors has challenged this view (see later discussion).

The type of cancer may play a role in the psychological effect on the child. Children with brain tumors are likely to experience more psychological distress, in large part because of the neurocognitive sequelae of their disease.²³ Similarly, those with severe medical late effects tend to have more depressive symptoms and poorer self-concept.²⁴

The involvement of mental health professionals in addressing the psychosocial needs of patients and their families can mediate the overall distress they experience. Optimal psychosocial care for patients with cancer includes opportunities to assess functioning and separate transient distress from more serious and disruptive emotional difficulties. Identification of those children with mood and behavioral difficulties who will require additional services is essential in providing good oncologic care. In assessing a child's mood, the clinician must be knowledgeable about the side effects of the treatments, which may include fatigue, decreased appetite, and

disturbed sleep. If a child does present with clinically significant depressive symptoms, the treatment follows the same course as it would in the physically well child; that is, with psychotherapy such as cognitive-behavioral therapy (CBT) and antidepressant medication as indicated.²⁵

Although no large studies have been conducted in children with cancer, selective serotonin reuptake inhibitor (SSRI) medications are the pharmacologic antidepressant treatment of choice, as they are in the population at large.²⁶ In an uncontrolled pilot study of 15 children with cancer and depression or anxiety, fluvoxamine was well tolerated and effective.²⁷ Fifty percent of pediatric oncologists at Children's Hospital of Philadelphia reported prescribing SSRIs for their patients.²⁸ In another small study, 7% of children involved in National Institutes of Health (NIH) research trials for cancer were found to have been prescribed antidepressant medication.²⁹ The investigators of this study noted increasing acceptance for psychopharmacologic treatment of subthreshold psychiatric disorders to improve quality of life, and concluded that in addition to psychological support always being indicated in the setting of anxiety or depression, there is a role for the judicious use of psychotropic medications.²⁹

Anxiety

Because of the need for frequent procedures and treatments (eg, blood draws and intravenous [IV] placements, as well as chemotherapy), the child with cancer often presents to mental health treatment with anticipatory anxiety and/or nausea and vomiting. Anticipatory anxiety without a nausea/vomiting component is initially addressed with behavioral interventions. Understanding the cause of the anxiety is helpful in determining what modifications will be most helpful. For preschool and school-age children, the worry may be about separation from a caregiver. They may demonstrate a greater resistance to being separated from parents or become more fearful of new people. They will want to know exactly where their parents will be before, during, and after. Distraction is a helpful and easy mechanism to alleviate anxiety. The use of handheld video games and watching videos has been shown to decrease anticipatory anxiety preoperatively for children and can be easily employed in the child's hospital room or waiting area.³⁰ Worries about pain are also foremost in a child's mind. Pain should be controlled or eliminated whenever possible, even when this may mean a delay in a procedure. The application of a topical anesthetic (EMLA cream) is standard practice in most pediatric oncology settings before venipuncture. In 1 recent study, the combination of EMLA with self-hypnosis further decreased the associated anticipatory anxiety.³¹ Regularly scheduled lumbar punctures and bone marrow aspirates are part of many childhood cancer protocols. To minimize the pain associated with these procedures they are often done with conscious sedation. Parents and staff should explain procedures in simple terms including where and when a procedure will occur and, if there is pain associated with the procedure, how it will be addressed.

Anticipatory anxiety with nausea/vomiting (ANV) affects many children despite advances in antiemetic medication. The child may feel nauseated or vomit on arriving at the outpatient clinic or hospital. One study reports 59% of children experienced mild to severe anticipatory nausea and vomiting despite the use of ondansetron.³² As with adults, ANV seems to fit the model of classic conditioning. The children with the most severe cases of ANV are those who experience postchemotherapy nausea and vomiting. However, there is a subset of children who do not experience postchemotherapy nausea and vomiting, but manifest ANV. In mild cases, effective behavioral approaches include thought stopping, hypnosis, distraction, and relaxation.³³ More severe cases of ANV in association with postchemotherapy nausea and vomiting may respond to increased use of antiemetics, including higher doses of ondansetron,

corticosteroids, and benzodiazepines. There are also some data to support the use of acupuncture in this population.³⁴

TREATMENT-RELATED ISSUES

In the psychiatric evaluation and treatment of children with cancer, several prominent areas of difficulty related to cancer treatment emerge, and include psychiatric effects of chemotherapeutic agents, neurocognitive effects of treatment from chemotherapy and cranial radiation, and issues related to adherence with treatment. Acute and chronic pain associated with cancer and cancer treatment can further compound psychological distress. Close attention to providing adequate pain control is essential and interventions that reduce pain will reduce suffering.³⁵ A review of pain management, however, is beyond the scope of this article.

