# Late and Acute Effects of Pediatric Cancer Therapy on the Oral Cavity

32

Christopher Rowland, Cesar A. Migliorati, and Sue C. Kaste

## Contents



**Abstract**

Pediatric cancer therapy has advanced to become curative for many types of cancer. The overall survival of patients treated for childhood cancer is now in the range of 90%. The May 2009 issue of the *Journal of Clinical Oncology* reported improved survival from about 30% in 1960 to 80% in 2004. An epidemiologic study (Mariotto et al. 2009) estimated that in the United States alone, there are more than 300,000 survivors of childhood cancer. However, this success has not come without a price. Pediatric cancer therapy is given during a time of growth, and late effects in the oral cavity can alter the growth and development of teeth and bones and affect overall health for the duration of a patient's life. The severity of these clinical and anatomical complications depends on tumor diagnosis, therapy exposure (chemotherapy, radiation, hematopoietic stem cell transplantation or a combination of several therapies), patient age and developmental status at the time of therapy and the resulting toxicity. In this chapter we will discuss some of the most important oral complications in pediatric oncology, with a focus on late effects of cancer and its treatment. Early complications will also be briefly described. Although the emphasis of this book is neurologic malignancy, oral complications occur in association with such malignancies because of the type of cancer therapy used. The prevention and management of these complications will be

C. Rowland (✉)
Division of Dentistry, Department of Surgery, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105, USA
e-mail: chris.rowland@stjude.org

C.A. Migliorati
University of Tennessee, Health Science Center, College of Dentistry, 857 Union Ave., suite N228, Memphis, TN 38163, USA
e-mail: migliorati@uthsc.edu

S.C. Kaste
Division of Diagnostic Imaging, Department of Radiological Sciences, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105, USA
e-mail: Sue.Kaste@stjude.org

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discussed, as well as the need for collaboration between dental providers and the oncology team for the improvement of outcomes.

## Introduction

Cancer therapies comprise chemotherapy, radiation, surgery and hematopoietic stem cell transplantation, used alone or in combination. Each can cause acute oral complications that can resolve after therapy or persist for many years (Brennan et al. 2010). In pediatrics, some of the complications affect the development of head and neck bones, cervical vertebral bodies, and oral cavity structures like the teeth and jaws (Kaste et al. 2009).

Chemotherapy can alter tissue development and integrity and can impair the function of oral tissues and salivary glands. This typically occurs during cancer treatment and usually resolves after therapy is discontinued (Majorana et al. 2000). Radiation therapy can cause the same effects, but part of the damage is permanent (Raney et al. 1999). Surgery physically alters craniofacial function and the physical appearance of the patient. High-dose chemotherapy and irradiation of the head and neck area can cause serious ulcerative lesions (oral mucositis). This acute toxicity of the oral soft tissues can be so severe that it requires modification or discontinuation of cancer treatment, thereby potentially affecting prognosis (Sonis 2009). Unlike the acute effects of therapy described above, late oral cavity effects in the pediatric population are usually related to altered growth and development of craniofacial structures and teeth (Kaste et al. 2009; Raney et al. 1999; van der Pas-van Voskuilen et al. 2009). In addition, salivary gland dysfunction, leading to a decrease in salivary secretion, increases the risk of caries and periodontal disease (Hong et al. 2010). The main factors that determine the severity of oral cavity effects are the patient's age, the toxicity of high-dose chemotherapy, the dosing and duration of radiation therapy and the anatomic areas of the head and neck that are irradiated. Severe late effects after hematopoietic stem cell transplantation include graft versus host disease, increased risk of secondary malignancies of the oral cavity, and adverse psychosocial complications (Bhatia et al. 2007; Curtis et al. 1997; Ferry et al. 2007; Leahey et al. 1999).

The oral cavities of pediatric patients can be devastated by cancer therapy due to high cell turnover. It has been reported that more than half of patients treated for rhabdomyosarcoma with multiagent chemotherapy developed dental toxicities (Kaste et al. 1995). Additional evidence has shown that 70% of patients who received chemotherapy for nephroblastoma were found to be at risk of dental sequelae (Marec-Berard et al. 2005). In another study, it was reported that 70% of children treated with chemotherapy, irradiation of the head and neck or hematopoietic stem cell transplantation (HSCT) for neuroblastoma developed dental abnormalities (Kaste et al. 1998). Other authors have found that among a group of children who underwent head and neck radiation therapy for rhabdomyosarcoma, 11/30 (~30%) experienced facial growth deficiencies and 7/30 (~20%) experienced dental abnormalities (Paulino et al. 2000). A study of long-term survivors of childhood cancer reported that patients with central nervous system tumors, neuroblastoma, and soft tissue sarcomas had the highest risk of oral cavity abnormalities (Kaste et al. 2009). Therefore, oral cavity and head and neck complications affect children treated for cancer. The severity and duration of these complications depend on the toxicity of the therapy used, the age of the children and the developmental stage of the skeleton, head and neck, and oral cavity structures. Below we will discuss pediatric oral cavity considerations before, during, and after cancer therapy, with an emphasis on late complications.

