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

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Most children with cancer are immuncompromised. The cancer itself may cause a variable degree of immunosuppression, but it is the cytotoxic antineoplastic therapy that is the main contributor. Many pediatric cancers are highly chemosensitive and radiosensitive, and their treatment usually involves chemotherapy or radiotherapy or both. The majority of children with cancer are treated with standard-dose chemotherapy, but children with high-risk hematologic malignancy, children with certain solid tumors, and children with disease relapse require high dose chemotherapy or radiotherapy followed by hematopoietic stem cell transplant (HSCT). These different forms of treatment have different influences on the immune system and the degree of immunodeficiency. Immune alteration is reflected by decrease in neutrophils, lymphocytes, immunoglobulin levels, and specific antibody against previous vaccinations. This results in increased susceptibility to and severity of infections.

Most of the vaccine-preventable diseases are now fortunately rare; however, the risk for some remains significant, in part because of increases in migration and travel. Furthermore, they can be associated with high

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morbidity and mortality, particularly in immunocompromised patients (eg, varicella zoster, measles). In view of the secondary immunodeficiency of children treated for cancer, particularly HSCT recipients, and their improved long-term survival after completion of treatment, it is important to ensure that they are protected against vaccine-preventable diseases. This can be achieved by optimizing the immunization strategy in children during immunosuppressive therapy and by reimmunization of children after completion of treatment. In view of the diversity of malignant diseases and their treatment protocols, it would be difficult to propose different immunization schedules for each disease. Rather, it is sensible to divide them into children treated with standard-dose chemotherapy and children treated with intensive chemotherapy followed by allogeneic or autologous HSCT.

Vaccinations in children treated with standard-dose chemotherapy

Children treated with standard-dose chemotherapy are at increased risk of infection. However, there are few data on the precise incidence of specific infections in this population. With regard to vaccine-preventable disease, there are data demonstrating an increase in incidence and severity of *Haemophilus influenzae* type b (Hib), pneumococcal, measles, and varicella infections [1–4].

Influence of cancer on immune function

Cancer itself, particularly leukemia and lymphoma, can have an adverse influence on immune function. Patients with acute leukemia may have myelosuppression at diagnosis; of particular significance is granulocytopenia. Some cancers may also affect adaptive immune functions; for example, leukemia and Hodgkin lymphoma, by the nature of their pathology, may have an adverse influence on lymphocyte function. However, there are few data to substantiate this assumption. Several studies show that total immunoglobulin concentrations, as well as specific antibody concentrations, to vaccine-preventable infections are normal at the time of diagnosis, suggesting that the effect of the cancer itself on the adaptive immune system is likely to be relatively small [5,6].

Influence of standard chemotherapy on immune function

Different cancers require treatment with different combinations of chemotherapy agents. Therapy for a single disease is risk-stratified based on patient factors, extent of disease, and tumor biology, so there may be variation in intensity of therapy for a single disease type. Therapy regimens that include agents such as cyclophosphamide, purine nucleoside analogs, or corticosteroids are immunosuppressive; they particularly have an effect on lymphocyte function. For example, treatment regimens for acute lymphoblastic leukemia (ALL) are targeted against lymphoid cells and can have an adverse