Corticosteroids

Corticosteroids are routinely used for the treatment of childhood cancers and their sequelae. In many chemotherapy protocols, including leukemias and lymphomas, corticosteroids play a central role. The appearance of adverse psychiatric symptoms is common in children who are receiving high-dose corticosteroids. These symptoms include changes in mood, sleep, and appetite.

Research in the area of psychiatric adverse effects to corticosteroids is much more extensive in adults than in children. The adult literature supports the role of corticosteroids in causing behavioral changes including depression, mood elevation, irritability, anger, insomnia, and excess talkativeness.^{36–42} Psychiatric sequelae are usually dose-dependent and studies have reported increased severity of psychiatric symptoms with higher doses of corticosteroids. Patients can become severely depressed, manic, psychotic and/or delirious. In the largest study of its type, severe psychiatric reactions were seen in 1.3% of patients receiving prednisone 40 mg per day or less; in 4% to 6% of patients receiving 41 to 80 mg per day; and in 18.4% of patient receiving more than 80 mg per day.⁴³

The use of corticosteroids in children has been studied in children with renal, pulmonary, and gastrointestinal diseases more commonly than in children with cancer.^{44–48} Effects seen in children with cancer are consistent with the behavioral changes seen in children with other illnesses and in the adult population. In children receiving prednisone at a dosage of 60 mg/m²/d for leukemia and lymphoma, increased irritability, argumentativeness, tearfulness, reports of “talking too much,” tiredness, low energy, and night waking were common symptoms, with a trend toward more symptoms in younger children.⁴⁹ In children with ALL, groups receiving prednisone 40 mg/m²/d and 120 mg/m²/d showed adverse changes in attention/hyperactivity, emotionality, sleep disturbance, depressed mood, listlessness, and peer relations, although there was no significant difference between the 2 steroid groups.⁵⁰

Sleep is also significantly affected by the use of corticosteroids. In an unblinded study of children receiving dexamethasone as part of their treatment of ALL, fatigue was worsened, and total sleep, nighttime awakenings, and restlessness were increased.⁵¹ Each child served as their own control by comparing 5-day periods on and off dexamethasone.

The child psychiatrist plays an important role in evaluating and managing corticosteroid-related psychiatric side effects during cancer. In mild cases, children may experience some sleep disturbance and irritability. Psychoeducation about the transient nature of symptoms and support of positive coping skills to adapt to these changes in the patient and family can be helpful. For more moderate cases in which

the child's sleep is more impaired or their behavior and mood are more significantly changed, medication interventions can be extremely helpful. There are numerous case reports of symptom-targeted pharmacotherapy or attempts at prophylaxis with mood stabilizers, antidepressants, and antipsychotics, with varying results. A small open-label trial of olanzapine in adults with manic or mixed symptoms secondary to corticosteroids showed benefit, lending support to the role of atypical antipsychotics.⁵² In our clinical practice, symptom-targeted medication interventions have been helpful in managing acute sleep difficulties, extreme irritability and sensitivity, and mood lability. Usually small doses of benzodiazepines or atypical antipsychotics for the duration of the corticosteroid dosing and a few days following are sufficient to manage the psychiatric sequelae of the corticosteroids. In a few cases, the severity of a child's depression or mania or the development of psychosis requires a reduction or discontinuation of the corticosteroids as well as acute psychopharmacologic intervention.

