Republic of Iraq

Ministry of Higher Education

and Scientific Research

University of Baghdad

College of Dentistry

Oral and Dental Consideration in Pediatric Cancer Patient

A Project Submitted to

The College of Dentistry, University of Baghdad,

Department of Pedodontics and Prevention Dentistry in Partial Fulfillment

for the Bachelor of Dental Surgery

By

Maryam Salah Abdul Mahdi

Supervised by:

Assist. Lec. **Noor Mohammed Hassan**

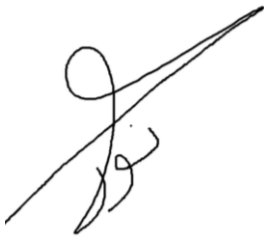
(B.D.S., M.Sc.)

(April, 2022) ١٤٤٣ هـ

Certification of the Supervisor

I certify that this project entitled "Oral and Dental Consideration in Pediatric Cancer Patient" was prepared by the fifth-year student **Maryam Salah Abdul Mahdi**, under my supervision at the College of Dentistry/ University of Baghdad in Partial Fulfillment of the graduation requirements for the Bachelor Degree in Dentistry.

Assist. Lec. Noor Mohammed Hassan



4/7/2022

Dedication

I dedicate this work to God,

my creator, my strong pillar, my source of inspiration and wisdom.

To Mom & dad,

Thank you for raising me to believe in God, myself and in my dreams.

To my family members

For teaching me to believe that everything is possible.

To my best friends

For making the world a better place, just by being in it...

Acknowledgment

First of all, I thank “Allah” almighty for granting me the will and strength to accomplish this project, and I pray that his blessings upon me may continue throughout my life, without “Allah”, I would not have had the wisdom or the physical ability to do so.

Deep thanks to **Prof. Dr. Raghad Abdulrazzaq Al-Hashimi**, Dean of the College of Dentistry, University of Baghdad, for his support to accomplish this project.

Deep thanks to **Prof Dr. Ali I. Al-Bustani**, the associate dean for scientific affairs.

I am indeed internally thankful to **prof. Dr. Ahlam Taha**, Head of the Department of pedodontics and Prevention, for her kindness and encouragement.

I would like to thank my supervisor **Assist. Lec. Noor Mohammed Hassan**, for her continuous guidance, generous advice, encouragement and wise supervision.

My great appreciation and thanks to **Assist. Lec. Mohammed k. Salih** for his kind effort and help.

Finally, thanks to all of the teaching staff of the Department of pedodontics and Prevention.

Table of Contents

List of Figures

List of Abbreviations

Abbreviation	Description
AAPD	American Academy of Pediatric Dentistry
ALL	Acute Lymphoblastic Leukemia
AML	Acute Myeloid Leukemia
ANC	Absolute Neutrophil Count
ANLL	Acute Non-Lymphoblastic Leukemia
CBC	Complete Blood Count
CML	Chronic Myeloid Leukemia
CSF	Cerebrospinal Fluid
CT	Computed Tomography
DNA	Deoxyribonucleic Acid
HBO	Hyperbaric Oxygen
HSCT	Hematopoietic Stem Cell Transplantation
ICCC	International Classification of Childhood Cancer
MRI	Magnetic Resonance Imaging
ORN	Osteoradionecrosis
PET	Positron Emission Tomography
RNA	Ribonucleic Acid
WHO	World Health Organization

Introduction

Oral health care is an integral part of interprofessional collaborative care for children and adolescents diagnosed with cancer **(Ritwk and Chrisentery, 2020)**. According to the World Health Organization (WHO), cancer will still be the top cause of mortality in children and adolescents. The chances of surviving a cancer diagnosis vary by country, in such a way that more than 80% of children with cancer were cured in high-income countries whereas in many low and middle-income countries, less than 30% were treated **(Lam *et al.*, 2019; WHO, 2021).**

The sequence of oral care prior to, during, and following cancer therapy consists of disease diagnosis together with dental examination/diagnosis and management of common oral diseases in the preparation for preventing and treating cancer. The type of cancer treatment and any probable oral side effects will determine the patient's follow-up plan **(Epstein *et al.*, 2012; Ray-Chaudhuri *et al.*, 2013).**

Baseline oral and dental health assessment should be received for children diagnosed with cancer before the initiation of cancer therapy in order to prevent debilitating complications during the immunosuppressed phase. Palliative care and treatment for mucositis, opportunistic oral infections, pain, and other oral complications associated with cancer therapy should be provided as necessary. Thus, pediatric dentists and pediatric oncology teams should work together for screening and treating dental and oral diseases **(Ritwik and Chrisentery, 2020).**

According to American Academy of Pediatric Dentistry (AAPD) Immunosuppressive therapy may cause many acute and long-term side effects in the oral cavity. Furthermore, any potential sources of dental infections and/or soft tissue trauma can compromise the medical treatment, leading to morbidity, mortality, and higher hospitalization costs. Therefore, it is imperative that the

pediatric dentist be familiar with the patient's medical history as well as oral manifestations of the underlying condition **(American Academy of Pediatric Dentistry, 2021).**

Aim of the Project

The goal of this project is to highlight the importance of oral and dental assessment in identifying, preventing, stabilizing, and treating oro-dental side effects that might affect a child's quality of life before, during, and after cancer therapy.

