



## Commentary

## Infections in children with cancer—old approaches and new

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Doctors Miflin and Kinsey have reviewed some of the challenges faced in the management of infections in children with malignancies. Survival rates for children with cancer have increased markedly over the past decades. Data from the Surveillance, Epidemiology and End Results (SEER) programme at the National Cancer Institute have shown overall survival rates exceeding 75% in children diagnosed with cancer between 1989 and 1998 [1]. As more children survive their cancers, the side-effects of cancer therapy become more evident and more important. Successful treatment of infections is one such example.

As the authors point out, children with cancer are at risk of unusual and life-threatening infections, in addition to the usual childhood illnesses. This occurs both because of the aspects of the cancer itself, and from immunosuppression caused by the therapy. The contemporary approach to the treatment of cancer in children involves treatment with chemotherapy, surgery or radiation therapy, or any combination of these modalities. Each causes side-effects that increase the susceptibility to infection. Surgery, for example, leaves wounds that provide entry portals for infection and may not heal well in the face of other therapies and active malignancy. Radiation therapy causes skin and mucous membrane breakdown, and occasionally bone marrow suppression. Chemotherapy is often myelosuppressive, depresses T and B cell function, and may also lead to mucous membrane disruption. Particularly in children with haematological malignancies, therapy can lead to prolonged periods of granulocytopenia and granulocyte dysfunction [2], both of which contribute to the increased infection risk. In addition to the usual opportunistic infections, children continue to be at risk for common childhood illnesses—colds and other viral infections, rhinitis, otitis media, just like normal children.

Children are different in many ways from adults, and children with cancer are different from adults with cancer. Not only do children have a different spectrum of malignant diseases, but the outcome of cancer treatment is often better in children. For example, children with

acute lymphoblastic leukaemia (ALL) have better survival rates than adults with ALL [1]. Infectious illnesses are also often different in children with cancer than in adult cancer patients. A comparison of febrile neutropenia episodes in children and adults treated in four trials from the European Organization for Research and Treatment of Cancer (EORTC) showed that although children and adults had equal incidences of bacteraemia and shock, children had a lower overall mortality rate with only 1% dying from infection compared with 4% in adults [3]. Although the children had lower mean neutrophil counts, the median period of neutropenia was shorter than in adults. Compared with adults, children were less likely to have an identifiable focus of infection; when they did, they were more likely to have upper respiratory tract disease and less likely to have lung infections. The approach to infection and antimicrobial therapy in children with cancer, then, is different from that in adult patients.

One of the crucial aspects in anticipating complications of the cancer and its therapy is assessment of the risk of infection faced by the individual child. Investigators have tried to determine the risks faced by children undergoing specific therapies, and under particular conditions. There are a number of established risk factors for infection. For example, it has been known for some time that the depth and duration of neutropenia has a direct impact and increases susceptibility to serious infections [4]. As cancer therapies have intensified, periods of neutropenia and overall immunosuppression have become longer and more profound. Children undergoing high dose chemo- or chemoradiotherapy, and stem cell transplantation, for instance, are clearly at a greatly increased risk for acquisition of bacterial, viral and fungal pathogens. New agents and approaches are continually advanced to meet the needs of children at risk for an often-changing array of pathogens.

In addition to identifying those children at highest risk, one of the benefits of risk assessment is to allow those at a lesser risk of serious infection to receive an appropriately smaller amount of empirical therapy.

Some of the drawbacks of intravenous inpatient antimicrobial therapy include drug side-effects, risk of nosocomially acquired infections, acquisition of resistant organisms, and increased financial expenditure [5]. In addition, many families prefer to be at home if it is safe for the patient. Recent reports have outlined features of subsets of patients with fever and neutropenia that seem to have a lower chance of serious infection. Santolaya and colleagues described a group of febrile neutropenic children with cancer, and identified risk factors for invasive bacterial infection [6]. There were 5 independent risk factors: C-reactive protein of 90 mg/dl or higher, hypotension, leukaemia in relapse, platelet count less than  $50 \times 10^9$  cells/l at presentation of fever, and chemotherapy within the previous 7 days. Others have described similar characteristics in groups of febrile neutropenic children that appear to be at a low risk [7–9]. Some physicians treat such patients with abbreviated courses of intravenous antibiotics, or oral antibiotics [10–13]. Aquino reports that up to 89% of ‘very low risk’ febrile, neutropenic children with cancer can be safely managed on an outpatient basis [13]. More studies are needed to try to delineate the most appropriate amount of therapy for each child.

In addition to new approaches and therapies, some of the older ones are still important. Doctors Kinsey and Mifflin review some preventive measures important in managing the immunosuppressed child with cancer. Handwashing is still one of the easiest and most effective tools. Handwashing has been shown to decrease the level of microbes on the skin, and to reduce morbidity and mortality from nosocomial infection [14,15]. Doctors, nurses, other professionals, and family members can reduce the risk of infections by frequent and thorough handwashing. Other approaches to hand decontamination, such as hand rubs and lotions, have been investigated and many are effective. Antimicrobial agents improve the effectiveness of the washing, reducing microbe levels further, and are recommended for high-risk locations such as the operating room and the cancer unit [16].

As Doctors Kinsey and Mifflin conclude, future developments in the management of infections in children with cancer will likely include improved diagnostic tools and strategies. New antimicrobial and antivirals, better pre-emptive therapies and, perhaps, intensive

treatments will contribute to the better care and outcomes of children with cancer.

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