Interferon

Interferon- α (IFN- α), an immunomodulator, is used to treat some pediatric malignancies including chronic myelogenous leukemia, giant cell tumors, and malignant melanoma.⁵³⁻⁵⁶ There is a paucity of data about IFN and depression in the pediatric population, and the assessment and treatment of children is based on the adult experience. Studies of interferons in adult patients, and particularly those with viral hepatitis, have shown evidence of psychiatric syndromes associated with treatment. Presentations include acute confusional states (delirium), depressive syndromes, and maniclike symptoms of irritability and agitation, and occasionally euphoria.⁵⁷⁻⁵⁹ A depressive syndrome similar to major depression is the most common psychiatric sequela of IFN and has been described in adults being treated for hepatitis C and cancer.⁶⁰ Psychiatrists consulted to evaluate patients who are receiving IFN need to be aware that the treatment may be causing the depression.⁶¹⁻⁶⁵ It is also important to recognize that making the diagnosis of depression in a patient receiving IFN can be challenging as fatigue and decreased appetite are 2 of the most common side effects associated with IFN. In addition, thyroid function should be monitored with high-dose IFN, because autoimmune thyroiditis secondary to IFN can lead to hypothyroidism and complicate the clinical picture.⁶⁶

Reports in the literature suggest that SSRI treatment of IFN-induced depression may be effective,⁶⁷⁻⁶⁹ and may be considered as a prophylactic treatment in patients with severe premorbid psychopathology,⁷⁰ or a history of depression during past IFN treatment.⁷¹ Although some studies have suggested wider prophylactic use in high-dose IFN patients,⁷² it is more common to treat depression in patients who become symptomatic during treatment.⁵⁹ In our clinical experience, children diagnosed with depression while on IFN have benefited from the use of SSRIs. For mild forms of depression, psychotherapeutic strategies can be beneficial. Psychoeducation for patients and families that symptoms may be transient and biochemically mediated rather than the result of a sudden giving up or self-pity is essential.⁶⁴

Neurocognitive Effects

Given the increased survival rates, a greater focus is being placed on the long-term sequelae of cancer treatment and in particular on the neurocognitive effects. More than 50% of children treated for a childhood malignancy are at risk for developing neurocognitive deficits.² Cranial radiation causes the most striking effects on the neurocognitive capabilities of the developing brain, as measured in long-term survivors; however, multiple aspects of treatment can contribute to neurocognitive decline

including primary CNS tumor effects, neurosurgical sequelae, and systemic and CNS-focused chemotherapies. Damage to developing cortical and subcortical white matter has been implicated as a key mechanism in the neurocognitive changes.^{73–76} In addition to the types of tumors and treatments, the following patient factors also play a role in who is at greatest risk of neurocognitive decline: female sex, younger age at treatment, genetic polymorphisms, and population and social risk factors.^{77,78} The largest body of research focuses on children who were treated for CNS malignancies and leukemia.^{9,73,75,79–83}

Cranial radiation therapy (CRT) causes the greatest damage to developing white matter and as a result has been shown to cause the greatest negative sequelae for the developing brain. Studies have shown a decrease in IQ of between 15 and 25 points in children with brain tumors who are treated with CRT.^{84,85} Children with ALL who have CNS involvement are also treated with CRT, and this population also shows significant cognitive decline over time. New protocols have been implemented to maintain the improved cure rates, but minimize the exposure to cranial radiation given the significant effect on cognition.⁸⁶ Protocols are using lower doses of cranial radiation, decreasing the tissue target volume, and postponing radiation in the highest risk groups or using early focal radiotherapy to minimize the cognitive effects. Newer forms and techniques for delivering radiation are also being used. For example, proton beam radiotherapy, as opposed to standard photon radiotherapy, may decrease the likelihood of significant neurocognitive decline, because there is no exit radiation dose thereby decreasing the volume of white matter involved.

Although cranial radiation is probably the most important single factor, brain tumors can also affect vital brain structures by direct mass effect or through sequelae of neurosurgery. A recent follow-up analysis of 24 patients who only required surgical resection of cerebellar tumors showed that although IQ was normal, neuropsychological testing showed deficits in attention, memory, processing speed, and visuospatial processing, and a variety of behavioral problems.⁸⁷ An investigation of patients treated for medulloblastoma showed that adverse factors such as neurologic deficits, meningitis, shunt infections, or the need for repeat surgery increased the risk for IQ deterioration after treatment, indicating that radiation and chemotherapy are not the only relevant considerations.⁸⁸ Furthermore, children who develop posterior fossa syndrome, a triad of mutism, ataxia, and behavioral changes postoperatively, are at greater risk for neuropsychological and psychosocial sequelae.^{89,90}

