Common Pediatric Cancers

Abstract: Pediatric cancers represent a spectrum of diseases. Much progress has been made in treating children with cancer, as demonstrated by the marked increase in cure rates and steady decline in mortality over the past 50 years. Such success is attributable to the collaborative efforts of multidisciplinary pediatric oncology teams across the country and throughout the world. The commitment to enroll children in cooperative group trials has expedited treatment results and facilitated improvements in treatment. A basic understanding of common pediatric malignancies is necessary for all health care practitioners, as many pediatric cancer patients survive their disease and reach adulthood.

In 1998, approximately 12,400 cases of cancer were diagnosed in patients younger than 20 years in the U.S. In that same year, 2,500 deaths from cancer occurred in this same age-group.[1] Despite its low incidence, cancer in children is important because most patients survive their disease and advance to adulthood. Survivors of pediatric cancers are at risk for secondary malignancies and long-term toxicities because of their multimodal treatment regimens; thus, these patients require monitoring throughout their life. This article describes the epidemiology, clinical presentation, diagnosis, and treatment modalities of the most common pediatric malignancies encountered in clinical practice.

Leukemia

Leukemia is the most common cancer diagnosis in patients under the age of 15 years. Each year in the U.S., there are about 3,250 new diagnoses of leukemia, of which 75% are acute lymphoblastic leukemia (ALL), and 19% are acute non-lymphocytic leukemia.[1] As recently as the 1950s, ALL was considered a fatal disease in children with few treatment options. Today, with the use of multimodal intensive chemotherapy regimens through cooperative group trials, more than 80% of patients diagnosed with pediatric ALL will achieve a cure. Cure rates are quickly approaching 90% in certain patient subgroups.[1,2]

Pediatric ALL has a peak incidence between 2 and 3 years of age and is more likely to affect boys than girls. Incidence is higher in Caucasian children when compared to other ethnic populations. Risk factors attributable to the development of ALL are prenatal exposure to ionizing radiation and certain genetic syndromes, but a myriad of other causative agents have been postulated (see **TABLE 1**).[1] The presenting signs and symptoms of ALL in children are numerous and are often consequences from the absence of normal hematopoiesis (see **TABLE 2**).[2-4] Along with physical examination, diagnostic evaluation should include drawing a complete chemistry panel and differential blood count to assist with the characterization of abnormal cells and ascertain abnormalities prior to therapy; obtaining chest radiography to determine the presence of disease in the lung; and performing a lumbar puncture and bone marrow aspirate and biopsy to identify the presence of leukemia in these areas. Other childhood illnesses can mimic ALL and must be ruled out as well (see **TABLE 3**).[2-4]

The biological characterization of ALL is necessary to establish the best treatment program. Leukemia cells should be characterized based on morphology, cytochemical stains, immunophenotyping, and cytogenetics. With this information, along with patient-specific characteristics, risk-directed therapy can be determined as well as the patient's overall prognosis. Patients considered standard-risk ALL comprise 60% of cases (event-free survival 80%); these patients are between ages 1 and 9 years with B-cell precursor or T-cell ALL presenting with white blood cell (WBC) counts less than 50,000 cells/mm^3. High-risk patients represent 30% of cases (event-free survival 70%) and are those with B-cell precursor or T-cell ALL presenting with WBC counts higher than 50,000 cells/mm^3 or are older than 9 years. Infants represent a very high-risk group; they account for 3% of ALL cases, and their event-free survival is less than 40%.[1-4]

Chemotherapy is the main treatment modality for children with ALL. It is divided into different phases, with each part consisting of multiagent chemotherapy regimens aimed at different goals (see **TABLE 4**).[2-4] Another

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treatment modality is radiotherapy. Once widely used to prevent and eradicate central nervous system (CNS) disease, radiotherapy is used less often for this purpose because its risks outweigh the benefits compared to instillation of selected chemotherapy agents (methotrexate, cytarabine, and hydrocortisone) directly into the cerebral spinal fluid. However, radiotherapy is used to treat the presence of leukemia in the testicle, but this is only seen in 1% of cases.[2]