## Oral Considerations Before Cancer Therapy

The oral cavity and oral structures should be evaluated before the start of cancer therapy so that the dentist can diagnose and treat existing oral/dental disease and implement interventions

**Table 32.1** Checklist of pre-therapy oral considerations

| |
|---|
| Oral examination by dental team |
| Radiographic evaluation |
| Oral hygiene instructions (brushing, flossing, fluoride, etc.) |
| Prescription of prophylactic agents (fluoride, mouth rinse, saliva substitutes, etc.) |
| Nutritional counseling (sugar intake, balanced meals, etc.) |
| Review of oral complications associated with planned cancer therapy |
| Optimization of oral health (caries control, dental extractions, treatment of infections) |
| Orthodontic appliance risk assessment |

to prevent or minimize oral complications. Collaboration between the dental and oncology teams is important in facilitating this preliminary evaluation. Depending on the type of cancer therapy that is going to be used and the expected toxicity, a proper dental care can be optimized for each patient. For example, the decision as to whether or not to extract teeth can be made by weighing expected toxicity and the risk of having to perform an emergency extraction of a decayed tooth during the myelosuppressive phase of cancer therapy. Thus, restorable decayed teeth could be immediately treated and teeth that are infected and non-restorable could be extracted before the patient becomes immunosuppressed or radiation therapy involving the oral cavity begins. In addition, oral hygiene education of both parents and children with focus on the importance of maintaining oral health during and after therapy can significantly improve treatment outcomes (Table 32.1).

Common effects of cancer therapy observed during treatment include oral mucositis, infections and bleeding. Early detection and control of oral disease is important to reduce the risk of acute dental and periodontal disease activation during myelosuppressive periods, improve the outcome of cancer therapy, and improve patient quality of life. When patients are treated with radiation therapy to the head and neck, the oral tissues should be protected and shielded. For example, the use of lead shields and collars can shield almost all oral structures from the radiation beam in patients with nasopharyngeal carcinoma. New radiation protocols using intensity-modulated radiation therapy protect and spare vital structures like the salivary glands from the radiation beam. Preventing radiation damage of the oral tissues can reduce oral sequelae (Peterson et al. 2010).

When oral complications like mucositis and xerostomia emerge during radiation therapy, oral intervention cannot always be completed. Ideally, patients should be screened before the start of radiation therapy. Potential or active lesions such as dental caries, abscesses, and ulcerations can be diagnosed and treated. Teeth that cannot be saved can be extracted. Plaque that accumulates on the tooth surface is composed of bacteria and its byproducts and is a source of infection that should be professionally removed.

During high-dose radiation therapy involving the craniofacial structures, normal blood flow and tissue oxygenation are compromised. Thus, the third molars (already developed in teenagers and young adults) and severely decayed teeth, which could become an additional source of plaque accumulation and infection during or after therapy, should be extracted before therapy starts. Such surgical procedures are contraindicated after radiation therapy has compromised tissue healing and imposed the risk of osteoradionecrosis.

There is an additional risk of oral complications if orthodontic appliances are not removed before cancer therapy. They can be a source of dental plaque build-up, making oral hygiene difficult. Therefore, the removal of orthodontic appliances should be considered, especially if treatment is expected to be myelosuppressive. Ideally, appliances should be removed a week before pre-transplant conditioning or initiation of radiation.

Oral hygiene procedures, specific oral hygiene products, and fluoride use should be discussed with patients and parents. There is increasing evidence that the use of high-dose fluoride in association with calcium phosphate increases the protection of tooth structures against demineralization (Papas et al. 2008). Implementation of an oral hygiene protocol will help to protect against the deleterious effects of impaired salivary gland function and reduced salivary secretion (Jensen et al. 2010).

If cancer therapy must be started urgently, pre-treatment evaluation of the oral cavity and optimization of oral health may not be possible. Recommended oral hygiene procedures should be made available to parents and oncology staff members and implemented as soon as possible. Although hygiene recommendations alone are not ideal for oral health prognosis, good hygiene will reduce the oral bacterial load and enhance tooth resistance against demineralization. Routine dental care can continue as the patient's health status improves after the completion of cancer therapy.