Review of Literature

1. Cancer

Childhood cancer is the world's 2nd most common cause of death among children. Cancer is a group of diseases in which cells divide continuously and excessively. There are many cancer types, usually categorized either by the type of cell from which the cancer originated or by the part of the body from which the abnormal cell originated. These cancer cells can penetrate nearby tissues and can migrate to other parts of the body via the blood or lymph systems **(Anjuga and Malathy, 2020; Matthews *et al.*, 2022)**.

The global burden of childhood cancer is a major health issue. Every year, almost 100 000 children die from cancer before the age of 15 years **(Sullivan *et al.*, 2013)**.

2. Factors Affecting the Incidence of Childhood Cancers

• Race

Race is the determining factor in cancer susceptibility. Black children show a lower frequency than white because pigmentation is obviously protective against UV-induced cancers **(Özdemir et al., 2017)**.

• Age

Age is an important independent unfavorable prognostic factor. Indeed, multiple studies have found that the older a person is, the greater the danger of dying from cancer **(Garinet et al., 2022)**.

• Gender

Boys are more affected than girls. Male to female ratio is 55% to 45% **(Hunger and Mullighan, 2015)**.

• **Developmental status**

Approximately 90% of cancers occur in low and middle-income countries, where health systems are generally poor, and malignancies go misdiagnosed and untreated as a result **(World Health Organization, 2021)**.

3. Causes of Childhood Cancer

The roots of childhood cancer are poorly investigated, although different forms of cancer are usually believed to have different causes. These are some of the established risk factors for childhood cancer development including (**Muresanu and khalchitsky, 2022**);

• **Genetic Factor**

Family history of cancer is an important factor to assess. The inherited genes can be transmitted from parent to child. Chemo- and radiotherapy have been linked to an increase in genetic risk in people who have previously had cancer.

• **Physical Factor**

Exposure to UV light, chronic viral infection and extremely high-frequency radiation (e.g., X-rays, gamma rays, and other diagnostic rays) all of these factors contribute to Deoxyribonucleic acid (DNA) alterations, which can lead to cancer.

• **Additional Factor**

These include lifestyle, bad habits and stress.

4. Cancer Diagnosis

Recent research on cancer has shown that cancer symptoms should be checked in the patient's blood or bone marrow. They may conduct tests such as **(Minesh, 2021)**:

- **Blood tests: -**

A complete blood count (CBC) is needed to examine the number and maturity of different types of blood cells. A blood smear is made to test for the presences of unusual or immature cells.

- **Bone marrow biopsy: -**

Test involves bone marrow biopsy taken from pelvic bone with a long needle. It is used to diagnose the type of leukemia that the patient has and how severe it is.

- **Spinal tap: -**

This involves fluid taken from the spinal cord to check if the cancer cells have spread to spinal cord.

- **Imaging tests: -**

Devices like Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) scans.

5. Types of Cancer in Children

Leukemia is the most common cancer occur in children follow by brain and spinal cord tumors, neuroblastoma, wilms tumor, lymphoma (including both Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma, bone cancer (including osteosarcoma and Ewing sarcoma) **(Street, 2019)**.

5.1 Leukemia

- **Definition**

Leukemia is a malignant neoplasm of hematopoietic cells originating in the marrow and spreading to the blood and other tissues, such as the lymph nodes, spleen, and liver. The characteristic feature of the neoplastic cells is that they retain the ability to proliferate but fail to differentiate normally into functional hematopoietic cells. This results in replacement of the normal bone marrow by the leukemic cells **(Zupanec and Tomlinson, 2010)**.

Leukemia may cause bone and joint pain, fatigue, weakness, pale skin, bleeding or bruising easily, fever, or infection **(American Cancer Society, 2021)**.

- **Types of Leukemia**

1. Acute Lymphoblastic Leukemia (ALL) is a malignancy of the lymphoid line of blood cells, which accounts for 75–80% of childhood leukemia **(Nabizadeh *et al.*, 2022)**.
2. Acute Myeloid Leukemia (AML) is an aggressive, heterogenous malignancy characterized by clonal expansion of bone marrow-derived myeloid progenitor cells, which accounts for 20–25% of childhood leukemia (**Ayyadurai *et al.*, 2022**).
3. Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative hematological cancer caused by an abnormal immature bone marrow stem cell, which accounts for less than 5% of childhood leukemia **(Suttorp *et al.*, 2021)**.

- **Oral Manifestations**

Oral manifestations occur frequently in leukemic patients and may be present as initial evidence of the disease or its relapse. The symptoms include gingival enlargement and bleeding, oral ulceration, petechia, mucosal pallor, trismus and oral infections **(Santos *et al.*, 2010; Reenesh *et al.*, 2012)**.

5.2 Brain and Central Nervous System Tumors

Most brain tumors in children start in the lower parts of the brain, such as the cerebellum or brain stem. They can cause headaches, nausea, vomiting, blurred or double vision, dizziness, seizures, trouble walking or handling objects, and other symptoms. Spinal cord tumors are less common than brain tumors in both children and adults **(Street, 2019)**.

Brain tumors can cause symptoms by impingement on normal tissue (usually cranial nerves) or by an increase in intracranial pressure caused either by obstruction of cerebrospinal fluid (CSF) or by a direct mass effect **(Thomas and Wofford, 2015)**.

5.3 Lymphoma

It arises in the lymph tissue in the body's immune system. The third most common malignancy in childhood (including both Hodgkin and non-Hodgkin) **(Thomas and Wofford, 2015)**.

Non-Hodgkin lymphoma and Hodgkin lymphoma often cause lymph nodes to swell, which can appear as a lump in the neck, armpit, or groin; other symptoms can include fatigue, weight loss, and fever **(American Cancer Society, 2021)**.

