Part 1: Screening and preventative practices for children undergoing oncology therapy; an oral health perspective

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Introduction

Cancer is rare in children compared to the adult population, but despite this, childhood cancer ranks second as the most common cause of death of children accounting for 17% of deaths behind injury in Australia (Australian Institute of Health and Welfare 2009; Baade et al 2010). In Australia, there are on average 157 per million Australian children under 15 years of age per year diagnosed with cancer (Baade et al 2010). This translates to 600-700 children under 15 years of age being diagnosed annually. This is comparable to the prevalence of childhood cancer in the Western world, with approximately 1 in 500 children being diagnosed with cancer before the age of 15 years (Fadda et al 2006).

Recent decades have seen the development of highly specific diagnostic procedures and the introduction and refinement of multimodal treatment strategies. These have resulted in increased cure rates and improved long term survival (Kaatsch 2010). Increased survival rates have come at the cost of increased patient morbidity (Wogelius et al 2008). Oral complications as a result of cancer therapy are well recognised and are among the possible causes of increased patient morbidity. Oral complications are classified as acute and late effects. Table 1 lists these potential acute and late oral complications.

Table 1: Potential Acute and Late Oral Complications of Oncology Therapy

<table>
<thead>
<tr>
<th>Acute</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral mucositis</td>
<td>Tooth agenesis</td>
</tr>
<tr>
<td>Salivary gland hypofunction</td>
<td>Microdont teeth</td>
</tr>
<tr>
<td>Xerostomia</td>
<td>Altered root development</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Developmental enamel defects</td>
</tr>
<tr>
<td>Oral and dental infections (fungal, viral,</td>
<td>Salivary gland hypofunction</td>
</tr>
<tr>
<td>bacterial)</td>
<td>Osteoradionecrosis</td>
</tr>
<tr>
<td>Altered taste sensation</td>
<td>Chronic graft versus host</td>
</tr>
</tbody>
</table>
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- Oral pain including muscle and joint
- Acute graft versus host
- Increased caries risk

- Altered craniofacial growth and development
- Malocclusion
- Compromised aesthetics
- Temporomandibular dysfunction
- Fibrotic remodelling
- Increased risk of oral cancer


Comprehensive care of patients with cancer is complex and involves many health care professionals all with the common goal of improving overall treatment outcomes. Joint collaboration between the Department of Paediatric Dentistry and Haematology and Oncology, at the Women’s and Children’s Hospital, Adelaide, South Australia have led to the development and validation of a specific oral care protocol for oncology patients. Results from the initial research concluded a 100% uptake of the oral health protocol by all oncology patients, a reduction in the incidence of oral mucositis and reduction of any additional oral complications such as dental caries and odontogenic infections (Qutob et al 2013). Retrospective analysis indicated that the protocol required further refinements and modifications. These were indicated in order to individualise specific care for those patients identified as high risk of developing oral complications.

The refined oral care protocol is made up of four key components:

a) Referral to a specialist paediatric dental team
b) Comprehensive dental assessment including caries risk assessment and appropriate recall
c) Implementation of a standardised oral care regime
d) Daily assessment of the oral condition of all in patients at risk of developing oral mucositis

PART A: Referral to a Specialist Paediatric Dental Team

It is recommended that all patients diagnosed with cancer are assessed by a specialist oral health practitioner in a timely manner to avoid complications that may arise from untreated dental disease (Rubenstein et al 2004; AAPD 2013; NCI 2013; Little et al 2008; da Fonseca & Hong 2008). Identification of those patients at risk of oral complications is recommended to form part of the overall initial management. This ensures that patient and parent education regarding appropriate oral care is provided specifically to those patients who require this service.

