Oral Health Care for People with Fanconi Anemia

Mark M. Schubert, DDS, MSD
Professor, Oral Medicine, University of Washington
Director, Oral Medicine Service, SCCA
Seattle, Washington

mschuber@seattlecca.org
Objectives

Provide a Brief Overview of Oral Issues for FA

- Review the oral and dental manifestations associated with Fanconi Anemia
- Review the basic oral and dental health care recommendations for patients with Fanconi Anemia
- Review the oral manifestations of AA / AML / MDS
- Review oral complications of chemotherapy, radiation, and hematopoietic cell transplantation
Oral Health Issues with FA

**Oral Health**

**Genetic Factors**
- Marrow Failure
- Acute Myelogenous Leukemia
- Myelodysplasia

**Hematologic Disease**
- Oral Cancers

**Oral Lesions / Dental Abnormalities**
- Missing teeth
- Extra teeth
- Small teeth
- Malpositioned teeth

**Non FA Oral Factors**

**Dental Diseases**
- Dental Decay
- Gingivitis / Periodontal Disease
- Salivary Gland Dysfunction

**Oral Complications of Oral Cancer Treatments**

**Oral complications of AML, MDS and HCT**
Oral Health Care for People with Fanconi Anemia

Oral and Dental Manifestations Associated with Fanconi Anemia
Oral Manifestations of Fanconi Anemia

Are there specific dental and skeletal developmental changes specific for FA?

- Dental development changes
- Skeletal development changes

Oral mucosal lesions

- Missing teeth
- Extra teeth
- Small teeth
- Abnormal root shape
- Orthodontic problems
- Skeletal abnormalities

- Oral Pigmentation
- Oral ulcers
Oral Manifestations of Fanconi Anemia

- **Dentition changes:**
  - Small teeth
  - Short roots / “V-shaped”
  - Missing teeth
  - Extra teeth

- **Oral pigmentation changes**

- **Oral ulcers / aphthous ulcers**

Minimal research to clearly document the specifics and frequency of oral and dental changes
Dental and Oral Manifestations of FA

Dentition Changes
- Missing teeth
- Extra teeth
- Small teeth
- Abnormal root shape
- Orthodontic problems
- Skeletal abnormalities

Skeletal Changes
Oral Ulcers and Oral Pigmentation

Oral Ulcers “Canker Sores”  Oral Pigmentation
Implications of oral and dental changes
- Not clear as to actual incidence rates
- Management: “Standard care protocols”

Tooth changes: *What is to be done?*
- Routine oral and dental examinations – be alert
- Plan and treat accordingly / Monitor

Oral ulcers
- Rule out: infection, marrow disease/immune disorder
- Prevent trauma / Topical steroids (?)

Oral Pigmentation
- Monitor / Minimal concerns
Basic Oral and Dental Health Care for Patients with Fanconi Anemia
What are the most common dental problems for FA patients?

- Dental Decay
- Gingivitis
- Periodontal Disease
Dental decay, gingivitis, and periodontitis
  - Very common problem for medically compromised patients
  - Affects oral health / oral function / systemic health,

Results in oral infections and pain
  - Bleeding / Abscesses / Tooth aches
  - Potential for systemic spread of infection

Tooth loss
  - Compromised function
  - Esthetics and self image

Social impact
  - Bad breath; missing teeth → affects self image

Dental treatment is expensive:
  - PREVENTION is clearly best
Routine Oral Hygiene

Standard oral hygiene works!

- **Bacterial plaque removal**
  - Tooth brushing: 2x/day
    - Hand tooth brushes
    - Electric toothbrushes
  - Flossing: 1x/day
    - Hand flossing
    - Flossers / floss holders

- Diet modifications
- Antibacterial oral rinses
- Topical fluorides

- **Routine dental exams / treatment**
Oral Hygiene: Recommendations

- Understand disease basics
- **Proper technique** is absolutely critical
- Get training – Customize techniques
- Follow-up assessments!
  - Assist children until child can completely carry out self care
  - Adults: Positive role models for children
- Consistent **DAILY** self-care
  - Brush 2x/day / Floss 1x/day
Oral Complications of Fanconi Anemia

Oral Squamous Cell Carcinoma
Fanconi Anemia: Oral Cancers

- Oral cancer
  - Related to FA genetic risk factors
  - Post hematopoietic cell transplant

- Abnormal presentation:
  - Occur at MUCH younger ages
  - Patients lack classic risk factors