5.4 Sarcomas

Sarcomas are tumors occurring in bones or soft tissue, such as muscles **(Thomas and Wofford, 2015)**.

Osteosarcoma, a bone cancer that most often occurs in adolescents, commonly appears as sporadic pain in the affected bone that may worsen at night or with activity and eventually progresses to local swelling. Rhabdomyosarcoma, a soft tissue sarcoma that can occur in the head and neck, genitourinary area, trunk, and extremities, may cause pain and/or a mass or swelling at the tumor site **(American Cancer Society, 2021)**.

5.5 Kidney cancers

wilm's tumor is the most common malignant renal tumor of childhood **(Thomas and Wofford, 2015)**. Wilm's tumor is also called nephroblastoma may appear as swelling or a lump in the abdomen, sometimes with blood in the urine **(American Cancer Society, 2021)**.

6. Staging of Cancer

Physical examination is used to determine the clinical stage, which is supplemented by CT, MRI. Inspection is frequently used to determine size, although radiographic imaging is usually used to describe deep extension more carefully. The TNM staging system is used to describe the amount and spread of cancer in a patient's body. In the TNM system, The T refers to the size and extent of the main tumor. The N refers to the number of nearby lymph nodes that have cancer. The M refers to whether the cancer has metastasized, Thus, stages of cancer can be summarized as **(Werning, 2011)**;

Stage I: Cancer is localized to a small area and hasn't spread to lymph nodes or other tissues.

Stage II: Cancer has grown, but it hasn't spread.

Stage III: Cancer has grown larger and has possibly spread to lymph nodes or other tissues.

Stage IV: Cancer has spread to other organs or areas of your body.

7. Cancer Treatment

- **Surgery**

Primary surgery is still the gold standard. Surgical options range from biopsy alone to complete removal, depending on the tumor's location and extent. Complete resection is an important surgical goal for most malignant tumors **(Rossetto, 2010)**.

- **Chemotherapy**

Chemotherapy is a drug therapy that is cytotoxic and that prevents malignant cell division and spread. Most chemotherapy agents kill malignant

cells in the active/ dividing phases of the cycle by damaging the Ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) that tell the cell how to copy itself **(Chordas and Graham, 2010)**.

- **Radiotherapy**

The use of ionizing radiation to treat cancer is known as radiotherapy. Due to very effective chemotherapy regimens and the recognition of the late effects of radiotherapy, which is of particular importance to the pediatric patient during the process of growth and development, radiotherapy has a diminishing role in the treatment of childhood cancers in general. However, about 20% of children and young people with cancer still require radiotherapy. It is the most common treatment for brain tumors and plays an important role in symptom relief **(Loch and Khorrami, 2010)**.

- **Hematopoietic Stem Cell Transplantation**

Hematopoietic stem cell transplantation (HSCT) is a procedure that involves replacing diseased, damaged, or missing hematopoietic stem cells (HSCs) with healthy HSCs. When the HSCs are diseased, allogeneic transplants are used (e.g., leukemia). It is an important treatment option for children with aggressive malignancies in first remission or recurrent disease **(Norville and Tomlinson, 2010)**.

8. Oral Assessment of Pediatric Cancer Patients

Oral assessment is fundamental to the management of patients with cancer. It involves taking a detailed history, performing a thorough examination, and the use of appropriate investigations **(Birnbaum and Dunne, 2000).**

8.1 History

The history should include questions about the most common oral symptoms. It is insufficient to simply ask about the presence of a symptom. The format of additional questioning will depend on the nature of the symptoms, for example, if a patient presents with pain, then the following parameters are useful to establish a diagnosis such as character, location, onset, radiation, intensity, duration, and exacerbating factors **(Davies and Epstein, 2010).**

A) Medical history:

It should include, but not be limited to, disease/condition (type, stage, prognosis), treatment protocol (surgery, chemotherapy, radiation, transplant), medications (including bisphosphonates), allergies, surgeries, hematological status (CBC), coagulation status, immunosuppression status **(National Cancer Institute, 2016).**

B) Dental history

It includes information such as habits, trauma, symptomatic teeth, previous care, preventive practices, oral hygiene, fluoride exposure and diet assessment **(American Academy of Pediatric Dentistry, 2021).**

- **Instruction**

Preventive measures include the use of fluoridated toothpaste, fluoride supplements if indicated, neutral fluoride gels/rinses, or applications of fluoride varnish for patients at risk for caries and/or xerostomia. A brush-on technique is convenient and may increase the likelihood of patient compliance with topical fluoride therapy **(Schubert and Peterson, 2009; Hong *et al*., 2010)**.

Dental practitioners should discuss the importance of a healthy diet to maintain nutritional status with an emphasis on foods that do not promote caries. Patients and parents should be advised about the high cariogenic potential of dietary supplements rich in carbohydrates and oral pediatric

medications rich in sucrose **(Hong *et al.*, 2010)**. They should also be instructed those sharp, crunchy, spicy, and highly acidic foods should be avoided during chemotherapy, radiation **(National Cancer Institute, 2016)**.

Oral hygiene includes brushing of the teeth and tongue two to three times daily with regular soft nylon brush or electric toothbrush, regardless of the hematological status. Ultrasonic brushes and dental floss should be allowed only if the patient is properly trained **(Lalla *et al.*, 2011; Peterson *et al.*, 2010)**.