Long-term cognitive effects from chemotherapeutic agents are most closely associated with methotrexate, whereas cytarabine and corticosteroids are implicated less strongly.^{77,81,83} CNS-directed therapy with methotrexate (administered intrathecally), a mainstay of leukemia treatment, has neurocognitive effects. These effects are hypothesized to be mediated by methotrexate interfering with the folate metabolic pathway, and may result in demyelination and other toxic effects.⁹¹ Several studies have examined the cognitive sequelae of CNS-directed chemotherapy. Children with ALL (who received CNS-directed therapy with methotrexate, but not cranial radiation) were compared with children with Wilms tumor (who experienced cancer but received no CNS-directed therapy) and sibling controls (who did not experience cancer but experienced the emotional distress of cancer in the family).⁹² Children with ALL showed problems with sustained attention, which correlated with teacher reports of poorer academic performance, particularly in mathematics. They also had increased internalizing behaviors on the Child Behavior Checklist, a parent report measure of social competence and behavior problems.⁹³ In this and other studies, the impairments are milder than are usually seen from cranial radiation, although intellectual and academic functioning is affected. The most common neurocognitive

deficits from chemotherapy are found in visual processing, visual-motor functioning, and attention and executive functioning, with female gender and young age (particularly less than age 3 years) as risk factors. Other findings include problems with academic performance, verbal abilities, and memory.^{94,95} Platinum-based chemotherapies (such as carboplatinum) affect hearing, and therefore can affect learning and academic performance.⁷⁷

In addition to morbidity-limiting strategies to minimize the neurotoxic effects (particularly cranial radiation), some investigators have examined interventions for neurocognitive effects after they have occurred.^{96,97} These have focused on cognitive remediation and psychopharmacologic interventions.

Cognitive remediation has been studied as a specific program combining techniques from the fields of brain injury rehabilitation, special education/educational psychology, and clinical psychology.⁹⁸ This program involves activities to strengthen attentional skills and information processing speed; metacognitive strategies to prepare for, approach, complete, and generalize tasks; and cognitive-behavioral strategies to target attention. A multisite, randomized, clinical trial of this program resulted in improved academic achievement and improved attention by parental report.⁹⁹ An alternative model of cognitive rehabilitation for patients who had stem cell transplantations failed to show a major effect compared with a control group.¹⁰⁰

Studies of pharmacologic interventions to treat attentional problems resulting from cancer treatment have focused on methylphenidate, with some promising results.^{101–104} Although stimulants are probably less efficacious in the childhood cancer survivor population than in the general attention-deficit hyperactivity disorder population (75% response rate),¹⁰⁵ a recent randomized, double-blind, placebo-controlled, crossover trial of childhood survivors of ALL and brain tumors showed a response rate of 45.28%.¹⁰⁶ Controlled studies, including 1 specifically geared to evaluate side effects, suggest that patients generally tolerate the medication well, with a subgroup who tolerate the medication less well demonstrating increased side effects.^{102,107}

COG recommends that a neuropsychological evaluation be done as part of entry into long-term follow-up and as clinically indicated for all childhood cancer survivors who received neurotoxic therapies. A complete list of recommendations by COG is available at <http://www.survivorshipguidelines.org>.¹⁰⁸ As in any child with academic difficulties and cognitive impairments, mental health professionals working with survivors of cancer have a role in educating family members and schools about deficits seen in this population, and advocating for appropriate accommodations and services. Studies show that the decline in IQ may not be apparent initially and can be progressive over time, highlighting the importance of following children longitudinally.

Adherence

Adherence to treatment regimens is a prominent issue with adolescents. Adolescents consistently show higher rates of nonadherence compared with children and adults in the treatment of cancer and other life-threatening illnesses.^{109–113} Risk factors for poor adherence with cancer treatment in adolescents have been identified, including low socioeconomic status of the family,^{113–115} barriers to communication such as cultural and linguistic differences,¹¹⁶ and mental illness, including depression in a parent and behavioral disturbances during the patient's childhood.¹¹⁷ Clinically, poor communication between adolescents and their parents around treatment seems to be a significant contributor to poor adherence. It is important to identify nonadherence issues early in treatment. Blood levels of a drug or its metabolites have been used to monitor adherence with oral medication regimens, such as 6-mercaptopurine in the treatment of ALL.^{114,115} A nonjudgmental inquiry about the patient's consistency in taking the

medication may be just as effective.¹¹³ Confusion about appropriate doses or about who is responsible for administering the medication may contribute to unintentional nonadherence.