The oral cavity is particularly susceptible to the effects of chemotherapy and radiotherapy and is reported to be a common source of sepsis in the immuno-suppressed cancer patient (NCI 2013; AAPD 2013). Odontogenic infections may act as the focus of septic infection in myelosuppressed patients (Hong & da Fonseca 2008). In addition, bacteraemia originating from the mouth has been reported to result in secondary infection of central venous lines (AAPD 2013). A possible cause of sepsis is untreated dental caries. Dental caries is prevalent among children being the “single most common chronic disease of childhood, occurring five times as frequently as asthma and seven times more commonly than hay fever” (United States Public Health Services 2000). Current data on the incidence of dental caries in Australia indicates that approximately 46% of 6 year olds have dental caries and the majority of these children have untreated dental caries. Ten percent of 6 year old children with dental caries had at least 10 teeth affected (Mejia et al 2012). It is reported that 34% of 12 year olds have at least one permanent tooth affected by dental caries (Armfield et al 2009; Mejia et al 2012). In addition to potential odontogenic infections, the range of acute oral manifestations is extensive. The potential effects of oral complications on the patient’s
overall health and prognosis are significant. In all cases where dental treatment is required, comprehensive multidisciplinary planning and management must be arranged (see Part 2 of this series). When possible all urgent dental treatment should be completed prior to the implementation of immunosuppressive treatment (AAPD 2013). Decisions regarding the management of any active disease are made in consultation with the oncology team and based on the risks of oral infection and or complications during the cancer treatment phase.

It is recognised that not all patients diagnosed with a malignancy are at the same risk of developing oral complications and patients diagnosed with cancer should have individualised oral care plans based on the cancer diagnosis and the associated risk of oral complications. This is represented in flowchart 1, which describes the initial referral pathway and oral care protocol. Patients that are identified as ‘at risk of oral complications’ and then further classified based on the malignancy and cancer treatment pathway. The importance of this initial first stage of referral is to identify active oral disease at an early phase, potentially avoiding unnecessary oral complications, as well as introducing the oral care protocol. In addition, the potential late effects and other oral complications as a result of cancer therapy can be identified and managed as a multidisciplinary specialist team. The referral pathway importantly also prevents the additional burden on patients and their families who are at low risk of developing dental disease and oral complications.

Flowchart 1: Referral to the Specialist Paediatric Dental Department

Surgery +/- Distant Radiotherapy

Chemotherapy +/- Distant Radiotherapy

Head and Neck Radiotherapy/ Bone Marrow Transplant

No Oral Care Protocol

Standardised Oral Care Protocol

Standardised Oral Care Protocol

Newly Diagnosed Comprehensive Dental Assessment: Outpatient Department

Newly Diagnosed Comprehensive Dental Assessment: Outpatient Department

No Dental Referral

See Flow Chart 2 For Details Regarding Dental Care During Chemotherapy

See Flow Chart 3 For Details Regarding Dental Care During Head and Neck Radiotherapy/ BMT

Flowchart 2: Dental Care During Chemotherapy

Flowchart 3: Dental Care During Head and Neck Radiotherapy/ BMT
PART B: Comprehensive Dental Assessment Including Caries Risk Assessment and Appropriate Recall

The paediatric oncology patient who is identified to be at risk of oral complications, presents with a number of individual considerations. The paediatric dentist plays a crucial role in supporting the oncology team by providing oral care, implementing and reinforcing oral care protocols/regimens, delivering emergency dental treatment and assisting in the management of oral complications (Hong & daFonseca 2008). Appropriate dental assessment requires an understanding of the patient’s diagnosis, intended oncology therapy and or surgical plan (Brennan et al 2008). The stage of growth and dental development of the patient at the time of oncology therapy can have a large influence on the presence and significance of late effects and thus also an influential factor in treatment planning decisions.