The patient's teeth should be gently flossed daily. If pain or excessive bleeding occurs, the patient should avoid the affected area, but floss the other teeth **(National Cancer Institute, 2016)**. Patients with poor oral hygiene and/or periodontal disease may use chlorhexidine rinses daily until the tissue health improves **(Hong *et al.*, 2010)**.

8.2 Oral Examination

1- In the oral cavity, any active or prospective sources of infection should be removed. Acute and chronic odontogenic diseases, including caries and periodontal disease, as well as teeth with a bad prognosis, must be treated definitively. The motivation for this strong treatment is that any slight odontogenic infection in a critically immunocompromised individual might progress to a systemic infection, which can often be fatal.

2- Ensure that the oral cavity is free of all possible sources of local irritation such as a sharp tooth cusp or a rough area on a restoration.

3- Look for evidence of the involvement of oral cavity by the malignancies (such as leukemia or metastatic tumor).

4- Educate the patient on the importance of dental treatment before starting cancer treatment, what to expect during cancer treatment, and long-term cancer treatment adverse effects.

9. Side Effect of Cancer Treatment

9.1 Early Oro-Dental Side Effects of Cancer Treatment:

A) Oral Mucositis

- **Definition**

Oral mucositis is a painful, inflammatory illness that affects the oral mucosa as a result of excessive chemotherapy dosages. This disease makes it difficult to swallow, speak, or brush your teeth, and it makes infection more likely. Mucositis is frequently mentioned as the worst adverse effect of treatment among patients who get chemotherapy or radiation to the head and neck **(Damm *et al.*, 2015)**.

- **Symptom**

Erythema, atrophy and ulceration are the first alterations in the oral mucosa as shown in (fig.1,2). Painful ulceration is generally seen. The ulcerative phase lasts around a week to ten days and, in most cases, heals on its own within three weeks of its onset. Mucositis can be painfully intolerable **(Bellm *et al.*, 2008)**.

Figure 1: Mucositis of lips with ulcers (Ahuja, Datta *et al.*, 2017).

Figure 2: Ulcers on palate and lips **(Ahuja, Datta *et al.*, 2017)**.

- **Management**

Mucositis care remains focused on palliation of symptoms and efforts to reduce the influence of secondary factors on mucositis **(Keefe *et al.*, 2007)**. The most common prescriptions for management of mucositis include **(Little *et al.*, 2012)**;

1. Good oral hygiene.
2. Analgesics.
3. Non-medicated oral rinses (e.g., 0.9 % saline or sodium bicarbonate mouth rinses four to six times/day).
4. Parenteral nutrition as needed.

B) Xerostomia

- **Definition**

Xerostomia is the subjective feeling of a dry mouth. It is characterized by low or almost no saliva **(Skolin, *et al.*, 2006)**.

Damage to salivary glands from medications or ionizing radiation is the underlying cause of xerostomia. Xerostomia increases caries risk, exacerbates mucositis, and increases risk for oral infections **(DaFonseca and Hong, 2008)**.

- **Management**

Sugar-free chewing gum or candy, sucking tablets, special dentifrices for oral dryness, saliva substitutes, frequent sipping of water, alcohol-free oral rinses, and/or oral moisturizers are recommended **(Amerongen and Veerman, 2003; Schubert and Peterson, 2009).**

C) Oral Infection

Children receiving cancer therapy easily develop opportunistic oral infections (fungal, bacterial, and viral) **(Glenny *et al.*, 2010).** Fungal species, most notably Candida species, are perhaps the most serious complication in the world of diseases. Systemic fungal infections have a much higher mortality rate than other diseases, with the majority of cases thought to have begun in the mouth **(Huber and Terezhalmy, 2005).** As showen in fig (3), herpes simplex lesion (cold sore) is one of the lesions that is usually found in the oral cavity of patients undergoing chemotherapy **(Alaizari *et al.*, 2015).**

Figure 3: Oral Candidiasis (Bakki *et al.*, 2021).

Oral Infection can be managed as follows (**Dafonseca and Hong, 2008; Alaizari *et al.*, 2015; Morgan *et al.*, 2017**): -

1. Nystatin is effective in treating oral candidiasis.
2. Systemic anti-fungal agents such as amphotericin B may be necessary.

3. Localized infections can be managed with chlorhexidine mouthwash and diligent oral hygiene.
4. Topical acyclovir is very helpful for herpes simplex lesions. Systemic Acyclovir is used to treat severe infections.

D)Neuropathic Pain

Children who receive chemotherapeutic agents may develop neuropathic pain that usually affects mandibular teeth. These children complain of deep pain in the jaw and teeth in the absence of an odontogenic source of pain. Such neuropathic pain is usually transient in children and diminishes or resolves after completion of chemotherapy. In the absence of a definitive cure for chemotherapy induced neuropathic pain, palliative care may be provided with over-the-counter pain medications **(Ritwik, 2018).**

E) Taste Disturbance

Dysgeusia is an alteration in taste and is associated with ageusia, which is the complete lack of taste, and hypogeusia, which is a decrease in taste sensitivity **(Minicucci, 2003).**

F) Dental caries

Children undergoing cancer therapy are at a high risk of developing dental caries **(Shen, Gao *et al.*, 2009)**. Damage to the salivary glands by radiotherapy and chemotherapy results in reduced salivary flow, which causes changes in the mouth ‘s environment and increases the chances of developing caries as shown in (fig. 4) **(Wong, Tsang *et al.*, 2011; McCaul, 2012).**

Figure 4: Radiation-associated caries (McCaul, 2012).