SUPPORT

The role of the family is central in children with cancer. As a child struggles with the intense period of stress associated with diagnosis and treatment, family members are the greatest potential source of support and strength for the child, but are also vulnerable themselves to the effects of the stress. Overall, parents of children with cancer seem to be quite resilient. A consistent theme reported in the literature is that functioning is preserved in cohesive, expressive families who provide high levels of support to their children and are able to access increased social support.

It has been theorized that cohesive families who display positive modeling and rewarding of competencies despite stress reduce symptomatic behaviors in children with illness.¹¹⁸ In a study following newly diagnosed children with cancer for 9 months, higher cohesion and expressiveness in families was correlated with lower psychological distress and higher social competence.¹¹⁹ Similarly, a prospective study of children undergoing stem cell transplantation showed that family cohesion and expressiveness were protective against child distress, especially if the parents did not exhibit high levels of depressive symptomatology.¹²⁰

In contrast, parents with poor social support are more likely to have lower emotional health scores¹²¹ and mothers with less social support satisfaction have been shown to have more distress.^{122,123} Poor social support has also been shown to be predictive of symptoms of posttraumatic stress in parents¹²⁴; increased social support during diagnosis and treatment may be protective against stress-related problems.¹²⁵ It is not completely clear if the benefit of social support for parents also reduces distress in the children themselves; 1 cross-sectional study indicated that social support of parents does not moderate the association between parent and child distress.¹²⁶ However, a prospective study by the same investigators indicated that maternal distress has a significant effect on the child, suggesting that helping to manage a mother's stress will help the child.¹²⁷

Siblings are often the forgotten members of the family while parents deal with the multiple demands of having a child with cancer. Many individual pediatric cancer centers have support groups to address this unmet need. An example of a sibling support program, accessible to all via the Internet, is the SuperSibs! program.¹²⁸ In studies looking at the experience of siblings, supportive relationships were cited as important,¹²⁹ and siblings who had better social support experienced fewer symptoms of depression and anxiety and fewer behavior problems than those with lower levels of support.¹³⁰

Parents often refer to the oncology staff as extended family and derive strength and support from the nurses, social workers, and physicians involved in their child's care. Care providers play an important role in helping families anticipate the many challenges of cancer treatment and manage them as they encounter these challenges. In addition to the powerful effects of caring personal interactions, it may be possible to use more formalized methods to bolster resilience. Some clinical interventions to support the psychosocial functioning of family members, such as problem-solving therapy and stress reduction techniques, have shown promise.¹³¹⁻¹³⁴

EDUCATION

School is one of the most important normalizing factors for children and adolescents. School provides structure and social contact as well as a place to gain the skills needed

for successful functioning later in life. Therefore, disruptions in school attendance because of treatment of cancer and the subsequent reintegration into the school setting are critical to address. Studies have consistently found that children with cancer are absent from school frequently and absenteeism is a problem at all stages of illness.¹³⁵ Teachers report no significant differences in overall behavioral functioning in school; however, parents and teachers observe increased difficulties in social functioning compared with peers, with regard to sensitivity and isolation.^{136–139}

Although it is anxiety provoking for many, returning to school after the diagnosis of cancer can promote healthy psychological functioning. One study showed that adolescents who returned to school compared with those who enrolled in home-based programs were happier and less socially isolated.¹⁴⁰ Many pediatric oncology centers provide support to children when they return to school, including school reentry programs. In our pediatric oncology center, a clinic nurse and social worker, with permission and guidance from the child and parents, will visit the school before the child's return. The team presents developmentally appropriate information about the child's illness and treatment and answers questions posed by the students and teachers. The child's classmates are given the opportunity to have an open discussion about childhood cancer and a chance to think about how best to treat their classmate when they return. Children, parents, and teachers find these visits helpful as they facilitate an educational discussion around cancer and decrease the burden on the child and family to explain the diagnosis and treatment. Reentry programs are helpful in increasing knowledge and confidence for teachers and improving self-esteem and mood in patients.^{141–143}

SURVIVORS

The landscape of childhood cancer has changed significantly in the past few decades and now most children diagnosed with cancer will survive. In 1997, 1 in 1000 adults were childhood cancer survivors, and this number is expected to increase.² The increased rate of survivorship has led to greater recognition of the long-term issues facing survivors. Cohort studies in the United States¹⁴⁴ and internationally^{145–147} have shed light on the many sequelae of childhood cancer, from second malignancies and organ toxicity to neurocognitive and psychological late effects. Understanding how to appropriately assess this population and effectively intervene when needed represents a burgeoning field. Long-term follow-up clinics for childhood cancer survivors are available in some cancer centers and are being developed in others. Multidisciplinary teams are needed to address the myriad of medical and psychological issues that arise. COG has published guidelines for appropriate care, available at <http://www-survivorshipguidelines.org>.¹⁰⁸ Mental health clinicians play a critical role in evaluating the psychosocial needs in the survivor population.

