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Paediatric Update

Commentary

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The effects of chemotherapy and irradiation on the oral mucosa are a continuing source of discomfort and morbidity in both children and adults [1–8]. The paper by Belfield and Dwyer provides a comprehensive review of the published work relating to mucositis. They have drawn attention not only to the paucity of good research on children in this field but also to the importance of accurate 'scoring' of oral complications for the objective evaluation of new treatments. A number of oral assessment scales have been developed for use in adults [9–13]. In current research, the reliability and validity of the Oral Assessment Guide [10] for scoring oral status in children following chemotherapy and radiotherapy is under assessment (Gibson and Cargill, personal communication) but as yet there is no agreed system. This work is likely to be important for the future best management of mucositis and for the evaluation of oral health-care protocols in children.

Pathophysiological concepts of mucositis [14] provide some attractive hypotheses. For example, sucking ice chips during the 'vascular phase' would seem to be a simple and effective approach for reducing mucositis or at least the symptoms associated with it, but the evidence is conflicting. In adults treated with edatrexate plus carboplatin the effect of mucositis seemed to be reduced by ice-chip cryotherapy [15,16], but the Cochrane Oral Health Review Group [17] concluded that there is only weak and unreliable evidence that ice chips prevent mucositis. There has been no prospective investigation of ice-chip therapy in children. Many other treatments have been advocated but no consensus has emerged. Glutamine mouth rinse was reported to reduce the duration and severity of mucositis after both chemotherapy and irradiation [18,19]. Later work concluded that oral glutamine may decrease the severity and duration of oropharyngeal mucositis in autologous bone-marrow transplant (BMT) patients but not in allogeneic BMT patients, possibly due to an interaction with methotrexate [18].

A trial of granulocyte macrophage-colony-stimulating factor (GM-CSF) versus placebo/no treatment suggests that GM-CSF may prevent mucositis rather than reduce its severity [17]. Later work suggested that mucositis was reduced by GM-CSF in adults treated with 5-fluorouracil but this was a small investigation and its results cannot be extrapolated to children. Overall, the evidence that GM-CSF prevents mucositis is inconclusive.

There have been many investigations on chlorhexidine mouth rinses [20,21]. Although chlorhexidine is not proved to prevent or reduce the severity of mucositis, it can reduce plaque accumulation and, subsequently, oral bacterial loading [20]. In addition to removing most or all foci of oral infection before immunosuppressive therapy, it is also important to reduce oral bacterial regrowth during periods of intense immunosuppression. The main portal of entry for opportunistic infection is through inflamed gingival and oral mucosal surfaces. Thus it is essential to keep the amount of bacterial dental plaque as small as possible; this is a field of mucositis research that has barely been considered [22,23].

Xerostomia, caused by radiation to the head and neck, is a particular problem. As a result, there is a shift in the spectrum of the oral bacterial flora towards Gram-negative bacteria and fungal species, particular *Candida*. Although *C. albicans* is the most common cause of candidiasis, an increasing proportion of serious infections have been attributed to non-*albicans* species, for example *C. tropicalis*. One of the reasons for this shift appears to be a change in antifungal treatment, exerting selective pressure. The use of prophylactic treatment with fluconazole has reduced the number of infections caused by *C. albicans* and *C. tropicalis* in BMT recipients [24,25] but has increased the rates of infection with *C. krusei* [26,27]. *C. krusei* together with

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C. glabrata are much less susceptible to fluconazole than are *C. albicans* and *C. tropicalis* [28]. Even though no established interpretative breakpoints are available, the candins, for example caspofungin acetate, have been found to have excellent antifungal activity [29].

Good oral hygiene reduces the effects of mucositis, but in small children good oral care is difficult to achieve because of the general malaise and poor co-operation caused both by the treatment itself and the resultant sore mouth. Small children cannot brush their teeth effectively and are unable to rinse properly, so the use of dressing sponges to deliver mouthwash to the mucosal surfaces in a non-traumatic way needs to be investigated. Chlorhexidine, which might help prevent opportunistic infections arising from the mouth, is unpleasant to use because of its ethanol base and the taste of the active constituent. Hence, there is a pressing need for the development of a non-alcohol, chlorhexidine-based mouth rinse. Adequate pain relief is a crucial element of good oral health care, as is professional help with tooth cleaning to reduce oral bacterial loading.

The long-term dental effects of high-dose chemotherapy and irradiation are well documented but are incompletely covered in the review. 'Late effects' include a variety of dental anomalies [30], diminished salivary secretion [31] and disturbances in craniofacial growth [32]. In children who have undergone conditioned BMT before the age of 12 months, sequelae can be particularly severe and include missing permanent teeth [33]. These problems can be managed effectively by dentists conversant with the complex of problems presented by these children, the long-term survivors of cancer therapy.

The paper by Belfield and Dwyer provides us with a timely assessment of the current knowledge base in a common and distressing problem for cancer patients. There are several important conclusions. First, to maximise the likelihood that cancer treatment regimens will be delivered 'on schedule' it is essential to provide a good standard of oral health, especially in children; most childhood cancers are now considered curable diseases and special attention to the oral mucosa, teeth and salivary glands may, by reducing morbidity, make a real difference to the prognosis. Secondly, the quality of life of cured patients is likely to be greatly improved by early and appropriate orodental interventions. For these reasons, every department of paediatric oncology should develop close contact with trained paediatric dentists to lead the oral-care programme. It is hoped that these two articles will help galvanise colleagues working in this field into developing or refining suitable assessment protocols. The efficacy of mouth-care therapies can and should subsequently be tested in properly designed and conducted, randomised controlled trials.

Editor's footnote: The 'take-home' messages of these two papers deserve reinforcement. Well-designed trials of orodental care in paediatric oncology are disappointingly thin on the ground. The problem is that most studies are institution based and the numbers of patients are usually small. Even if randomised, these studies have limited power to answer even a single research question with the necessary high degree of statistical probability. National and international co-operation is urgently needed in this field. Agreement on a 'common language'—an internationally agreed 'orodental assessment scale'—would be an appropriate first step in this direction. The *European Journal of Cancer* encourages such trials and, since oral discomfort is one of the worst symptoms for cancer patients, especially children, receiving chemotherapy, will pay particular attention to any submitted papers dealing with this topic.

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