G) Oral Bleeding:

Oral bleeding is caused by thrombocytopenia, impairment of coagulation factors, and/or impaired vascular integrity. Management should include local methods (e.g., pressure packages, gelatin sponges) and institutional interventions (e.g., platelet transfusions, aminocaproic acid) **(Anjuga and Malathy, 2020)**.

H) Lip Care

Children who are receiving chemotherapy and/or radiation treatment often develop dry lips and angular cheilitis. Lanolin-based creams and ointments are beneficial in moisturizing the lips of these patients **(Anjuga and Malathy, 2020)**.

9.2 Late Oro-Dental Effects from Cancer Therapy:

A) Dental Developmental Abnormalities

Root stunting is the term to describe shortening of the roots of the teeth which is common in pediatric patient receiving cancer therapy. Other developmental abnormalities include microdontia (abnormally small teeth) and hypodontia (partial absence of teeth) **(Doğan *et al.*, 2001; Figliolia *et al.*, 2008).**

The severity of dental anomalies depends on **(Bagattoni *et al.*, 2014; Wilberg *et al.*, 2016)**.

1. The age of the child.
2. The stage of dental development at the time of cancer chemotherapy and/or radiation therapy,
3. The intensity of cancer therapy.

B) Trismus

Generally, reduced incisal opening of less than 35 mm is considered as trismus **(Dijkstra *et al.*, 2006)**. Tongue blades can be used to gradually increase the mandibular opening **(Bensadoun *et al.*, 2010)**. Continuity of stretching exercises can help minimize the oral restrictions due to trismus as shown in (fig.5) **(McCaul, 2012; Effinger *et al.*, 2014)**.

Figure 5: The use of tongue blade to address trismus (McCaul, 2012).

C) Osteoradionecrosis

Is defined as non-healing exposed bone present for at least 3 months in an area which has been previously irradiated (fig.6). ORN is caused by trauma to the irradiated jaw (such as tooth extraction) but can also occur spontaneously. ORN increase risk of mortality and significant morbidity; sever pain, pathological fracture and oro-cutaneous fistula may develop **(McCaul, 2012)**.

Surgical debridement and supplementary therapies such as antibiotics and hyperbaric oxygen (HBO) therapy are commonly used to prevent or cure ORN **(Peterson *et al.*, 2010)**.

Figure 6: Osteoradionecrosis (McCaul, 2012).

10. Dental Guidelines for Management Childhood Cancers in Dental Clinic

10.1 Hematological considerations:

- **Absolute neutrophil count:**

If Absolute neutrophil count (ANC) more than 2,000 per cubic millimeter /mm³: There is no need for antibiotic prophylaxis **(National Cancer Institute, 2016; Little *et al.*, 2018)**.

1000 to 2000/ mm³: Use clinical judgment based on the patient's health status and planned procedures **(American Academy of Pediatric Dentistry, 2021)**.

Less than 1,000 /mm³: defer elective dental care. In dental emergency cases the patient may need hospitalization for dental management **(Da Fonseca, 2018)**.

- **Platelet count**

If platelet count is more than 75,000 per mm³ no additional support is needed; 40,000 to 75,000/mm³ platelet transfusions may be considered pre- and 24 hours post-operatively. Localized procedures to manage prolonged bleeding may include sutures, hemostatic agents, pressure packs, and/ or gelatin foams, less than 40,000/mm³: defer care **(American Academy of Pediatric Dentistry, 2021)**.

10.2 Dental procedures:

Ideally, all dental care should be completed before cancer therapy is initiated. When that is not possible, temporary restoration may be placed and non-acute dental treatment may be delayed until the patient's hematological status is stable **(Lalla *et al.*, 2011; National Cancer Institute, 2016)**.

- **Prioritizing procedures**

Priorities should be infections, extractions, periodontal care (e.g., scaling, prophylaxis), and sources of tissue irritation before the treatment of carious teeth, and replacement of faulty restoration. Incipient to small carious lesions may be treated with fluoride or sealants until final therapy is available **(Lalla *et al.*, 2011)**.

- **Pulp therapy in primary teeth**

Many clinicians choose to provide a more definitive treatment in the form of extraction instead of performing pulp therapy in primary teeth because pulpal/periapical infections during immunosuppression periods can become life-threatening **(Lalla *et al.*, 2011)**.

- **Endodontic treatment in permanent teeth**

Symptomatic non-vital permanent teeth should receive root canal treatment at least 1 week before initiation of therapy to allow sufficient time to assess treatment success before the chemotherapy. Endodontic treatment of asymptomatic non-vital permanent teeth may be delayed **(Lalla *et al.*, 2011; Da Fonseca, 2018; Little *et al.*, 2018)**.

- **Extractions**

Extraction is indicated in the following cases **(Lalla *et al.*, 2011; Little *et al.*, 2018)**;

1. Non-restorable tooth with poorly prognosis.
2. Teeth with periodontal pockets greater than six millimeters.
3. Symptomatic impacted teeth.
4. Teeth exhibiting acute infections.
5. Mobile teeth.
6. Significant bone loss, involvement of the furcation.

Perform extraction with minimal trauma and surgical procedures must be as atraumatic as possible. If there is documented infection associated with the tooth, antibiotics should be administered for about 1 week. At least 2 weeks, tooth should be removed (or at least seven to 10 days) before therapy is initiated to allow adequate healing. Trim bone at wound margins to eliminate sharp edges and obtain primary closure (**Schubert *et al.*, 2009; Lalla *et al.*, 2011; Little *et al.*, 2018)**.

