Managing the morbidity of multimodality therapy in head and neck cancers

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Indian Scenario

- India is one of the high incidence zones in head & neck cancer

- In India, the most common H&N cancers are those of oral cavity and pharynx

- Infact, mouth and pharynx cancers are 3\textsuperscript{rd} most common cancer in males and 4\textsuperscript{th} most common in females in the developing countries
HNSCC CANCER

Patterns of failure

- Loco regional failure 75 - 90 %
- Distant Mets 05 -10 %
- Second Primary 10 - 20 %
General Management Guidelines: HNSCC Cancers

- Highest loco-regional control
- Anatomical with functional Preservation

- Stage I / II disease - Single modality (Surgery or RT)
- Stage III / IV disease – Combined modality

* Surgery + RT (in most patients)
* Chemotherapy + RT in selected patients
Why is combined treatment necessary?

- Advanced lesions (85% are stage III and IV cancers)

- Single modality of treatment gives unsatisfactory results

- Failure to control disease above clavicle (loco regional)
Combined Modality Treatment: Possible regimes

- RT $\rightarrow$ Surgery (Pre-op RT)
- Surgery + RT (Intra-operative RT)
- Surgery $\rightarrow$ RT (Post-op RT)$\pm$CT
- Radical RT$\pm$CT $\rightarrow$ Salvage Surgery
HNSCC CANCER

Multidisciplinary Team

Radiation Oncologist
Surgical Oncologist
Medical Oncologist
Radiologist
Medical Physicists
Radiotherapy Technologist
Dentistry / Prosthodontics
Speech and Swallowing therapy
Physical Medicine & Rehabilitation
Social Services
## Paradigm Shift in Cancer Mx

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Chemotherapy</th>
<th>Radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical</td>
<td>Nil</td>
<td>Wide Field</td>
</tr>
<tr>
<td>Conservative</td>
<td>H Dose</td>
<td>Involved F</td>
</tr>
<tr>
<td>NIL ?</td>
<td>Targeted</td>
<td>Conformal</td>
</tr>
</tbody>
</table>

**ERA OF RADICAL SURGERY GONE**
CLINICAL IMPLICATIONS

• Increasing incidence: intensification of therapy due to combined modality approach with overlapping toxicities.
• Most debilitating acute complication.
• Major drawbacks to patient (discomfort) and physician (challenging to manage).
  – Frequent treatment interruptions: inferior control rates.
  – Hospitalizations for alimentation support.
  – Pain control requiring potent narcotic cover.
  – Predisposition to neutropenic sepsis and life threatening complications.
  – Increased use of feeding tube replacement.
  – Increased cost: higher utilization of hospital resources.
  – Significantly impairs quality of life during treatment (difficulty in speaking, swallowing, maintaining oral hygiene).
  – Increased mortality rates.
A Challenge for The Radiation Oncologist!!!

Tumor
- Very Close proximity Of Tumor and Critical structures
- Total Dose Delivery Limited by Tolerance of Normal structures
- Dosimetric Challenges Due to Varying Contour/Tissue Heterogeneity

Patient
- Compromised Tolerance To Treatment
- Poor Nutritional Status and Weight Loss
- Inadequate oral Intake
- Treatment Induced Complications/side effects
Critical Structures

- Spinal Cord
- Brain Stem (and Cranial Nerves)
- Optic Chiasm and Nerves
- Brain (Temporal Lobes)
- Mandible (+TMJ)
- Eyes (Lens and Retina)
- Ear (Middle Ear, Inner Ear)
- Salivary Glands (Parotid, Submandibular, Sublingual)
- Tongue/Oral Cavity/Lips
- Larynx
- Pharynx/Esophagus

- Anterior Pharyngeal Constrictor muscle
Side Effects

• Early reactions
  – **Mucositis**
    – Dermatitis
    – Increasing hoarseness
    – Dysphagia
    – Laryngeal edema
  – **Xerostomia**
    – Laryngeal edema
    – Subcutaneous fibrosis
    – Pharyngeal stricture
    – ORN

• Late reactions
MUCOSITIS
Oral mucositis

- Oral mucositis (OM) is defined as “inflammation of oral mucosa resulting from cancer therapy typically manifesting as atrophy, swelling, erythema and ulceration” (Raber-Durlacher et al, 2010).