Treatment regimens for leukemia are intensive. Associated sequelae with these regimens can include tumor lysis syndrome, fever/neutropenia, infections, gastrointestinal toxicities (e.g., nausea, vomiting, diarrhea, and severe mucositis), anemia/bleeding, neurotoxicity, and organ damage (e.g., renal, liver and cardiac compromise, and pancreatitis).[2,3] The maintenance phase alone is usually two years for girls and three years for boys (boys have a higher relapse rate, hence the need for more therapy).

Table 1

Causative Agents Implicated (Evidence Is Inconclusive or Limited) in the Development of Pediatric ALL

Being born to mother of advanced maternal age (> 35 years)
High birth weight (> 4,000 g)
Being the firstborn or only child
Being born to a mother who smoked before or during pregnancy
High consumption of meats, particularly, cured meats
Being born to parents who experienced certain occupational exposures
Experiencing a postnatal infection
Living near electromagnetic fields

Brain Tumors

Brain tumors are the most common solid tumors occurring in pediatric patients and represent a heterogeneous group of malignancies. In patients under the age of 20 years, the most common group of brain tumors is the astrocytomas (52%), followed by primitive neuroectodermal tumors (PNET; 21%), brainstem gliomas (15%), and ependymomas (9%). The most common astrocytoma diagnosed in children is low-grade astrocytoma; medulloblastoma is the most frequently seen PNET. Approximately 2,200 brain tumors are diagnosed annually in patients younger than 20 years in the U.S., making it the second most common malignancy in children. Identifiable risk factors for brain tumors in children are ionizing radiation to the head and certain genetic conditions (i.e., neurofibromatosis, tuberous sclerosis, Li-Fraumeni syndrome, and Turcot's syndrome), but these factors account for only a few cases. Certain brain tumors in children (ependymomas and medulloblastoma) have a slight gender preponderance (male greater than female sex) and racial predilection (Caucasians >African-Americans), particularly in those under 10 years of age.[1]

Given the heterogeneity of this malignancy, signs and symptoms associated with brain tumors vary with size and location of tumors as well as the developmental age of the child. Slightly more than half of all brain tumors in children arise in the posterior fossa (infratentorial), and associated symptoms often relate to an increase in intracranial pressure. Such symptoms are headaches, lethargy, nausea and vomiting most pronounced in the morning upon arising, visual disturbances, and unsteady gait. In contrast, the signs and symptoms seen in patients with supratentorial tumors are frequently correlated with the area of the brain that is affected. These patients may present with symptoms such as seizures, personality changes, impaired judgment, memory loss, hemiplegia, hormonal insufficiency, and hydrocephalus.[5-7]

The preferred diagnostic exam to ascertain the size and location of brain tumors in children is magnetic resonance imaging (MRI). It is favored over computed tomography (CT) for neurosurgical planning because MRI provides better definition of the tumor and can pinpoint associated edema and involvement, if any, of surrounding tissues. Tissue sampling is necessary to establish the histological diagnosis by the pathologist. The tumor is subsequently graded based on characteristics (e.g., histological appearance relative to normal brain tissue, rate of growth, vascularity), which, in turn, directs the postsurgical treatment plan and the patient's overall prognosis. The surgeon's role is to remove as much of the tumor as possible

Table 2

Clinical Findings Associated With Pediatric ALL

Fever
Infections (relating to neutropenia)
Generalized malaise and pallor (relating to anemia)
Loss of appetite and weight loss
Early bruising and bleeding, particularly from mucous membranes (relating to thrombocytopenia)
Abdominal pain and distention (including hepatomegaly and splenomegaly)
Bone and/or joint pain
Lymphadenopathy
Headache (may be indicative of CNS disease)