- **Orthodontic treatment**

The following strategies should be considered when providing orthodontic care for patients with dental sequelae **(Zahrowski, 2007)**; -

1. Use appliances that minimize the risk of root resorption,
2. Use lighter forces,
3. Terminate treatment earlier than normal,
4. Choose the simplest method for the treatment needs.

Orthodontic care may start or resume after completion of all therapy and after at least a two-year disease-free survival when the risk of relapse is decreased **(Da Fonseca, 2018).**

- **Periodontal considerations**

Partially erupted molars can become a source of infection because of pericoronitis. The overlying gingival tissue should be excised if the dentist believes it is a potential risk and if the hematological status permits **(Schubert *et al.*, 2009; Little *et al.*, 2018)**.

11. Dental and Oral Care After Cancer Therapy

The goals of a dental/oral examination following treatment are **(American Academy of Pediatric Dentistry, 2021)**; -

- To maintain optimal oral health.
- To educate to the patient/parents about the importance of optimal oral and dental care for life.
- To address and/or treat any dental issues that may arise as a result of the long-term effects of immuno-suppressive therapy.

The child should be seen at least every 6 months (or in shorter intervals if issues such as xerostomia, or trismus are present). Patients who have experienced moderate or severe mucositis be followed closely for malignant transformation of their oral mucosa (e.g., oral squamous cell carcinoma) **(Euvrard *et al.*, 2003; Elad *et al.*, 2008)**.

Long-term management Xerostomia, trismus and risk of radiation caries and ORN are lifelong and patients require close follow-up long after being discharged from 5-year cancer follow-up. A combination of effective planning prior to cancer treatment and effective follow-up care should result in good functional and aesthetic oral and dental outcomes **(McCaul, 2012)**.

12. Recommendations for Children Following Cancer Therapy

1. The teeth and tongue should be brushed at least twice each day with a soft bristled nylon toothbrush. If the child can swish and spit the mouth rinse, it should be recommended as an adjunct to brushing and flossing **(Ritwik, 2018)**.

2. Maintaining a healthy body weight and following well-balanced diets. Decreasing the intake of high-fat processed foods, refined starches, sugars, and red and processed meat; and increasing the intake of fruits and vegetables **(Laha *et al.*, 2022)**.

Conclusion

The key to success in maintaining a healthy oral cavity during cancer therapy is patient compliance. Consequently, it is vital to educate the caretaker and child about the importance of oral care to minimize discomfort and maximize the chances for a successful outcome. Moreover, parents should also be educated about the deleterious effects of indulging the child with unhealthy foods, the potential carcinogenicity of pediatric medications and nutritional supplements, and late effects of the treatment on the craniofacial growth and dental development.

It is important for the pediatric dentist to realize that these issues are rarely discussed by the physicians and nurses involved in the patient's care. Thus, the participation of a pediatric dentist in the hematology/oncology team is of paramount importance.

Oral complications such as mucositis and infections should be anticipated during cancer treatment. As the survival rates of childhood cancers

improve, it is important for these patients to have an established dental home where long-term oral and dental complications of cancer treatment, such as dental anomalies, orthodontic problems, and risk for oral cancer and salivary gland tumors, can be appropriately managed.

The oral health profession plays an important role in reinforcing cancer prevention strategies and in screening oral and systemic factors for future risk for cancers. Interprofessional collaborative care between the dental and medical team is imperative in all phases of care for children diagnosed with cancer and for children diagnosed with risk factors for future neoplasia.

References

(A)

- American Academy of Pediatric Dentistry, 2021. Dental management of pediatric patients receiving immunosuppressive therapy and/or radiation therapy. *The Reference Manual of Pediatric Dentistry*. Chicago, Ill.: American Academy of Pediatric Dentistry, p.471-9.
- American cancer society, 2021. Cancer facts and figures. Atlanta: *American Cancer Society*, p.12-13.
- Anjuga, E.S. and Malathy, L., 2020. Dental Care for The Patients with Childhood Cancer and Survivors–A Short Review. *European Journal of Molecular & Clinical Medicine*, 7(10), p.682,688
- Ayyadurai, V.S., Deonikar, P., McLure, K.G. and Sakamoto, K.M., 2022. Molecular Systems Architecture of Interactome in the Acute Myeloid Leukemia Microenvironment. *Cancers*, 14(3), p.756.

(B)

- Bagattoni, S., D'Alessandro, G., Prete, A., Piana, G., & Pession, A. 2014. Oral health and dental late adverse effects in children in remission from malignant disease. A pilot case-control study in Italian children. *European Journal of Paediatric Dentistry*, 15(1), 45–50.
- Bakki, S.R., Rajendra Santosh, A.B. and Muddana, K., 2021. Fungal infections of oral cavity: diagnosis, management, and association with COVID-19. SN comprehensive clinical medicine, 3(6), pp.1373-1384.
- Bensadoun, R.J., Riesenbeck, D., Lockhart, P.B., Elting, L.S., Spijkervet, F.K. and Brennan, M.T., 2010. A systematic review of trismus induced by cancer therapies in head and neck cancer patients. *Supportive Care in Cancer*, 18(8), pp.1033-1038.
- Birnbaum, W. and Dunne, S.M., 2000. *Oral Diagnosis*: The clinician's guide. Wright.

(C)

- Chordas, C. and Graham k. Chemotherapy. In:Tomlinson, D. and Kline, N., 2010. *Pediatric oncology nursing*. Heidelberg: Springer.Ch.9.