## Oral Considerations During Cancer Therapy

The oral care team plays an important role in the prevention and management of oral complications (McGuire et al. 2006). It is important that patients maintain good oral hygiene throughout cancer therapy to reduce the risk of oral complications, including dental caries, periodontal disease and infection. During active therapy, the dental team has limited interaction with the patient, and physicians and nurses are more likely to note changes in the oral cavity. Routine patient evaluations should include attention to oral hygiene and evaluation of the oral cavity for complications. The medical staff can also encourage the patient and parents to maintain daily hygiene procedures. High-dose chemotherapy and radiation can lead to the development of acute oral complications such as dental or periodontal infection, bleeding, dryness and mucositis. When these complications are diagnosed, the oral care team should be advised so that the complications can be addressed promptly (Table 32.2).

Prevention and management of oral mucositis can be a challenge. Oral mucositis can be so severe as to limit the administration of cancer treatment, thus increasing the risk of an adverse treatment outcome and potentially death (Sonis 2005). Oral mucositis is frequently accompanied by bleeding and offers oral bacteria an entryway into the systemic circulation, thus placing immunosuppressed patients at risk of life-threatening infection. Oral mucositis can also be intensely painful and distressing. Patients may have difficulty eating, swallowing and performing oral hygiene. When severe oral toxicity is expected (as in hematopoietic stem cell transplantation), patient-controlled analgesia (PCA) with morphine can be initiated (Keefe et al. 2007). After 2–3 weeks of therapy (radiation or chemotherapy), patients may experience dryness of the mouth. This uncomfortable symptom can also influence oral health and eating habits. Thus, minimizing the risk of oral complications and diagnosing them early is of great importance (Table 32.3).

**Table 32.2** Observation of the oral cavity by medical staff: What to look for

| |
|---|
| Ability to swallow, eat solids and/or drink liquids |
| Mouth pain, oral discomfort, bleeding |
| Color and consistency of saliva |
| Oral mucosa: soreness, redness, ulcers, lesions and dryness |
| Scalloped tongue |
| Signs of infection (e.g., herpes simplex, candidiasis) |

**Table 32.3** Evaluation of the oral cavity during cancer therapy

| |
|---|
| Examination by dental team every 3–6 months |
| Radiographic evaluation (as recommended by the ADA) |
| Monitor salivary function |
| Emphasize oral hygiene instructions (brushing, flossing, etc.) |
| Monitor therapeutic agents and prescribe other therapies as needed |
| Review nutritional counseling |
| Discuss dental complications of therapy if noted |
| Correct dental caries and infections |

*ADA* American Dental Association

## Oral Considerations After Cancer Therapy

After completion of cancer treatment, children may experience problems with teeth, gingival tissue, salivary glands, and bone. Chemotherapy and radiation can cause long-term effects in the oral

cavity, but the risk of acute oral complications from high-dose chemotherapy decreases with bone marrow recovery. Pediatric patients who undergo HSCT receive immunosuppressive therapy for prolonged periods, increasing the risk of opportunistic infections in the oral cavity. Additional complications after high-dose chemotherapy include chronic salivary gland dysfunction and dryness, graft-versus-host disease and second primary tumors of the oral cavity (Demarosi et al. 2005).

Age is an important factor in the development of oral complications; the younger the patient, the greater the risk. The detrimental effect of therapy is caused by inhibition of the normal development of the oral structures, which include teeth, bone, temporomandibular joint, muscles of mastication, salivary glands, and oral mucosa (Holtta et al. 2005a, b).

## Complications Affecting the Teeth

Odontogenic complications may affect different parts of the tooth structure (Fig. 32.1). The crown is composed of the enamel (outer surface) and dentin (internal portion). The root is composed of cementum (outer surface) and dentin (internal portion). The root canal is the space that contains the nerve and blood vessels within the tooth structure. When therapy is administered during the development of dentition, developmental arrest or defects in all three structures (crown, root, root canal) may result. This interruption in development can lead to partial development or complete absence of the tooth (Table 32.4).