(prognosis often correlates with the extent of tumor resection) and to place a ventriculoperitoneal shunt to alleviate persistent hydrocephalus.[5-8]

Following surgery, radiotherapy and/or chemotherapy are frequent therapeutic options for children. Radiotherapy is often reserved for patients over the age of 2 to 3 years old, as its use is associated with an increase in morbidity in younger patients, which usually manifests itself as neurocognitive deficits and impaired growth and development. Chemotherapy has a role in certain tumor subtypes and in patients who are not candidates for radiotherapy. Commonly employed chemotherapies include cisplatin, carboplatin, cyclophosphamide, ifosfamide, etoposide, lomustine, procarbazine, and vincristine. However, the delivery of chemotherapy across the blood-brain barrier is challenging. Future directions for brain tumor therapies are ongoing investigations examining the utility of temozolomide, camptothecin analogs (irinotecan and topotecan), angiogenesis inhibitors, and retinoids.[5-8]

Table 3

Childhood Illnesses That Can Present Like Pediatric ALL

Juvenile rheumatoid arthritis
Infectious mononucleosis
Idiopathic thrombocytopenia purpura
Aplastic anemia
Pertussis
Acute infectious lymphocytosis
Non-Hodgkin's lymphoma
Rhabdomyosarcoma
Neuroblastoma
Retinoblastoma

Neuroblastoma

Derived from the embryonic neural crest cells, neuroblastoma is a malignancy that involves the sympathetic nervous system. Neuroblastoma is the most common extracranial solid tumor in children and remains the most typically diagnosed neoplasm during infancy. Approximately 650 children are diagnosed with this disease each year in the U.S., and the exact cause of this tumor remains unknown. However, because a majority of cases occur at a very young age (mean age of diagnosis is 2 years old), exposures before conception and during gestation have been postulated as a leading risk factor for neuroblastoma and warrant further investigation.[1]

Signs and symptoms of neuroblastoma are directly related to the sites of tumor involvement. Frequently, tumors arise from the adrenal gland (retroperitoneal area); thus, abdominal pain and a firm, palpable, nontender mass are often hallmarks of the disease. Thorax is another site of tumor involvement, which is more likely to exist in infants. Associated symptoms present in patients with neuroblastoma often relate to paraneoplastic syndromes. Such symptoms are intractable secretory diarrhea, relating to tumor secretion of vasointestinal peptide (VIP), and excessive catecholamine secretion, which can be an uncommon cause of tachycardia and hypertension. Renal vessel compression can occur with large tumors and is also another cause for hypertension. Metastatic disease is present at the time of diagnosis in approximately two thirds of patients. The sites of involvement can be bones, bone marrow, lungs, liver, brain, and soft tissues. Poor prognostic factors are summarized in **TABLE 5**.[9,10]

Table 4

Phases of Pediatric ALL Therapy

Name	Goal	Representative Therapies
Induction	Restoration of normal hematopoiesis	Vincristine, glucocorticoid (prednisone or dexamethasone), and asparaginase An anthracycline (daunorubicin or doxorubicin) may be added for patients at high risk
Consolidation	Continuation of response and strengthening of remission as well as directing therapy at CNS	Methotrexate, cytarabine, asparaginase, cyclophosphamide, thioguanine, mercaptopurine, and etoposide
Intensification	Eradication of minimal residual disease and resistant leukemia cells	Vincristine, glucocorticoid (prednisone or dexamethasone), asparaginase, anthracycline (daunorubicin or doxorubicin), cytarabine, cyclophosphamide, thioguanine, and mercaptopurine
Maintenance	Maintenance of remission	Vincristine, prednisone, methotrexate, and mercaptopurine

Diagnostic evaluation for neuroblastoma includes CT scans and skeletal surveys to determine tumor location and bone marrow aspirates/biopsies to confirm the presence of bone marrow involvement. The measurement of urinary excretion of catecholamine metabolites can aid in the diagnosis.[9,10] The current staging system used in clinical practice is the International Neuroblastoma Staging System.[10,11] Both treatment strategies and overall prognosis depend on the stage of disease and age of the child.