(D)

- Davies, A. and Epstein, J. eds., 2010. *Oral complications of cancer and its management*. Oxford University Press Oxford.
- Dijkstra, P.U., Huisman, P.M. and Roodenburg, J.L.N., 2006. Criteria for trismus in head and neck oncology. *International journal of oral and maxillofacial surgery*, 35(4), pp.337-342

- Doğan C, Haytaç C, Antmen B, Şaşmaz I, 2001. A: Oral health status in children with acute lymphoblastic leukemia and lymphoma. *Turkish Journal of Haematology*, 18(3):179-183.

(E)

- Effinger, K.E., Migliorati, C.A., Hudson, M.M., McMullen, K.P., Kaste, S.C., Ruble, K., Guilcher, G.M., Shah, A.J. and Castellino, S.M., 2014. Oral and dental late effects in survivors of childhood cancer: a Children's Oncology Group report. *Supportive Care in Cancer*, 22(7), pp.2009-2019.
- Elad, S., Thierer, T., Bitan, M., Shapira, M.Y. and Meyerowitz, C., 2008. A decision analysis: the dental management of patients prior to hematology cytotoxic therapy or hematopoietic stem cell transplantation. *Oral oncology*, 44(1), pp.37-42.
- Epstein JB, Thariat J, Bensadoun RJ, Barasch A, Murphy BA, Kolnick L, Popplewell L, Maghami E., 2012. Oral complications of cancer and cancer therapy: from cancer treatment to survivorship. CA: *a Cancer journal for Clinicians*, 62, p. 400–422.
- Euvrard, S., Kanitakis, J. and Claudy, A., 2003. Skin cancers after organ transplantation. *New England Journal of Medicine*, 348(17), p.1681-1691.

(F)

- Figliolia, S.L.C., Oliveira, D.T., Pereira, M.C., Lauris, J.R.P., Mauricio, A.R., Oliveira, D.T. and Mello de Andrea, M.L., 2008. Oral mucositis in acute lymphoblastic leukaemia: *analysis of 169 paediatric patients. Oral diseases,* 14(8), p.761-766.

(G)

- Garinet, S., Wang, P., Mansuet-Lupo, A., Fournel, L., Wislez, M. and Blons, H., 2022. Updated Prognostic Factors in Localized NSCLC. Cancers, 14(6), p.140

- Glenny, A. M., Gibson, F., Auld, E., et al. 2010. The development of evidence-based guidelines on mouth care for children, teenagers and young adults treated for cancer. *European Journal of Cancer*, 46(8), p. 1399–1412.

(H)

- Hong, C.H., 2008. Considerations in the pediatric population with cancer. *Dental Clinics of North America*, 52(1), p.155-181.
- Hunger, S., Mullighan, C., 2015. Acute Lymphoblastic Leukemia in Children. *New England Journal of Medicine*, 373(16), pp.1541-1552.

(L)

- Laha, F., Ribalta, A., Arribas, L., Bellver, M., Roura, E., Guillén-Rey, N., Megias-Rangil, I., Alegret-Basora, C., Tresserra-Rimbau, A. and Zamora-Ros, R., 2022. A Review of Web-Based Nutrition Information in Spanish for Cancer Patients and Survivors. Nutrients, 14(7), p.1441.
- Lalla, R.V., Brennan, M.T. and Schubert, M.M., 2011. Oral complications of cancer therapy. *Pharmacology and therapeutics for dentistry*, 6, p.782-798
- Lam, C.G., Howard, S.C., Bouffet, E. and Pritchard-Jones, K., 2019. Science and health for all children with cancer. *Science*, 363(6432), p.1182-1186.
- Loch, I. and Khorrami J. Radiotherapy. In:Tomlinson, D. and Kline, N., 2010. *Pediatric oncology nursing*. Heidelberg: Springer.Ch.10.

(M)

- Matthews, H.K., Bertoli, C. and de Bruin, R.A., 2022. Cell cycle control in cancer. *Nature Reviews Molecular Cell Biology*, 23(1), p.74-88.

- McCaul, L.K., 2012. Oral and dental management for head and neck cancer patients treated by chemotherapy and radiotherapy. *Dental update*, 39(2), p.135-140.
- Minesh Khatri, MD., 2021. Leukemia. [online] WebMD. Available at: <https://www.webmd.com/cancer/lymphoma/understanding-leukemia-basics> [Accessed 26 April 2022].
- Minicucci, E.M., Lopes, L.F. and Crocci, A.J., 2003. Dental abnormalities in children after chemotherapy treatment for acute lymphoid leukemia. *Leukemia research*, 27(1), p.45-50.
- Morgan, J.E., Hassan, H., Cockle, J.V., Lethaby, C., James, B. and Phillips, R.S., 2017. Critical review of current clinical practice guidelines for antifungal therapy in paediatric haematology and oncology. *Supportive Care in Cancer*, 25(1), p.221-228.
- Muresanu, C. and Khalchitsky, S., 2022. Updated Understanding of the Causes of Cancer, and a New Theoretical Perspective of Combinational Cancer Therapies, a Hypothesis. DNA and Cell Biology.