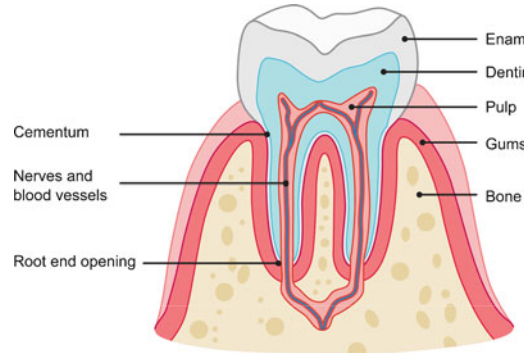


**Fig. 32.1** Structural diagram of a tooth

Normal tooth development involves the formation of a primary set of teeth that exfoliate between the ages of 6 and 12 years of age and are replaced by the permanent teeth. When the primary teeth are affected by cancer therapy, the permanent teeth may still develop normally. Panorex films show the developing dentition in Fig. 32.2 and Fig. 32.3. Figure 32.2 is a panorex of the normal developing dentition of a 6 year old. Figure 32.3 is a normal panorex of a teenage patient. During development of the enamel or dentin, oncotherapeutic exposures can adversely affect crown development, causing hypocalcification of the tooth structure, defects in the surface, and anatomical malformation. Clinically, these effects appear as discoloration, malformation,

**Table 32.4** Late effects in the oral cavity after therapy

| Disease | Dental sequelae | % | Source |
|---|---|---|---|
| Rhabdomyosarcoma | Root stunting | 54 | Kaste et al. (1995) |
| | Microdontia | 23 | |
| | Hypodontia | 50 | |
| | Multiple issues | 36 | |
| | Cosmetic or functional | 23 | |
| Nephroblastoma | Root stunting | 44 | Marec-Berard et al. (2005) |
| | Enamel hypoplasia | 22 | |
| | Microdontia | 18 | |
| | Hypodontia | 7 | |
| Neuroblastoma | Caries | | Hutton et al. (2010) |
| | Microdontia (below 3.5 years old) | | |

Adapted from Lopes et al. (2006)

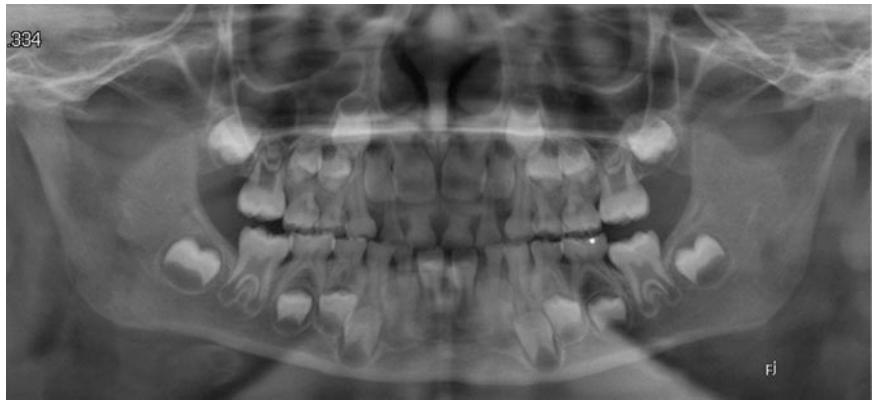

**Fig. 32.2** Panorex of a 6 year old showing normal mixed dentition. The patient underwent placement of a small restoration in left mandibular second primary molar

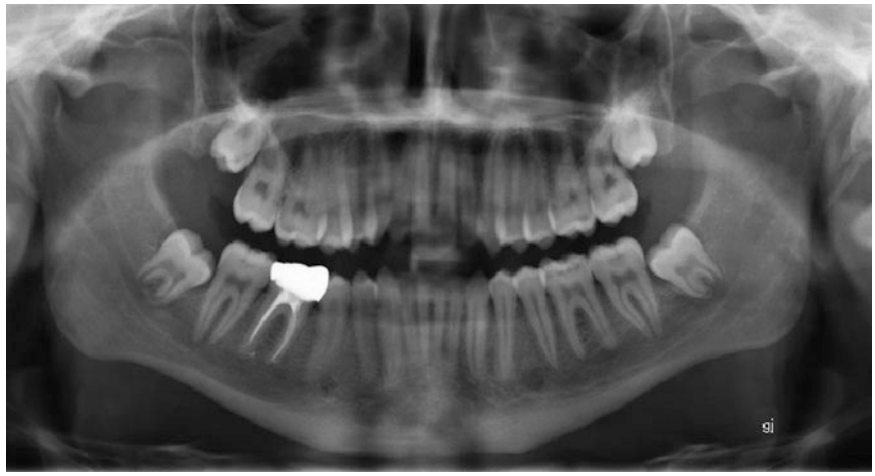

**Fig. 32.3** Normal panorex of a teenager. Patient has undergone root canal therapy and placement of a crown right mandibular first molar

and abnormal size of the tooth (Holtta et al. 2002). When the tooth structure is compromised, formation of dental caries is facilitated. For example, patients less than 3.5 years of age who undergo HSCT for lymphoma and solid tumors, particularly neuroblastoma, have teeth that are microdontic (small) and show a significant number of caries (Hutton et al. 2010) Caries can be exacerbated by xerostomia if the salivary glands and secretion of saliva are affected in patients treated with high-dose chemotherapy and radiation therapy (Fig. 32.4).