The AAPD (2013) states the following three objectives for the pre-treatment dental assessments in children diagnosed with cancer:

i) To identify and stabilise or eliminate existing and potential sources of infection and local irritants in the oral cavity; without needlessly delaying the cancer treatment or inducing complications;

ii) To communicate with the oncology team regarding the patient’s oral health status, plan, and timing of treatment; and

iii) To educate the patient and parents about the importance of optimal oral care in order to minimise oral problems/discomfort before, during, and after treatment and about the possible acute and late effects of the therapy in the oral cavity and craniofacial complex

This initial assessment determines whether there is any active dental disease. A thorough dental evaluation, involving both clinical and radiographic examination including assessment of intraoral soft tissues and bony structures is essential in the determination of dental disease and its urgency in treatment. Baseline records to monitor the effect of radiotherapy and/or chemotherapy on the oral / craniofacial and dental structures allow for future assessment of dental late effects following cancer therapy. Assessment for intraoral malignancy or leukaemic infiltrates also forms part of this assessment (Brennan et al 2008).

Important preventive advice and strategies are discussed and include discussions relating to both oral hygiene and diet. Advice is given regarding raising awareness of high cariogenic supplements and medications containing sucrose (AAPD 2013, Little 2008). A personalised fluoride program may be indicated (AAPD 2013). Trismus prevention can also be discussed where relevant (AAPD 2013).

Strategies to manage soft tissue changes (mucositis, bleeding, xerostomia and infections) in an attempt to decrease patient morbidity should be discussed. Individualised care with regard to prevention of candida and herpes simplex infections is recommended.

Dental Caries Risk Assessment

It is essential to determine an individual patient’s risk of developing dental caries to determine and implement an appropriate preventative and management system (Pitts et al 2011). Assessment of all factors involved in the disease process of dental caries helps to define a patient’s level of risk. This process is called caries risk assessment (CRA) and it is used to determine the probability that caries will occur in the future. CRA guides the clinician in decision making from the level of diagnostic procedures indicated, prevention and early intervention (Ramos-Gomez et al 2007; Jenson et al 2007).

For the purpose of the allocation of risk status among this population of patients undergoing active oncology therapy the Caries Management System (CMS) has been selected. The CMS was developed at The Department of Paediatric Dentistry, Women’s and Children’s Hospital, North Adelaide, South Australia.
University of Sydney and is described as a “10 step, risk based, non-invasive strategy to arrest and remineralise early lesions and enhance caries primary prevention” (Evans et al 2008). This system involves the assessment of each patient’s diet, plaque distribution, and signs of caries as shown in bitewing radiograph images (Evans & Dennison 2009).

### Table 2: 10 Step Summary of the Caries Management System

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Diet assessment</td>
</tr>
<tr>
<td>2.</td>
<td>Plaque assessment</td>
</tr>
<tr>
<td>3.</td>
<td>Bitewing radiographic survey</td>
</tr>
<tr>
<td>4.</td>
<td>Diagnosis and risk assessment</td>
</tr>
<tr>
<td>5.</td>
<td>Preparation of treatment plan</td>
</tr>
<tr>
<td>7.</td>
<td>Oral hygiene coaching</td>
</tr>
<tr>
<td>8.</td>
<td>Topical fluoride application (professional and home care)</td>
</tr>
<tr>
<td>9.</td>
<td>Monitoring of plaque control and treatment outcomes at each visit</td>
</tr>
<tr>
<td>10.</td>
<td>Recall program tailored to caries risk status</td>
</tr>
</tbody>
</table>

(Evans et al 2008)

The CMS is based on the principle that caries management needs to include consideration of the patient at risk, the status of each lesion, patient management, clinical management and monitoring (Evans et al 2008; Evans & Dennison 2009). The CMS determines caries risk of children and adolescents solely on the severity and extent of their presenting clinical and radiographic signs. Standardised scales; the ICDAS II and Mejare (1999) radiographic system is used to determine the extent of caries. Children are diagnosed as simply low risk or at risk (Evans & Dennison 2009).