(N)

- Nabizadeh, F., Momtaz, S., Ghanbari-Movahed, M., Qalekhani, F., Mohsenpour, H., Aneva, I.Y., Bishayee, A., Farzaei, M.H. and Bishayee, A., 2022. Pediatric acute lymphoblastic leukemia management using multitargeting bioactive natural compounds: A systematic and critical review. *Pharmacological research*, p.106116.
- National Cancer Institute, 2016. Oral complications of chemotherapy and head/neck radiation. *Health Professional Version*.
- Nieuw Amerongen, A. and Veerman, E., 2003. Current therapies for xerostomia and salivary gland hypofunction associated with cancer therapies. *Supportive care in cancer*, 11(4), p.226-231.

- Norville R. and Tomlinson D. Hematopoietic Stem Cell Transplantation. In:Tomlinson, D. and Kline, N., 2010. *Pediatric oncology nursing*. Heidelberg: Springer.Ch.11.

(O)

- Özdemir, B.C. and Dotto, G.P., 2017. Racial differences in cancer susceptibility and survival: more than the color of the skin. *Trends in cancer*, 3(3), p.181-197.

(P)

- Peterson, D.E., Doerr, W., Hovan, A., Pinto, A., Saunders, D., Elting, L.S., Spijkervet, F.K. and Brennan, M.T., 2010. Osteoradionecrosis in cancer patients: the evidence bases for treatment-dependent frequency, current management strategies, and future studies. *Supportive care in cancer*, 18(8), p.1089-1098.

(R)

- Ray-Chaudhuri, A., Shah, K. and Porter, R.J., 2013. The oral management of patients who have received radiotherapy to the head and neck region. *British dental journal*, 214(8), p.387-393.
- Reenesh, M., Munishwar, S. and Rath, S.K., 2012. Generalised leukaemic gingival enlargement: *a case report. Journal of oral & maxillofacial research*, 3(3).
- Ritwik, P., 2018. Dental care for patients with childhood cancers. *Ochsner Journal*, 18(4), pp.351-357.
- Ritwik, P., Chrisentery-Singleton, T.E., 2020. Oral and dental considerations in pediatric cancers. *Cancer Metastasis Rev* 39, p.43–53
- Rossetto L. C. Surgical Approaches to Childhood Cancer. In:Tomlinson, D. and Kline, N., 2010. *Pediatric oncology nursing*. Heidelberg: Springer. Ch.12.

(S)

- Schubert MM, Peterson DE. Oral complications of hematopoietic cell transplantation. In: Appelbaum RF, Forman SJ, Negrin RS, Blume KG, eds 2009. *Thomas' Hematopoietic Cell Transplantation:* Stem Cell Transplantation. 4th ed. Oxford, UK: Wiley-Blackwell; 1589-607.
- Shen C, Gao Y, Xu T, Wang X, Ying H, Hu C 2009: Carcinoma of the Nasopharynx in Young Patients: A Single Institution Experience. *Clinical Oncology*, 21(8):617-622.
- Smith MA, Ries LAG. Childhood cancer: incidence, survival, and mortality. In: Pizzo PA, Poplack DG, eds 2002. *Principles and Practice of Pediatric Oncology*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 1-12.
- Street, W., 2019. Cancer facts & figures 2019. *American Cancer Society*: Atlanta, GA, USA, 76.
- Sullivan, R., Kowalczyk, J.R., Agarwal, B., Ladenstein, R., Fitzgerald, E., Barr, R., Steliarova-Foucher, E., Magrath, I., Howard, S.C., Kruger, M. and Valsecchi, M.G., 2013. New policies to address the global burden of childhood cancers. *The Lancet Oncology*, 14(3), p. e125-e135.
- Suttorp, M., Millot, F., Sembill, S., Deutsch, H. and Metzler, M., 2021. Definition, epidemiology, pathophysiology, and essential criteria for diagnosis of pediatric chronic myeloid leukemia. Cancers, 13(4), p.798.

(T)

- Teguh, D.N., Levendag, P.C., Voet, P., van der Est, H., Noever, I., de Kruijf, W., van Rooij, P., Schmitz, P.I. and Heijmen, B.J., 2008. Trismus in patients with oropharyngeal cancer: relationship with dose in structures of mastication apparatus. Head & Neck: *Journal for the Sciences and Specialties of the Head and Neck*, 30(5), p.622-630.

- Thomas W. McLean and Marcia M. Wofford. Oncology., 2015.In: Marcdante, K. and Kliegman, R., n.d. *Nelson essentials of pediatrics*. 7th ed. Section 21.

(W)

- Werning, J., 2011. *Oral Cancer*. New York: Thieme, pp.66,67.
- Wilberg, P., Kanellopoulos, A., Ruud, E., Hjermstad, M.J., Fosså, S.D. and Herlofson, B.B., 2016. Dental abnormalities after chemotherapy in long-term survivors of childhood acute lymphoblastic leukemia 7–40 years after diagnosis. *Supportive care in cancer*, 24(4), p.1497-1506.
- Wong, H.M., Chu, C.H. and Chan, G.C.F., 2011. Caries experience of paediatric oncology patients in Hong Kong. In IADR-SEA Division Annual Scientific Meeting. *International Association for Dental Research*.
- *World Health Organization*, 2021. Cure All framework: WHO global initiative for childhood cancer: increasing access, advancing quality, saving lives.

(Z)

- Zahrowski, J.J., 2007. Bisphosphonate treatment: an orthodontic concern calling for a proactive approach. *American Journal of Orthodontics and Dentofacial Orthopedics*, 131(3), p.311-320.
- Zupanec, S., Tomlinson, D. Leukemia. In:Tomlinson, D. and Kline, N., 2010. *Pediatric oncology nursing*. Heidelberg: Springer.Ch.1.