When a tooth erupts into the oral cavity, problems can be identified and treated upon visual evaluation of the crown structure. Radiographs are the most effective tools to assess the development of root structure and pulpal tissue. Developmental defects of the root can be devastating and can go unnoticed in the absence of radiographic evaluation. Some of these defects include root stunting, "thistle tube-like" malformation and dilacerations (Fig. 32.5). Root stunting is the most destructive effect, as it disrupts dental eruption patterns and can cause future loss of the tooth (Duggal 2003; Vaughan et al. 2005). Root stunting also interferes with orthodontic treatment, as the underdeveloped root structures

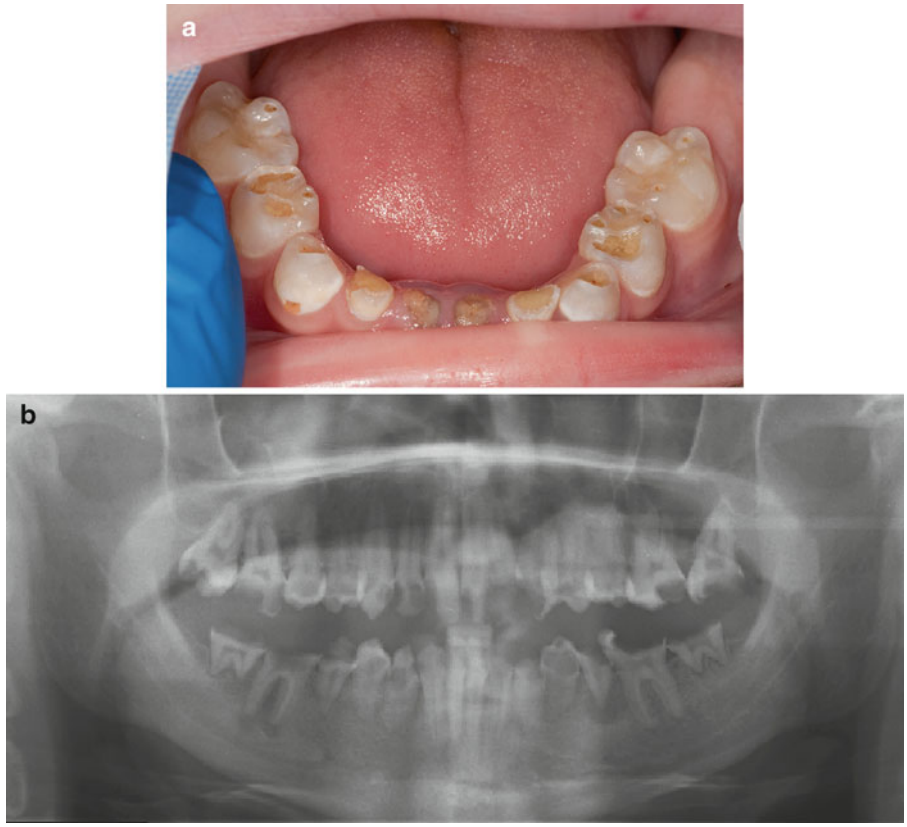


**Fig. 32.4** Clinical (**a**) and radiographic (**b**) aspects of severe tooth decay associated with radiation therapy and xerostomia

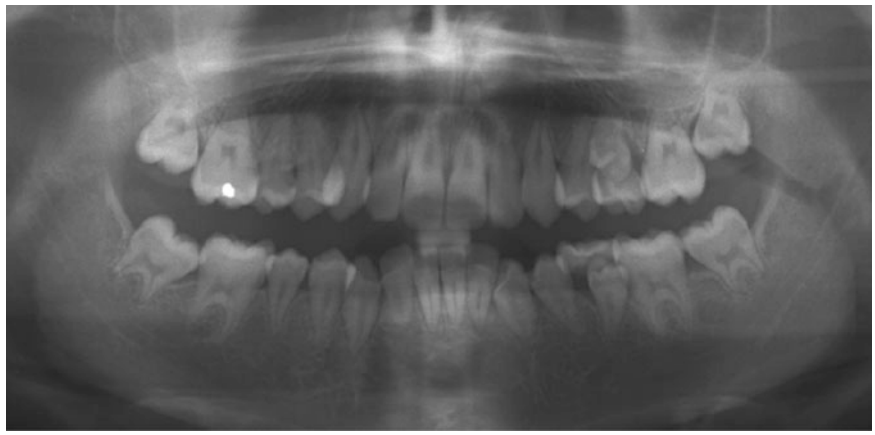

**Fig. 32.5** Panoramic radiograph showing root stunting (arrested tooth development)

may be inadequate for secure fixation of an orthodontic appliance.

