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Acute lymphoblastic leukemia (ALL), the most common type of cancer in children, is a heterogeneous disease in which many genetic lesions result in the development of multiple biologic subtypes. Today, with intensive multiagent chemotherapy, most children who have ALL are cured. The many national or institutional ALL therapy protocols in use tend to stratify patients in a multitude of different ways to tailor treatment to the rate of relapse. This article discusses the factors used in risk stratification and the treatment of pediatric ALL.

Acute Myeloid Leukemia	21
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Acute myeloid leukemia (AML) is a heterogeneous group of leukemias that result from clonal transformation of hematopoietic precursors through the acquisition of chromosomal rearrangements and multiple gene mutations. As a result of highly collaborative clinical research by pediatric cooperative cancer groups worldwide, disease-free survival has improved significantly during the past 3 decades. Further improvements in outcomes of children who have AML probably will reflect continued progress in understanding the biology of AML and the concomitant development of new molecularly targeted agents for use in combination with conventional chemotherapy drugs.

Acute Leukemias in Children with Down Syndrome

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and Paresh Vyas

Children with Down syndrome have an increased risk for developing both acute myeloid as well as lymphoblastic leukemia. These leukemias differ in presenting characteristics and underlying biology when compared with leukemias occurring in non-Down syndrome children. Myeloid leukemia in children with Down syndrome is preceded by a preleukemic clone (transient leukemia or transient myeloproliferative disorder), which may disappear spontaneously, but may also need treatment in case of severe symptoms. Twenty percent of children with transient leukemia subsequently develop myeloid leukemia. This transition offers a unique model to study the stepwise development of leukemia, and of gene dosage effects mediated by aneuploidy.

Indications and Donor Selections for Allogeneic Stem Cell Transplantation in Children with Hematologic Malignancies

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Rupert Handgretinger, Joanne Kurtzberg, and R. Maarten Egeler

Allogeneic stem cell transplantation (SCT) is the only curative approach for many patients with advanced or high-risk leukemia. Advances in supportive care and management of graft-versus-host disease have resulted in improvements in outcomes of related and unrelated donor SCT, creating controversies as to which strategy might be the optimal therapy for individual patients. This article discusses the indications and donor selection strategies for SCT in patients with malignant hematologic disease.

Neuroblastoma: Biology, Prognosis, and Treatment

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Julie R. Park, Angelika Eggert, and Huib Caron

Neuroblastoma, a neoplasm of the sympathetic nervous system, is the second most common extracranial malignant tumor of childhood and the most common solid tumor of infancy. Neuroblastoma is a heterogeneous malignancy with prognosis ranging from near uniform survival to high risk for fatal demise. Neuroblastoma serves as a paradigm for the prognostic utility of biologic and clinical data and the potential to tailor therapy for patient cohorts at low, intermediate, and high risk for recurrence. This article summarizes our understanding of neuroblastoma biology and prognostic features and discusses their impact on current and proposed risk stratification schemas, risk-based therapeutic approaches, and the development of novel therapies for patients at high risk for failure.

Central Nervous System Tumors

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Roger J. Packer, Tobey MacDonald, and Gilbert Vezina

Central nervous system (CNS) tumors comprise 15% to 20% of all malignancies occurring in childhood and adolescence. They may present in a myriad of ways, often delaying diagnosis. Symptoms and signs depend on the growth rate of the tumor, its location in the central nervous system (CNS), and the age of the child. This article describes the presentation, diagnosis and management of these tumors.

Cancer Immunotherapy: Will Expanding Knowledge Lead to Success in Pediatric Oncology?

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Terry J. Fry and Arjan C. Lankester

The past 25 years have seen an increase in our understanding of immunology and further expansion in the clinical use of immunotherapeutic modalities. How immunotherapy will be integrated with chemotherapy, radiation, and surgery remains to be established. Although there have been successes in the field of immunotherapy, they have been inconsistent, and it is hoped that increased understanding of the basic principles of immunology will improve the consistency of beneficial effects. In this article, we briefly provide a general overview of our current understanding of the immune system, with a focus on concepts in tumor immunology, followed by a discussion of how these concepts are being used in the clinic.

Vaccinations in Children Treated with Standard-Dose Cancer Therapy or Hematopoietic Stem Cell Transplantation

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Soonie R. Patel, Julia C. Chisholm, and Paul T. Heath

Most children with cancer are immunocompromised during therapy and for a variable period after completion of therapy. They are at an increased risk of infections, including vaccine-preventable infections. There is a reduction in immunity to vaccine-preventable diseases after completion of standard-dose chemotherapy and after hematopoietic stem cell transplant. It is important to protect these children against vaccine-preventable diseases by reimmunization.

Good Clinical Practice and the Conduct of Clinical Studies in Pediatric Oncology

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Susan Devine, Ramzi N. Dagher, Karen D. Weiss, and Victor M. Santana

This article discusses the principles that guide good clinical practice standards, with particular emphasis on how they to relate

to pediatric oncology research and recent efforts at harmonization. The authors review the clinical trials process and the roles of the participants, highlighting the pivotal role of the clinical investigator and the research team, and briefly review the historical aspects of drug development regulations in the United States and the current regulatory paths for pediatric oncology drug development. Where relevant, historical events that underlie many of the regulations and their current applications are described, and practical examples are provided.

Rethinking Pediatric Assent: From Requirement to Ideal

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Yoram Unguru, Max J. Coppes, and Naynesh Kamani

Physician-investigators are required to obtain informed consent from adult participants in their studies. Inclusion of children in research legally requires informed permission of a child's parent or guardian. It is increasingly recognized that a child need not assume a passive role when included in research, but that his or her active involvement should be sought, as expressed by the child's assent to partake in clinical research. This article briefly explores the history of assent and the central role of assessing a child's understanding of research and preference for participating in decisions related to their care, as necessary components of meaningful assent.

Integration of Palliative Care Practices into the Ongoing Care of Children with Cancer: Individualized Care Planning and Coordination

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Justin N. Baker, Pamela S. Hinds, Sheri L. Spunt,
Raymond C. Barfield, Caitlin Allen, Brent C. Powell,
Lisa H. Anderson, and Javier R. Kane

Most parents of children with cancer have dual primary goals: a primary cancer-directed goal of cure and a primary comfort-related goal of lessening suffering. Early introduction of palliative care principles and practices into their child's treatment is respectful and supportive of these goals. The Individualized Care Planning and Coordination Model is designed to integrate palliative care principles and practices into the ongoing care of children with cancer. Application of the model helps clinicians to generate a comprehensive individualized care plan that is implemented through Individualized Care Coordination processes as detailed here. Clinicians' strong desire to provide compassionate, competent, and sensitive care to the seriously ill child and the child's family can be effectively translated into clinical practice through these processes.

Challenges After Curative Treatment for Childhood Cancer and Long-Term Follow up of Survivors

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Childhood cancer survivors are at increased risk of serious morbidity, premature mortality, and diminished health status. Proactive and anticipatory risk-based health care of survivors and healthy lifestyles can reduce these risks. In this article, the authors first briefly discuss four common problems of survivors: neuro-cognitive dysfunction, cardiovascular disease, infertility and gonadal dysfunction, and psychosocial problems. Second, the authors discuss the concept of risk-based care, promote the use of recently developed evidence-based guidelines, describe current care in the United States, Canada, and the Netherlands, and articulate a model for shared survivor care that aims to optimize life long health of survivors and improve two-way communication between the cancer center and the primary care physician.

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