With increased risk for an oral cancer: BE ALERT and AWARE

Stay alert: Abnormal non healing lesions
Dentists and hygienists ACTIVELY involved
Consider use of adjunctive tests
Oral Cancer: A Few Basic Considerations

- No one single clinical appearance
  - Red / White / Red and White
  - Lump / A Bump
  - An Ulcer / A Growth
  - Firm / Not So Firm
  - Pain / No Pain
  - Single Lesion / Multiple Lesions

What is the one single characteristic?
THE LESION DOES NOT HEAL AND GO AWAY!!
Oral Squamous Cell Carcinoma
# Location of Oral Cancer After HCT

## Tumors after bone marrow transplant, reported in the literature

<table>
<thead>
<tr>
<th>No</th>
<th>BMT age (yr)</th>
<th>Gender</th>
<th>Cancer age (yr)</th>
<th>Cancer type</th>
<th>Interval (yr)</th>
<th>Result</th>
<th>Age (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>F</td>
<td>25, 29</td>
<td>Cheek, tongue</td>
<td>5, 9</td>
<td>D</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>F</td>
<td>24</td>
<td>Tongue</td>
<td>10</td>
<td>A</td>
<td>32</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>F</td>
<td>18</td>
<td>Buccal</td>
<td>9</td>
<td>D</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>F</td>
<td>23, 24</td>
<td>Vulva, tongue</td>
<td>14, 15</td>
<td>A</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>M</td>
<td>12</td>
<td>Tongue</td>
<td>6</td>
<td>D</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>M</td>
<td>11</td>
<td>Tongue</td>
<td>3</td>
<td>D</td>
<td>11</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>M</td>
<td>16</td>
<td>Tongue</td>
<td>8</td>
<td>A</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>19</td>
<td>M</td>
<td>33</td>
<td>Tongue</td>
<td>14</td>
<td>D</td>
<td>33</td>
</tr>
<tr>
<td>9</td>
<td>NA</td>
<td>M</td>
<td>NA</td>
<td>Tongue</td>
<td>5</td>
<td>A</td>
<td>NA</td>
</tr>
<tr>
<td>10</td>
<td>8</td>
<td>M</td>
<td>13</td>
<td>Tongue</td>
<td>5</td>
<td>D</td>
<td>13</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>M</td>
<td>25</td>
<td>Pharynx</td>
<td>15</td>
<td>D</td>
<td>25</td>
</tr>
<tr>
<td>12</td>
<td>–</td>
<td>M</td>
<td>19</td>
<td>Tongue</td>
<td>NA</td>
<td>D</td>
<td>19</td>
</tr>
<tr>
<td>13</td>
<td>–</td>
<td>F</td>
<td>34</td>
<td>Larynx</td>
<td>21</td>
<td>A</td>
<td>34</td>
</tr>
<tr>
<td>14</td>
<td>7</td>
<td>M</td>
<td>9</td>
<td>Tongue</td>
<td>2</td>
<td>A</td>
<td>11</td>
</tr>
</tbody>
</table>

A, alive; BMT, bone marrow transplant; D, deceased; F, female; M, male; NA, not available.

Updated from Ref. 1 with the addition of Refs. 17 and 18.

### SITE # Cases
- **Tongue:** 11
- **Buccal:** 2
- **Pharynx/Larynx:** 1
- **Multiple times:** 2

**Age at HCT:** 10.7 yo (7 - 20)
**Age cancer dx:** 20.2 yo (9 - 34)
**Year post HCT:** 9.3 yrs (2 - 15)

---

Alter BP. Fanconi’s Anemia, transplantation, and cancer. Pediatr Transplantation 2005;9(suppl 7) 81-86
Bone Marrow Disorders

- Severe marrow aplasia
- Acute Myelogenous Leukemia (AML)
- Myelodysplastic Syndromes
Normal Hematopoesis

- Multipotential hematopoietic stem cell (Hemocytoblast)
  - Common myeloid progenitor
    - Erythrocyte
    - Mast cell
    - Myeloblast
    - Basophil
    - Neutrophil
    - Eosinophil
    - Monocyte
    - Macrophage
    - Thrombocytes
  - Common lymphoid progenitor
    - Small lymphocyte
    - B lymphocyte
    - Plasma cell
    - T lymphocyte
    - Natural killer cell (Large granular lymphocyte)
Blood Cell Types: Basic Functions