Surgery is targeted at establishing the diagnosis, obtaining tissue samples for biological evaluation, and removing the tumor, if possible. For early-stage disease, surgery alone can be curative. Radiotherapy is being used less frequently because of the increased use of dose-intensive chemotherapy; however, it may be added to therapy for patients with more advanced disease. Chemotherapy remains the backbone of treatment for patients with neuroblastoma, and multiagent regimens usually consist of cyclophosphamide, ifosfamide, doxorubicin, etoposide, cisplatin, and carboplatin.[9,10] A more recent treatment approach for patients with advanced disease is high-dose chemotherapy with autologous stem cell rescue followed by 13-*cis*-retinoic acid (isotretinoin) therapy.[12] Retinoids have been shown to act as differentiating agents in neuroblastoma cells, causing the cells to mature into more benign cells.

Glossary

Angiogenesis: formation of new capillary blood vessels

Diaphyses: shaft of a long bone

Enucleation: surgical removal of an entire tumor or organ, such as an eye, without rupture

Hematopoiesis: development of blood cells through the proliferation and differentiation of stem cells (often occurs in the bone marrow)

Hemiplegia: paralysis occurring on one side of the body

Hydrocephalus: dilatation of the cerebral ventricles that is accompanied by an accumulation of cerebral spinal fluid within the skull causing head enlargement and brain compression

Infratentorial: below the tentorium cerebelli (fold in the dura mater that separates the cerebellum and the posterior part of the cerebrum)

Leukocoria: appearance of a white pupil in the eye

Metaphysis: conical section of bone between the end and the shaft of long bones

Nephrectomy: surgical removal of the kidney

Paraneoplastic syndromes: clinical conditions occurring in patients with cancer that are often an indirect result caused by the tumor or its products

Strabismus: condition where one eye cannot focus with the other

Supratentorial: above the tentorium cerebelli

Ventriculoperitoneal (VP) shunt: surgical procedure involving the insertion of a catheter that shunts excess cerebral spinal fluid from the ventricles of the brain into the peritoneal cavity

The Sarcomas

Pediatric sarcomas, defined as malignant neoplasms arising from embryonic mesenchymal cells that give rise to connective tissue, can be divided into two groups: soft tissue sarcomas and bone sarcomas. The three most common sarcomas in patients under the age of 20 years are rhabdomyosarcoma, a soft tissue sarcoma, as well as osteosarcoma and Ewing's sarcoma, both of which are bone sarcomas. Together, the three tumor types account for about 10% of all newly diagnosed pediatric cancers in the U.S. Although they share a common pathological origin, their characteristics and treatment vary slightly.[1,13]

Constituting more than half of all soft tissue sarcomas in children, rhabdomyosarcoma is a highly aggressive tumor. Most patients are younger than 10 years at the time of diagnosis, and most cases are sporadic.[1,13] Osteosarcoma and Ewing's sarcoma have a peak incidence during the second decade of life, and diagnosis frequently coincides with puberty when adolescents experience growth spurts. Risk factors for Ewing's sarcoma, whose cause remains unknown, have not been established. On the contrary, the development of osteosarcoma has been linked to previous exposure to ionizing radiation; the development of Paget's disease; a history of hereditary retinoblastoma; and the presence of Li-Fraumeni syndrome, a familial cancer syndrome associated with mutations in the p53 tumor suppressor gene, which itself is a risk factor for some cases of rhabdomyosarcoma.[1,14,15] There are no distinct gender or racial differences in the development of rhabdomyosarcoma or osteosarcoma. Ewing's sarcoma, however, is very rare in African-American and Asian-American children.[1]