The pulpal tissue and the root canal can be adversely affected in a number of ways. The canal can be obliterated and enlarged, and the dental pulp can become necrotic. If the dental pulp becomes necrotic the existing obliteration of the pulp chamber will make the necessary root canal therapy impossible. As a consequence, the tooth will have to be extracted. Taurodontism is an abnormality commonly noted after therapy of young patients (Lopes et al. 2006). This abnormality is a benign elongation of the body of the root canal chamber. However, necrosis of the pulp can be a rare complication.

## Complications of Bones of the Head and Neck

The bone structure of the oral cavity is composed of the maxilla and mandible. These structures are best evaluated through imaging such as panoramic radiographs and cephalometric studies. The panoramic view will reveal bone density, bone height, and general development from a frontal view, whereas the cephalometric film shows growth and deficits of the mandible and maxilla (Fig. 32.4).

The maxilla and mandible can be affected independently during radiation therapy, depending on the anatomic distribution and scatter of the radiation beam. In children, for example, some retardation of growth may result from doses as low as 10 Gy, depending upon the age at irradiation and the conditions of exposure. Other skeletal changes have been observed after therapeutic irradiation in childhood at doses exceeding 20 Gy. However, the susceptibility of these tissues to subsequent trauma months or years later may be increased, but precise dose-response data for such long-term effects are fragmentary (International Commission on Radiological Protection 1984). The area primarily affected by radiation therapy is that included in the radiation ports. Shielding of vital areas in the head and neck prior to radiation can help to prevent future complications. The treatment of rhabdomyosarcomas of the head and neck with multiagent chemotherapy can result in defects that require orthodontic and structural correction in 23% of patients (Kaste et al. 1995). Radiation therapy to the head and neck can cause deficient mandibular growth leading to retrognathia, while irradiation of the sinus cavity can cause maxillary hypoplasia. Because the opposing mandible will develop normally, bone development will show a discrepancy that may necessitate future orthodontic therapy and, in severe cases, orthognathic surgery to correct jaw positioning and occlusion. If altered jaw formation is noted, referral to an orthodontist for evaluation is recommended (Estilo et al. 2003).

Irradiated bone can pose a problem when tooth extraction is needed. Patients who have received more than 50 Gy of radiation to the head and neck are at risk of osteoradionecrosis (ORN). When invasive dental procedures like dental extractions or surgery involving bone manipulation are needed in areas within the radiation fields, the use of hyperbaric oxygen therapy (HBO) could reduce the risk of ONR. The usual HBO protocol is 20 hyperbaric chamber treatments of 90 min each before oral surgery and ten treatments afterward. However, it must be considered that this protocol is still in search of scientific support (Peterson et al. 2010). The overall risk of ORN of the jawbones is low but may persist indefinitely. The mandible is at higher risk because of its limited blood supply.

Osteonecrosis of the jaw is observed in cancer patients with skeletal metastasis of solid tumors (breast, prostate, and lung) and multiple myeloma as well as in patients with osteoporosis who take bisphosphonates. Bisphosphonates do not appear to affect the pediatric population in this manner; no pediatric cases have been reported to date (Brown et al. 2008).

Like other joint structures, the temporomandibular joint may be affected by radiation. Some of the complications are trismus, joint adhesion, and joint necrosis. The main functional complication is trismus, or limited opening of the jaw. Trismus hinders oral hygiene, compromises the patient's ability to eat and masticate properly, and interferes with dental treatment. The muscles of mastication can also

be affected, with the development of scar tissue. Physical therapy can improve mouth opening and the range of motion of the jaw. All of these developmental complications affect the overall health and quality of life of the patient. Maintaining good oral and maxillofacial function is important for eating, swallowing, speech, and good oral hygiene.