White Blood Cells
- Neutrophils: Infections
- Macrophages: Infections, Allergy
- Eosinophils: Infections, Allergy
- Basophil: Inflammatory reactions

Lymphocytes
- T-Lymphocytes: Immune coordination, Killer cells / other
- B-Lymphocytes: Antibody production

Platelets: Bleeding

Red Blood Cells: O₂ / CO
Approximately 15-20% or 1 out of 5 of patients with marrow failure will initially present with “oral lesions or problems”!
Marrow Aplasia and Leukemia

- **Loss of marrow function and leukemia**

- **Infections**: White blood cells / Immune function
  - Gingival and periodontal disease
  - Dental abscesses
  - Mucosal infections

- **Bleeding, petechiae, bruising**: Platelets

- **Pallor, fatigue, headache**: Red blood cells

- **Leukemic infiltrates (AML)**
Hematologic Malignancies

Early Oral Signs & Symptoms:
→ Are vague and non-specific

Later Oral Signs & Symptoms:
→ Become way more obvious & can become quite severe
Marrow Diseases: Oral Manifestations

- **Oral infections**
  Gingival, Periodontal, Pulp / Root Canal, Mucosal Types: *Bacterial, Viral, and Fungal*

- **Hemorrhage**
  Gingival bleeding / Petechia / Ecchymosis
  Prolonged bleeding with brushing / flossing

- **Ulcerations**
  Necrotizing Ulcerative Gingivitis
  Mucosal Ulcerations

- **Gingival infiltrates with leukemic cells**

- **Lymphadenopathy** – enlarged lymph nodes

- **Neurological symptoms**
  Numbness, tingling, jaw pain, “toothaches”
The following slides graphically show oral lesions associated with leukemia

WARNING!

Viewer Discretion is Advised
Aplastic Anemia

Pale gingival
Oral Bleeding

- Petechial Hemorrhage
- Ecchymosis – Blood Blisters
- Gingival Bleeding
Oral Bleeding
Oral Hemorrhage

• **Risk factors for oral bleeding:**
  - Low platelet counts: disease / chemotherapy
  - Medications: NSAIDS / Anticoagulants
  - Pre-existing infection – especially gingival
  - **Trauma:** petechiae / ecchymosis (blood blisters)
  - Usually “medically insignificant”

• **Scary for patients and family**
Leukemia: Bacterial Infections

Periodontal disease

Unusual organisms

Necrotizing ulcerative gingivitis “Trench Mouth”

Unusual organisms
Leukemia: Oral Herpes Simplex
Leukemia: Fungal Infections
Oral Infections

Prevention and Management

- Prophylactic regimens: prevent infection
  - *Acyclovir* - *Antifungal* - *Antibacterial Protocols*
- Clinical presentation: What does it look like?
- Culture lesions to diagnose → then treat to the identified organisms
- Empiric therapy vs directed therapy
Accumulation of myeloid leukemic cells in infected gum tissue – leukemic cells attracted to gum tissue → don’t work, more cells called in, swelling.
Leukemic Infiltrates and Bleeding
Neutropenic Ulcerations / Infections
AML: Infection, Ulcers, and Bleeding
Oral Complications of Cancer Therapy

- Head and Neck Radiation
- Chemotherapy
- Hematopoietic Cell Transplantation
Oral Complications of Cancer Treatments

Oral complications vary significantly with various cancer therapies

- **Oral Cancer**
  - Surgery
  - Radiation with / without chemotherapy

- **Systemic Chemotherapy (MDS/AML)**

- **Hematopoietic Cell Transplant**
  - Chemotherapy / total body irradiation
    - Myeloablative conditioning regimens
    - Non-myeloablative conditioning regimens
Oral Cancer Treatment: Oral Complications

- **Surgery:** physical disability
- **Radiation +/- chemotherapy**
  - Addition of Chemotherapy
    - Worsens oral mucositis
    - Increases risk for oral infections
    - Prolongs recovery of acute complications
  - Mucositis
  - Salivary gland dysfunction* (IMRT)
  - Fibrosis / trismus*
  - Bone damage: Osteoradionecrosis*
  - Oral infection (candidiasis, HSV)