Because rhabdomyosarcoma can occur anywhere, symptoms at diagnosis vary based on tumor site (see **TABLE 6**).[13,16] Osteosarcoma and Ewing's sarcoma are usually associated with pain and swelling of the affected bone and/or joint. Constitutional symptoms, e.g., fever, anorexia, and weight loss, can be present but are rare. Most often occurring in the metaphyses of long tubular bones, about half of all osteosarcoma cases are located in the distal femur or proximal tibia (or around the knee). In contrast to osteosarcoma, Ewing's sarcoma occurs relatively equally in long bones (usually affecting the diaphyses of long bones) and flat bones, with the pelvis being the most common site followed by the femur, tibia, and humerus. Ewing's sarcoma can also arise in soft tissue.[13-15]

Patients with osteosarcoma and Ewing's sarcoma are

more likely to have metastatic disease at presentation compared to patients with rhabdomyosarcoma (20% to 25% vs. 15%). Common sites of metastatic spread for patients with rhabdomyosarcoma and Ewing's sarcoma are bone, bone marrow, and lungs, with regional lymph nodes being an additional site for rhabdomyosarcoma. Osteosarcoma patients almost exclusively experience metastatic spread to their lungs and rarely have metastatic disease to their bone.[13-15]

Table 5

Factors Associated with a Poor Prognosis in Neuroblastoma

Age > 1 year old
Advanced disease (stage 3 or 4)
Urinary catecholamine ratio of VMA/HVA <1
Serum ferritin >143 ng/mL
Lactate dehydrogenase >1,500 U/mL
Neuron specific enolase >100 ng/mL
N-*myc* oncogene amplification
Diploid karyotype (DNA index = 1)
Allelic loss or deletion associated with chromosome 1

VMA, vanillylmandelic acid; HVA, homovanillic acid

Diagnoses of sarcomas are made definitively based on fresh tissue samples evaluated by a pathologist. Diagnostic evaluation of the area involved with the tumor should be performed and can be plain radiographic films, CT, or MRI. These tests can also detect the presence of metastatic disease to the lungs. Bone scans can detect bone disease, and if bone marrow involvement is suspected, a bone marrow biopsy and aspirates should be obtained. For osteosarcoma and Ewing's sarcoma, patients are staged according to the grade of their tumor, tumor location, and the presence of metastatic disease. Patients with rhabdomyosarcoma are stratified according to site and size of tumor, presence of lymph node disease, and metastases.[13-15,17]

Treatment regimens for sarcomas are multimodal. Surgery is indicated initially for patients with rhadomyosarcoma when the tumor can be safely resected. For patients with Ewing's sarcoma and osteosarcoma, surgery is often used adjuvantly to remove residual disease that has been debulked by chemotherapy. Radiotherapy is used in those with rhabdomyosarcoma and Ewing's sarcoma to assist with local control, but it is rarely used in osteosarcoma patients (except in a few cases of pulmonary metastases) because this tumor is not radiosensitive.[17-19]

Chemotherapy is the foundation of sarcoma treatment and is administered to many patients before and after surgery. Patients with rhabdomyosarcoma often receive a combination of vincristine, dactinomycin, and cyclophosphamide as initial therapy. Doxorubicin, ifosfamide, and etoposide have also been used. Newer agents, e.g., topotecan and irinotecan, are being investigated. Chemotherapy protocols for Ewing's sarcoma parallel those for rhabdomyosarcoma, with active agents including vincristine, doxorubicin, cyclophosphamide, etoposide, and ifosfamide. Osteosarcoma patients frequently receive chemotherapy regimens using doxorubicin, cisplatin, high-dose methotrexate, ifosfamide, and etoposide.[17-19]