The use of the CMS allows for the identification of those patients that are at caries risk from those that are not. Patients have an individualised prevention protocol implemented where appropriate. Caries management systems such as those developed by the ADA, AAPD and the CAMBRA system were not selected in this situation as they consider epidemiological factors that can complicate clinical application and also can group all children with special health care needs as high risk and thus does not allow for identification of those children at increased risk within this subpopulation (ADA 2011; AAPD 2014; Featherstone et al 2007). Grouping all patients as high risk and providing increased recall and prevention accordingly could add to patient burden and over treatment. The CMS also allows for reassessment at recall periods and transition of patients down to low risk or up to high risk accordingly (Evans & Dennison 2009). The table below summarises those paediatric patients that are low risk and at caries risk as per the CMS.
### Table 3: Determination of ‘Low’ and ‘At Risk’ Paediatric Patients with the CMS

<table>
<thead>
<tr>
<th>Age of Patient</th>
<th>Low Risk</th>
<th>At Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&lt;6 years of age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>New patient:</strong></td>
<td>• dmfs = 0</td>
<td>• dmfs &gt; 0</td>
</tr>
<tr>
<td></td>
<td>• ICDAS II &lt; 2</td>
<td>• Demineralised enamel, ICDAS II &gt; 1</td>
</tr>
<tr>
<td></td>
<td>• No radiolucencies</td>
<td>• Radiolucency in the outer half of enamel or greater</td>
</tr>
<tr>
<td></td>
<td>• No sites with plaque index = 3</td>
<td>• Sites with plaque index = 3, where dmfs = 0</td>
</tr>
<tr>
<td><strong>Recall patient:</strong></td>
<td>• &lt;1 new lesions per year</td>
<td>• &gt;1 new lesions per year</td>
</tr>
<tr>
<td></td>
<td>• No progression of existing lesions</td>
<td>• Progression of existing lesions</td>
</tr>
<tr>
<td><strong>&gt;6 years of age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>New patient:</strong></td>
<td>• dmfs + DMFS = 0</td>
<td>• dmfs + DMFS &gt;0</td>
</tr>
<tr>
<td></td>
<td>• ICDAS II &lt; 2</td>
<td>• Demineralised enamel, ICDAS II &gt;1</td>
</tr>
<tr>
<td></td>
<td>• No radiolucencies</td>
<td>• Radiolucency in the outer half of enamel or greater</td>
</tr>
<tr>
<td></td>
<td>• No sites with plaque index = 3</td>
<td>• Sites with plaque index = 3 where dmfs + DMFS = 0</td>
</tr>
<tr>
<td></td>
<td>• No hypomineralised or hypoplastic 6’s or 7’s</td>
<td>• Hypomineralised or hypoplastic 6’s or 7’s where dmfs + DMFS = 0</td>
</tr>
<tr>
<td><strong>Recall patient:</strong></td>
<td>• &lt;1 new lesions per year</td>
<td>• &gt;1 new lesions per year</td>
</tr>
<tr>
<td></td>
<td>• No progression of existing lesions</td>
<td>• Progression of existing lesions</td>
</tr>
</tbody>
</table>

(Evans & Dennison 2009)

Following the completion of the initial dental assessment and treatment as needed, the need for continued dental review and appropriate recall scheduling can be determined. At this point the type and intensity of oncology therapy planned becomes an influential factor. Patients that are having low intensity chemotherapy for a short duration do not require ongoing high frequency dental review. Such practice adds burden to the families and is not an efficient means of utilising hospital resources. Flow chart 2 below illustrates the process form the point of referral, through dental treatment to appropriate recall scheduling and or discharge of patients undergoing chemotherapy.
Patients that are undergoing radiotherapy and bone marrow transplants are at increased risk of oral complications. Flowchart 3 below describes the dental care provided to these patients. Both of the protocols rely on communication between the oncology and dental departments should patients have acute or chronic oral complications requiring dental assessment and management between recall periods.