*Represents a permanent disability/risk
Oral Cancer Treatment Time Line

**Staging Treatment Planning**
- **Diagnosis**
- Time 0

**Surgery and Recovery**
- 4 weeks
- 8 weeks

**Radiation Therapy**
- 16 weeks

**Acute Recovery**
- 20-22 weeks

**Chronic Complications**
- 42 weeks
- Years

**Pre Radiation Dental Health Stabilization**

**Acute Complication Management**
- **Mucositis**
- **Xerostomia**
- **Taste dysfunction**
- **Candida**
- **Swallowing**
- **Soft tissue necrosis**

**Chronic Complication Management**
- **Xerostomia**
- **Xerostomia decay**
- **Taste dysfunction**
- **Candida**
- **Swallowing**
- **Osteonecrosis**
- **Soft tissue necrosis**
- **Fibrosis / Trismus**
Oral Complications of Chemotherapy

- **Direct damage to oral tissues**
  - Oral mucosa: Mucositis
  - Salivary gland dysfunction
  - Taste dysfunction
  - Altered development of teeth in children

- **Indirect damage → oral complications**
  - Oral ulcerations (direct + indirect damage)
  - Oral infections: Bacterial / Fungal / Viral
  - Oral bleeding
The Relevance of Stem Cell Research?
HCT Time Line

Pre Transplant Planning

1-4 Weeks

Transplant Conditioning

2-7 Days

Acute Oral Complications

Mucositis
Xerostomia
Taste dysfunction
Swallowing
Acute GVHE

100 Days

Chronic Oral Complications

Chronic GVHD
Xerostomia
Xerostomia decay
2nd Malignancies
Growth / Development

Years

Pre Transplant Dental Health Stabilization

Acute Oral Complication Management

Chronic Oral Complication Management
Hematopoietic Cell Transplantation

- **Oral complications HCT**
  - Pre-existing dental disease-related
    - Tooth decay, gingivitis, and periodontitis
  - Direct damage from conditioning regimens
  - Indirect damage from conditioning regimens
  - Specific allogeneic HCT complications
    - Acute and Chronic Graft vs Host Disease
    - Risk of “second malignancies” post HCT
  - Chronic oral complications of HCT
Oral Complications of HCT

- Mucositis
- Infections  
  - Viral  
  - Fungal  
  - Bacterial  
- Hemorrhage
- Salivary Gland Dysfunction
- Drug Reactions
- Neurotoxicity (rare)
- Taste Dysfunction
- GVHD Acute & Chronic
- Benign Mucosal Lesions
- Dental Growth & Development  
  - Dentition - Skeletal
- Oral Cancers
Oral Complications of HCT

Early Post-Transplant

- Mucositis
- Infections
  - Viral
  - Fungal
  - Bacterial
- Hemorrhage
- Salivary Gland Dysfunction
- Drug Reactions
- Neurotoxicity \(^{(rare)}\)

- Taste Dysfunction
  - GVHD Acute & Chronic

- Benign Mucosal Lesions
  - Dental Growth & Development
  - Dentition - Skeletal

- Oral Cancers
Oral Complications of HCT

Late Post-Transplant

- Mucositis
  - Infections
    - Viral
    - Fungal
    - Bacterial
- Hemorrhage
  - Salivary Gland Dysfunction
  - Drug Reactions
  - Neurotoxicity (rare)

- Taste Dysfunction
  - GVHD Acute & Chronic
- Benign Mucosal Lesions
  - Dental Growth & Development
  - Dentition - Skeletal
- Oral Cancers

Late Post-Transplant
Oral Complications of HCT

- **Mucositis**: *Severity related to conditioning toxicity*
  - Pain symptom management
    - Saline rinses / topical anesthetics / pain medications
  - Palifermin
Oral Complications of HCT

- **Oral infections**: Infectious disease protocols
  - Standard infection prevention protocols

- **Oral bleeding**:
  - Prevention of infection and trauma
  - Platelet transfusions

- **Salivary gland dysfunction**
  - Symptom management / Taste stimulation
  - Sialagogues
  - Dry mouth (Xerostomia) decay: Prevention
Salivary Gland Dysfunction - Xerostomia Decay
Oral Complications of HCT

- **Taste dysfunction**
  - Supportive care recommendations
  - Diet adjustment
  - Recovers in 1-3 months after transplant

- **Dental growth and development**
  - Age at transplant (less 12-14 years old)
  - Monitor
  - Manage as indicated
Oral Graft vs Host Disease:
- Acute GVHD, chronic GVHD
- Diagnosis: clinical exam (*biopsy*)
- Symptom management: steroids
- Complicates recognition of oral cancers
A Few Key Take Home Points
Dental Health Considerations