Wilms' Tumor

The most common renal neoplasm in children is Wilms' tumor. Also referred to as nephroblastoma, Wilms' tumor usually occurs in patients under 5 years of age, with a mean age of diagnosis of 3 years old. Most patients (90% to 95%) have the disease in one kidney. Recent demographic data suggests incidence does not vary according to gender, but a racial predilection does exist because the incidence in Asians is about 50% less than in Caucasians and African-Americans. In the U.S., the current overall relative five-year survival rate for children diagnosed exceeds 90%.[1] The main reason for this is the National Wilms' Tumor Study (NWTS) Group. With the collaborative effort of practitioners in standardizing their patient care according to set treatment plans and judiciously collecting outcome data, modifications for future treatment based on their findings have continually decreased morbidity and mortality (see TABLE 7).[1,20,21]

Table 6

Signs and Symptoms of Rhabdomyosarcoma

Tumor Location	Signs and Symptoms
Head and neck region	Nausea, vomiting, headache, cranial nerve palsies, proptosis, ophthalmoplegia, epistaxis, sinus obstruction with or without nasal discharge, and hypertension
Genitourinary tract	Hematuria, urinary obstruction, vaginal discharge, painless scrotal or inguinal enlargement, and constipation
Extremities	Swelling of the affected area that may or may not be accompanied by pain, tenderness and/or redness

Children with Wilms' tumor most often present with a nontender abdominal flank mass, which is usually detected by a family member. Other symptoms at presentation may be hematuria and hypertension, the latter

Table 7
Summary of Significant Findings in the NWTS Collaborations

Study (Registration Dates)	Significant Conclusions
NWTS-1 (1969 – 1973)	1. In children less than 2 years old with stage I favorable histology, postoperative radiation had no benefit. 2. The combination of vincristine and dactinomycin was more effective than either drug alone in stage II-III disease.
NWTS-2 (1974 – 1978)	1. For children with stage I favorable histology, 15 months of vincristine and dactinomycin was no more effective than 6 months of therapy. 2. The addition of doxorubicin to vincristine and dactinomycin improved relapse-free survival rates in stage II-IV disease.
NWTS-3 (1979 – 1986)	1. For stage I disease, 11 weeks of vincristine and dactinomycin without radiation is effective therapy. 2. For stage II favorable histology disease, vincristine and dactinomycin without radiation for 15 months was equivalent to vincristine and dactinomycin with radiation or with doxorubicin. 3. For patients with stage II favorable histology, the addition of abdominal radiation did not improve survival. 4. 1,000 cGy abdominal radiation was equivalent to 2,000 cGy in stage III favorable histology. 5. For stage III favorable histology, the addition of doxorubicin to vincristine and dactinomycin was more beneficial than vincristine and dactinomycin together. 6. The addition of cyclophosphamide to vincristine, dactinomycin and doxorubicin did not improve survival in stage IV favorable histology but the addition of cyclophosphamide to the three drug regimen may benefit those patients with stage II-IV anaplastic histology.
NWTS-4 (1986 – 1994)	1. Pulse-intensive chemotherapy regimens are as effective as standard regimens. 2. For stage II-IV favorable histology, 6-month therapy is as effective as 15 months.
NWTS-5 (1995 – 2002)	Final results pending.

resulting from increased renin productions. Fever, anorexia, and weight loss occur infrequently and are typically indicative of advanced disease. Diagnostic work-up usually begins with an abdominal ultrasound followed by a CT scan to determine the size and location of the mass. Since the most common site for metastatic disease is the lungs, chest evaluation is often recommended. Pulmonary involvement can be confirmed by chest radiography or CT scan, but CT scans remain controversial for this purpose.[20,21]

Surgery, usually in the form of nephrectomy, is frequently the first part of treatment for patients with Wilms' tumor. The surgeon's goal is to remove as much tumor as possible and to provide details of the tumor involvement necessary for staging. Chemotherapy consisting of vincristine and dactinomycin with or without doxorubicin commonly follows for patients with intermediate-stage and advanced-stage disease. The addition of other agents such as etoposide, cyclophosphamide, ifosfamide, or carboplatin is usually reserved for patients with relapsed disease or patients initially diagnosed with unfavorable histology with diffuse anaplasia. Radiotherapy is used for those with advanced-stage disease and in the setting of pulmonary metastases.[20,21]