**Flowchart 3: Protocol for Dental Care for Patients Undergoing Radiotherapy and Bone Marrow Transplant**

* Review period is to be selected based on clinical judgement and prevention program in place. More frequent review may be required for management of acute oral complications

**PART C: Implementation of a standardised oral care regime and recall period for those patients at risk of developing oral complications due to their planned oncology therapy and individual caries risk**

Oral hygiene and prevention such as fluoride, is not only important in the prevention of dental caries and gingivitis (Ayele et al 2013; Mackler & Crawford 1973). It is also recommended by the Multinational Association for the Supportive Care in Cancer Mucositis Study Group MASCC that oral care protocols be used to prevent oral mucositis in all age groups and across all cancer treatment modalities (Lalla et al 2014).

A standardised oral care regimen is essential to reduce the prevalence and severity of potential oral complications such as oral mucositis in patients undergoing oncology therapy (Cheng et al 2002; Cheng et al 2004; Hogan 2009; Qutob et al 2013). Systematic review performed by Qutob et al (2013) that assessed oral care protocols in relation to oral mucositis, five articles were found that supported the use of oral care
protocols to prevent oral mucositis in children. Of these five articles four reported a statistically significant reduction in the rates of occurrence of oral mucositis ranging from 22-40% (Qutob et al 2013; Cheng et al 2001; Cheng et al 2004; Cheng & Chan 2003). The severity of oral mucositis experienced is also reported to be reduced among those patients on an oral care protocol (Cheng et al 2001; Cheng et al 2004). It is essential to educate the patients and parents on the importance of oral hygiene and the benefits of preventative oral care to reduce oral complications (Hong & da Fonseca 2008; Petersen et al 2011; AAPD 2013).

Table 4 below describes the preventative oral care regimen that is recommended. This is based around the maintenance of dental health with good oral hygiene practices comprised of toothbrushing with age and caries risk appropriate fluoridated toothpastes and the use of 0.2% alcohol free chlorhexidine mouthrinse twice daily.

Patients are encouraged to brush at all times possible, despite haematological status and replace their toothbrush monthly. Only when brushing and rinsing is not possible jumbo probe swabs should be used to apply the 0.2% Alcohol Free Chlorhexidine mouthrinse. This oral protocol has been successfully implemented and had a reported compliance rate of 100% (Qutob et al 2013). Clinical success has also been observed with notable improvements in the children’s oral hygiene and reduction in severe oral mucositis (Qutob et al 2013).

Table 4: Women’s and Children’s Oral Care Protocol for Oncology Patients

| Dental Visits | Attend the paediatric dental department shortly after cancer diagnosis to assess child’s oral health prior to start of cancer therapy
|              | Attend follow up dental visits as determined by caries risk |
| Teeth Brushing | Brush teeth and tongue 2-3 times daily, each session lasting at least 2 minutes with a soft nylon toothbrush |
|              | Brushing should continue regardless of the child’s blood cell and platelet counts |
|              | Toothbrushes are to be air dried between uses |
|              | Replace tooth brush every month and/or after neutropenic cycle |
|              | Use super soft tooth brushes or oral sponges ONLY when the child cannot tolerate a toothbrush and should be soaked with aqueous 0.2% alcohol-free Chlorhexidine mouth rinse (regular teeth brushing with soft brush should resume once tolerated) |
|              | Use Small pea sized amount of 1000ppm fluoridated toothpaste to brush teeth in children over 18 months of age |
|              | - In children at high risk of dental caries fluoridated toothpaste may be introduced at an earlier age |
|              | - Children over 6 years of age at high risk of dental caries may be encouraged to use higher concentrations of fluoridated toothpaste or additional oral care products |
|              | - Use a mint-free tooth paste if the child has stinging sensation |
| Mouth Wash | Rinse 2 times daily with aqueous 0.2% alcohol-free Chlorhexidine mouth wash after brushing to reduce gum bleeding |
|            | NOTE: Infants or children, who are unable to rinse their mouths should use jumbo probes soaked in the recommended mouth wash |