- **Standard oral hygiene works!**
  - Brushing twice a day
  - Flossing once a day
  - Adjunctive dental care
    - Antibiotic oral rinses
    - Topical fluorides / Fluoride varnishes

- **Routine dental examinations**
  - Pediatric dentists
  - General dentists

Realize YOU will likely have to educate dentists and hygienists
  - Written materials
  - Discussions
Pre Cancer Treatment Oral / Dental Health

- Full dental and oral exam
- Stabilize / Eliminate oral disease
  - Caries
  - Gingivitis
  - Periodontitis
- Education and Training
  - Oral hygiene / self oral care
- Complications of cancer treatments:
  - Radiation therapy - Chemotherapy - Transplantation
    ➔ What – When – How managed
  - Anticipate: Prevent / Manage comprehensively

This has to be REALISTIC and FLEXIBLE
Oral Health Care for People with Fanconi Anemia

Mark M. Schubert, DDS, MSD
Oral Medicine Service
Seattle Cancer Care Alliance

mschuber@seattlecca.org

206 288 1333
Oral Health for People with Fanconi Anemia

Oral Health for Fanconi Anemia Patients

Appendix

Additional Slides
Tooth Brushing

- **Soft toothbrush**
  - Manual brushes
  - Electric brushes

- **Brushing techniques**
  - Bass sulcular technique
  - Scrubbing techniques

- **Interproximal brushes**

- **Toothpastes**

- **Remineralizing**
  - Fluorides
  - Calcium / phosphate
Tooth Brushing

Goal: Remove bacterial plaque from teeth and gums

- Soft tooth brush: manual or electric
- Toothpaste
- Brushing techniques:
  - Pediatric brushing
  - Bass sulcual brushing
- Flossing: manual or with flossers
Flossing

- **Floss**
  - Waxed / Unwaxed
  - Fine / Extra-fine
  - Glide™

- **Hand flossing**
- **Flossers**
Adjunctive Oral Hygiene Aids

- Interproximal brushes
- Tongue scrapers
- Antibacterial rinses
  - Chlorhexidine
  - Doxycycline / Minocycline
- Water irrigators
Salivary Gland Dysfunction

- **Risk factors**
  - Previous cancer treatments
  - Radiation conditioning regimens
  - Graft versus Host Disease
  - Medications

- **Infections / Microbial shifts**
  - Oral candida colonization
  - Shift to higher levels of cariogenic flora

- **Xerostomia Decay: Flora + loss of remineralization**

- **Management:**
  - Both comfort and oral health
  - Secretagogues (pilocarpine, cevimeline, bethanechol)
  - Caries prevention protocols (fluoride, OH, chlorhexidine)
  - Antifungal therapy as indicated
Alter BP. Fanconi’s Anemia, transplantation, and cancer. Pediatr Transplantation 2005;9 (suppl 7) 81-86
## Oral Signs/Symptoms AML

<table>
<thead>
<tr>
<th>Sign / Symptom</th>
<th>AML* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>109 (93)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>53 (45)</td>
</tr>
<tr>
<td>Laryngeal Pain</td>
<td>44 (38)</td>
</tr>
<tr>
<td>Oral Bleeding</td>
<td>51 (43)</td>
</tr>
<tr>
<td>Petechiae</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Oral Ulcerations</td>
<td>4 (22)</td>
</tr>
<tr>
<td>Gingival Infiltrates</td>
<td>5 (27)</td>
</tr>
<tr>
<td>Mucosal Pallor</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Tooth Mobility</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Toothache</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

Management

- Prophylactic regimens: prevent infection
  - *Acyclovir - Antifungal - Antibacterial Protocols*

- Clinical presentation: What does it look like?

- Culture lesions to diagnose → then treat to the identified organisms

- Empiric therapy vs directed therapy
Oral Hemorrhage

**Management:**
- Improve oral health – *eliminate gingivitis*
- Direct pressure / Mouth guards
- Topical hemostatic agents
- Platelet transfusions
Leukemic Infiltrates: Management

Gingival Infiltrates

**Improve oral hygiene**
- Brushing and flossing
- Antimicrobial rinses
- Systemic Antibiotics

- **Do not STOP** oral hygiene -- Modify protocol with medical / oral status

Generally will resolve with chemotherapy

Hopefully patients are already healthy and it is merely a matter of maintaining gingival health

Staging of oral hygiene care components
Adapt and up-date / Support patient health