## Complications Associated with Saliva and Salivary Glands

Salivary gland function and saliva production can be severely affected by cancer therapy (Jensen et al. 2010). Chemotherapy typically affects the glands during treatment, and dryness of the oral cavity can persist for a short time after completion of treatment. Progressive improvement may lead to complete normalization of gland function and saliva production. However, xerostomia is a serious problem for patients after irradiation of the head and neck that involves the salivary glands. The dose of radiation and the extent of glandular involvement determine whether normal function and saliva production can be restored. Among its multiple functions, saliva is a natural cleansing agent of the oral mucosal tissues and teeth. Salivary buffering capacity maintains a neutral ph, protecting teeth from the acidity of sugars (Sreebny 2000). When salivary glands are functionally impaired and saliva production is decreased or absent, an acidic oral environment that is detrimental to the teeth can develop. Patients with dry mouth after radiation therapy are at very high risk of caries, which can be rampant (Fig. 32.4) and affect every tooth in the mouth (Purdell-Lewis et al. 1988). This condition is very difficult to treat and usually leads to complete tooth loss and the need for dentures. Thus, attention should be paid to the salivary glands and saliva production before cancer therapy begins, especially if radiation therapy of the head and neck that involves the salivary glands is necessary. During the pre-treatment evaluation, patients must be educated about the importance of maintaining good oral hygiene during cancer treatment and for life. Preventive measures include good oral hygiene even during therapy, the use of saliva substitutes, alcohol-free mouth rinses, and non-irritating toothpastes with high fluoride content. There is, however, no substitute for good brushing techniques and regular follow-up at the dental office. The patient must understand that more frequent visits to the dentist are needed during therapy. The dentist has the important role of early detection and treatment of dental and other oral problems and monitoring their progression.

In addition to good oral hygiene and periodic follow-up visits to the dentist, other issues must also be considered. Dental visits should be more frequent than that for general pediatric populations. Access to dental care maybe limited for patients with low income, less education, and no medical insurance (Casillas et al. 2010). Patients who have completed cancer therapy are likely to be in these categories. Further, in some cases, dentists may decline to treat cancer patients due to lack of adequate training. Thus, lack of access to dental care may lead to the long-term failure of a patient's oral and dental health after cancer therapy (Kaste et al. 2009).

## References

Bhatia S, Francisco L, Carter A et al (2007) Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: report from the bone marrow transplant survivor study. Blood 110(10):3784–3792

Brennan MT, Elting LS, Spijkervet FK (2010) Systematic reviews of oral complications from cancer therapies, oral care study group, MASCC/ISOO: methodology and quality of the literature. Support Care Cancer 18(8):979–984

Brown JJ, Ramalingam L, Zacharin MR (2008) Bisphosphonate-associated osteonecrosis of the jaw: does it occur in children? Clin Endocrinol 68(6):863–867

Casillas J, Castellino SM, Hudson MM et al (2010) Impact of insurance type on survivor-focused and general preventive health care utilization in adult survivors of childhood cancer: the childhood cancer survivor study (CCSS). Cancer 117(9):1966–1975

Curtis RE, Rowlings PA, Deeg HJ et al (1997) Solid cancers after bone marrow transplantation. N Engl J Med 336(13):897–904

Demarosi F, Lodi G, Carrassi A et al (2005) Oral malignancies following HSCT: graft versus host disease and other risk factors. Oral Oncol 41(9):865–877

Duggal MS (2003) Root surface areas in long-term survivors of childhood cancer. Oral Oncol 39(2):178–183

Estilo CL, Huryn JM, Kraus DH et al (2003) Effects of therapy on dentofacial development in long-term survivors of head and neck rhabdomyosarcoma: the memorial sloan-kettering cancer center experience. J Pediatr Hematol Oncol 25(3):215–222

Ferry C, Gemayel G, Rocha V et al (2007) Long-term outcomes after allogeneic stem cell transplantation for children with hematological malignancies. Bone Marrow Transplant 40(3):219–224

Holtta P, Alaluusua S, Saarinen-Pihkala UM et al (2002) Long-term adverse effects on dentition in children with poor-risk neuroblastoma treated with high-dose chemotherapy and autologous stem cell transplantation with or without total body irradiation. Bone Marrow Transplant 29(2):121–127

Holtta P, Alaluusua S, Saarinen-Pihkala UM et al (2005a) Agenesis and microdontia of permanent teeth as late adverse effects after stem cell transplantation in young children. Cancer 103(1):181–190

Holtta P, Hovi L, Saarinen-Pihkala UM et al (2005b) Disturbed root development of permanent teeth after pediatric stem cell transplantation. Dental root development after SCT. Cancer 103(7):1484–1493