The use of Chlorhexidine mouthrinse is somewhat controversial in the literature. Systematic review has reported mixed results for the use of chlorhexidine rinses in the prevention of oral mucositis in children.
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However, these studies did not necessarily report on the use of chlorhexidine rinse as part of an oral care protocol. There was evidence ranging from fair in support to insufficient to allow any conclusions to be drawn for its use (Qutob et al 2013). A chlorhexidine mouthrinse is recommended in an oral care regimen due to its antibacterial and antifungal properties (Fathilah et al 2012; Lanzos et al 2011; Epstein et al 1992). An alcohol free mixture is used in keeping with recommendations from MASCC that alcohol free rinses are used during periods of oral mucositis as alcohol containing rinses can be irritating to the oral tissues (Rubenstein et al 2004).

**Part D: Daily Assessment of the Oral Condition of All Patients at Risk of Developing Oral Mucositis**

A final component of the oral care protocol is the use of a standardised oral assessment scale. It is recommended that patients at risk of oral mucositis have daily oral assessments with a standardised oral assessment tool. The scale currently recommended is the ChIMES scale; to allow for patient reported outcomes, in addition to the WHO scale; for grading of severity of oral mucositis. Patient reported outcomes are becoming more prominent in cancer clinical trials, especially those that are involved with supportive cancer care. Successful clinical trials that assess the prevention and treatment of oral mucositis depend upon a reliable, valid and sensitive oral assessment instrument (Tomlinson et al 2010). See table 5 below for the ChIMES scale and WHO scale as used with this oral care protocol.

<table>
<thead>
<tr>
<th>Table 5: Standardised Daily Oral Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Assessment with ChIMES and WHO scale</strong></td>
</tr>
<tr>
<td><strong>1. Pain:</strong> Which one of the following faces best describes the pain from your mouth today?</td>
</tr>
<tr>
<td><img src="image" alt="Face Pain Rating" /></td>
</tr>
<tr>
<td><strong>2. Function:</strong> Which one of the following faces best describes how hard it is for you to swallow your saliva because of your sore mouth or throat today?</td>
</tr>
<tr>
<td><img src="image" alt="Face Function Rating" /></td>
</tr>
<tr>
<td><strong>3. Function:</strong> Which one of the following faces best describes how hard it is for you to eat because of your sore mouth or throat today?</td>
</tr>
<tr>
<td><img src="image" alt="Face Function Rating" /></td>
</tr>
</tbody>
</table>

**World Health Organisation Grading of Oral Mucositis**

<table>
<thead>
<tr>
<th>0</th>
<th>No symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sore mouth, +/- erythema, no ulceration</td>
</tr>
<tr>
<td>2</td>
<td>Erythema, ulcers, can tolerate a solid diet</td>
</tr>
<tr>
<td>3</td>
<td>Extensive erythema, ulcers, liquids only</td>
</tr>
<tr>
<td>4</td>
<td>Unable to eat or drink</td>
</tr>
</tbody>
</table>

Adapted from Tomlinson et al 2010

The ChIMES scale has been validated for use in the paediatric population (Tomlinson et al 2010; Tomlinson et al 2009). Implementation of a standardised means of recording the findings of oral assessments allows for the identification of patients that are affected by oral mucositis at an early stage and appropriate supportive therapies to be implemented. The WHO scale is also included in combination to allow for...
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grading of mucositis as possible. Compliance of utilisation of this scale by nursing staff has been reported to be up to 87% in prospective research (Qutob et al 2012).

Conclusion

A multidisciplinary approach is needed to provide paediatric oncology patients with the best possible treatment. A paediatric dentist is an important member of this team when patients are at increased risk of oral complications. The framework above provides a system by which the patients at risk of oral complications can be identified and a timely referral for dental assessment and management can be arranged. Caries risk assessment and setting of an appropriate recall program combined with a standardised basic oral care regimen and regular intraoral assessments are all crucial components in preventing, identifying and managing complications. These factors also allow for individualised prevention programs where indicated and for services to be targeted appropriately to maximise resources and decrease the appointment burden on low risk patients.

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