Several studies have looked at psychological functioning in childhood cancer survivors. Initial reports were encouraging and in a review by Eiser and colleagues²² of 20 studies that compared survivors of childhood cancer with population norms or control groups, there was a lack of significant social and emotional dysfunction. However, more recent studies have raised some concern about the psychological functioning in childhood cancer survivors. Increased awareness of the occurrence of avoidance, hyperarousal, and intrusive thoughts in survivors of childhood cancer has brought attention to the role of posttraumatic stress symptomatology.¹⁴⁸ A Danish study showed that childhood brain tumor survivors had higher rates of psychiatric hospitalization for psychosis and somatic causes, but not depression, compared with the general public and other childhood cancer survivors.¹⁴⁹ There also seems to be an

increased risk of suicidal ideation. In an uncontrolled sample of 226 childhood cancer survivors, Recklitis and colleagues¹⁵⁰ found a significantly increased lifetime risk of suicidal ideation in childhood cancer survivors compared with sibling controls.

The Childhood Cancer Survivorship Study (CCSS), a multisite study funded by the National Cancer Institute of a cohort of 20,276 patients and 3500 sibling controls provides the most comprehensive data about psychosocial outcomes.² Reports using these data have noted significant psychosocial issues in this population. Hudson and colleagues¹⁴⁴ found moderate to severe impairment existed in some aspect of mental health, with significantly higher levels of cancer-related anxiety observed in patients with Hodgkin disease, sarcomas, and bone tumors. Brain tumor survivors from the CCSS cohort showed increased distress and depression compared with siblings.¹⁵¹ Survivors of a variety of other tumors, including leukemia, lymphoma, neuroblastoma, and bone tumors, were found to have increased depression, somatization, and distress compared with siblings.¹⁵² The data from this cohort also supported Recklitis' earlier findings of increased suicidal ideation in the childhood cancer survivor population.¹⁵³ Surveillance of psychosocial outcomes in survivors is essential, especially as cancer treatments continue to evolve and the number and makeup of the survivorship population changes.

CARE AT THE END OF LIFE

Although most children with cancer survive, childhood cancer remains the leading cause of illness-related death in childhood and is the second leading cause of death in children, behind accidents.² The reality of cancer as a sometimes terminal illness affects patients, families, and caregivers alike. Oncology teams utilize the services of social workers, psychologists, psychiatrists, chaplains, and child life specialists to assist the child, family, and staff with the challenges faced at the end of life. These care providers can facilitate family conversations about death between parents and with the child.¹⁵⁴ Conversations about dying and end-of-life care are inherently difficult and often avoided, but data support having open conversations with children. Kreicbergs and colleagues¹⁵⁵ found that parents of children with severe malignant disease who had conversations with their children about dying did not regret these conversations.

Children with cancer experience significant physical and psychological symptoms and suffering at the end of life.¹⁵⁶ Despite this, palliative care services are available at only 58% of institutions caring for pediatric oncology patients, highlighting 1 obstacle to offering optimal care to all children treated for cancer.¹⁵⁷

Many of the difficulties encountered in the terminal phase of children with cancer are common to all children at the end of life. See the article by Knapp and colleagues elsewhere in this issue for further exploration of this topic.

SUMMARY

Overall, children with cancer are resilient, but as shown in this article, there are confronted with several challenges adjusting to their illness, dealing with treatment-related effects, and for some facing end-of-life care. Recent decades have brought about tremendous improvements in survival outcomes for children with cancer. As a result, mental health clinicians not only need to understand the immediate psychosocial issues but also appreciate and anticipate the long-term sequelae for a child with cancer. Mental health clinicians play a critical role in providing the assessment, support, and treatment needed in the childhood cancer population. Continued research in this field is imperative.

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