Retinoblastoma

Retinoblastoma is the most common intraocular tumor of childhood. This tumor accounts for less than 3% of pediatric malignancies, but it is nonetheless important because it serves as a prototype for the role of genetics in the development of pediatric cancers. Evaluation of patients with retinoblastoma led to the discovery of the retinoblastoma (Rb) gene and concept of tumor suppressor genes. Patients with the Rb gene, which is often associated with deletions on chromosome 13, have a greater than 90% chance of developing this intraocular tumor.[1,22]

Of the estimated 200 annual cases in the U.S., the median age at diagnosis is 2 years, and cases are rarely seen after the age of 6. To date, no significant racial or gender predilection has been elucidated. Retinoblastoma at diagnosis may be found in only one eye (unilateral) or both (bilateral). Bilateral disease accounts for approximately 25% of all cases and is always inherited. Unilateral disease may be hereditary or sporadic. Com-

pared with sporadic disease, the hereditary form of retinoblastoma is often diagnosed at a younger age due to clinical presentation and vigilance in screening methods.[1,22]

The two most common signs and symptoms of retinoblastoma are leukokoria (often referred to cat's eye reflex or white eye), resulting from retinal detachment, and strabismus, which is frequently caused by secondary pressure from the tumor. Less common symptoms reported are ocular cellulites, eye pain, vitreous hemorrhage, glaucoma, and poor vision. Metastatic disease occurs when the tumor spreads along the optic nerve, invading the subarachnoid space of the CNS or involving lymphatic or hematological seeding, and can be associated with headache, nausea, vomiting, anorexia, and weight loss.[22,23]

Clinically, retinoblastoma can be diagnosed with ophthalmoscopic examination. The classical finding is solitary or multiple yellow-white retinal tumors associated with the fundus. Pupillary dilatation and complete examination of the patient's retina is required and usually performed under general anesthesia because retinal detachment and vitreous hemorrhage can complicate the evaluation. The presence of metastatic disease can be confirmed by a CT or MRI of the globe, orbits, and CNS.[22,24]

Introduced in 1963, the Reese-Ellsworth classification system remains the most commonly used staging system in clinical practice.[25] This system, which is highly dependent on radiotherapy as the main treatment modality, is more indicative of the prognosis of life rather than preservation of vision. Because therapeutic strategies and treatment techniques for retinoblastoma have evolved over the past 40 years, a revised staging system is necessary to more accurately predict clinical outcomes.[22,24]

Treatment of retinoblastoma is complex, highly individualized, and reliant on multiple modalities. Surgical techniques, namely enucleation, are used when vision preservation of the affected eye is not possible. Radiotherapy (plaque radiotherapy or external beam radiotherapy) is frequently prescribed in clinical practice. However, due to unwanted side effects such as orbital deformities and development of secondary malignancies, chemotherapy is starting to gain favor for low-stage tumors. Specific chemotherapy agents used to treat retinoblastoma have included vincristine, carboplatin, etoposide, or teniposide and cyclophosphamide. Other treatment techniques are cryotherapy, laser photocoagulation, and thermotherapy. Overall, survival exceeds 90% in those patients with limited disease confined to the globe.[22,24]

Summary

A working knowledge of common pediatric malignancies is necessary for today's pharmacist. As more children with cancer become adult survivors, pharmacists are increasingly called on to address the needs of these patients, for whom chronic toxicities and long-term sequelae are at least as critical as the acute toxicities that pharmacists have traditionally considered (see elsewhere for a review of these toxicities).[26-30] Pharmacists must have knowledge of these long-term effects, which may not be readily recognizable, to provide a continuum of care to this patient population. ■

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