Hong CH, Napenas JJ, Hodgson BD et al (2010) A systematic review of dental disease in patients undergoing cancer therapy. Support Care Cancer 18(8):1007–1021

Hutton A, Bradwell M, English M et al (2010) The oral health needs of children after treatment for a solid tumour or lymphoma. Int J Paediatr Dent 20(1): 15–23

ICRP (1984) Principles for limiting exposure of the public to natural sources of radiation. ICRP publication 39. Ann ICRP 14(1):1–8. http://www.icrp.org/publication.asp?id=ICRP%20Publication%2039

Jensen SB, Pedersen AM, Vissink A et al (2010) A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: management strategies and economic impact. Support Care Cancer 18(8):1061–1079

Kaste SC, Hopkins KP, Bowman LC (1995) Dental abnormalities in long-term survivors of head and neck rhabdomyosarcoma. Med Pediatr Oncol 25(2): 96–101

Kaste SC, Hopkins KP, Bowman LC et al (1998) Dental abnormalities in children treated for neuroblastoma. Med Pediatr Oncol 30(1):22–27

Kaste SC, Goodman P, Leisenring W et al (2009) Impact of radiation and chemotherapy on risk of dental abnormalities: a report from the childhood cancer survivor study. Cancer 115(24):5817–5827

Keefe DM, Schubert MM, Elting LS et al (2007) Updated clinical practice guidelines for the prevention and treatment of mucositis. Cancer 109(5): 820–831

Leahey AM, Teunissen H, Friedman DL et al (1999) Late effects of chemotherapy compared to bone marrow transplantation in the treatment of pediatric acute myeloid leukemia and myelodysplasia. Med Pediatr Oncol 32(3):163–169

Lopes NN, Petrilli AS, Caran EM et al (2006) Dental abnormalities in children submitted to antineoplastic therapy. J Dent Child (Chic) 73(3):140–145

Majorana A, Schubert MM, Porta F et al (2000) Oral complications of pediatric hematopoietic cell transplantation: diagnosis and management. Support Care Cancer 8(5):353–365

Marec-Berard P, Azzi D, Chaux-Bodard AG et al (2005) Long-term effects of chemotherapy on dental status in children treated for nephroblastoma. Pediatr Hematol Oncol 22(7):581–588

Mariotto AB, Rowland JH, Yabroff KR et al (2009) Long-term survivors of childhood cancers in the United States. Cancer Epidemiol Biomarkers Prev 18(4):1033–1040

McGuire DB, Correa ME, Johnson J et al (2006) The role of basic oral care and good clinical practice principles in the management of oral mucositis. Support Care Cancer 14(6):541–547

Papas A, Russell D, Singh M et al (2008) Caries clinical trial of a remineralising toothpaste in radiation patients. Gerodontology 25(2):76–88

Paulino AC, Simon JH, Zhen W et al (2000) Long-term effects in children treated with radiotherapy for head and neck rhabdomyosarcoma. Int J Radiat Oncol Biol Phys 48(5):1489–1495

Peterson DE, Doerr W, Hovan A et al (2010) Osteoradionecrosis in cancer patients: the evidence base for treatment-dependent frequency, current management strategies, and future studies. Support Care Cancer 18(8):1089–1098

Purdell-Lewis DJ, Stalman MS, Leeuw JA et al (1988) Long term results of chemotherapy on the developing dentition: caries risk and developmental aspects. Community Dent Oral Epidemiol 16(2):68–71

Raney RB, Asmar L, Vassilopoulou-Sellin R et al (1999) Late complications of therapy in 213 children with localized, nonorbital soft-tissue sarcoma of the head and neck: a descriptive report from the intergroup Rhabdomyosarcoma studies (IRS)-II and - III. IRS group of the Children's cancer group and the pediatric oncology group. Med Pediatr Oncol 33(4):362–371

Sonis S (2005) New trends in the management of oral mucositis. J Natl Compr Canc Netw 3(Suppl 1): S54–S56

Sonis ST (2009) Mucositis: the impact, biology and therapeutic opportunities of oral mucositis. Oral Oncol 45(12):1015–1020

Sreebny LM (2000) Saliva in health and disease: an appraisal and update. Int Dent J 50(3):140–161

Van der Pas-van Voskuilen IG, Veerkamp JS, Raber-Durlacher JE et al (2009) Long-term adverse effects of hematopoietic stem cell transplantation on dental development in children. Support Care Cancer 17(9):1169–1175

Vaughan MD, Rowland CC, Tong X et al (2005) Dental abnormalities after pediatric bone marrow transplantation. Bone Marrow Transplant 36(8):725–729