- Symptoms of mucositis vary from pain and discomfort to an inability to tolerate food or fluids.

- Mucositis may also limit the patient’s inability to tolerate either chemotherapy or radiation therapy, resulting in dose-limiting toxicity and hence drastically affecting cancer treatment and outcome.

Neoplasia 2004; 6, 423–431
Oral mucositis - an unmet medical need

- Estimated that about 40% of patients treated with standard chemotherapy develop mucositis

- Almost all patients (97%) receiving radiation therapy to the head and neck areas develop oral mucositis*

Neoplasia 2004; 6, 423–431
*Clinical Medicine and Diagnostics 2013; 3(4): 82-87
SITE & TIME OF OCCURRENCE OF MUCOSITIS

**Chemotherapy induced:**
- 7-14 days after initiation.
- Non-keratinized mucosal sites (SP, FOM, ventral tongue) affected.
- Granulocytopenia aggravates risk of infection.
- Resolution by 2-3 weeks.
- Mirrored by the recovery of neutrophil count.
- Generalized, affects entire alimentary tract.

**Radiotherapy induced:**
- Conventional: begins at 1-2 weeks, ulcerative mucositis develops after 30 Gy.
- Accelerated: peaks within 3 weeks.
- Interstitial implant: begins 7-10 days, peaks after 2 weeks.
- Limited to the field of radiation.
- Resolves 3-6 weeks after completion of RT.
CT V/S RT INDUCED OM

**Fig. 1** Clinical differences in onset, severity, and resolution of chemotherapy- and radiation-induced oral mucositis. In some patients treated with radiotherapy, oral mucositis may last for longer periods and may become chronic. Hyperfractionated radiotherapy, combined chemoradiation regimens, or radiotherapy combined with a targeted agent may lead to increased mucositis severity (not depicted).
RISK FACTORS- CT RELATED

1. Increasing number of cycles.
2. Previous episodes of CT induced mucositis.
5. High dose CT & BM transplant.
6. Other concurrent therapy: RT, biologic therapy.
7. Focused (regional) delivery: intra-arterial, liposomal conjugates, intraperitoneal.
RISK FACTORS- RT RELATED

1. Total cumulative dose.
2. Dose per fraction.
3. Volume of irradiation.
4. Overall treatment time.
5. Technique of RT (conformal vs. non-conformal. external vs. brachytherapy)
6. Quality of radiation (photons, electrons, protons).
8. Counseling and reassurance.
Effect Of Radiotherapy And Chemotherapy On The Risk Of Mucositis During Intensity-modulated Radiation Therapy For Oropharyngeal Cancer.

- Radiotherapy and chemotherapy act independently in determining acute mucosal toxicity; cCHT increases the risk of mucosal Grade 3 toxicity $\approx 4$ times over radiation therapy alone, and it is equivalent to an extra $\approx 6.2$ Gy to 21 cc of OM over a 7-week course.

Int J Radiat Oncol Biol Phys. 2012 May 1;83(1):235-42
Figure 3: Impact of Oral Mucositis—OM induced by chemotherapy and/or radiotherapy can have a negative impact on patients physically, nutritionally, psychologically, and socially, and caregivers may need support also.
# Table 3: Scales Used to Assess OM

<table>
<thead>
<tr>
<th>Grade</th>
<th>WHO</th>
<th>RTOG</th>
<th>NCI CTC</th>
<th>OMAS Ulceration/erythema</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Soreness with erythema</td>
<td>Erythema, ulcers, can eat solids</td>
<td>Painful erythema, edema, or ulcers, but can eat/swallow</td>
<td>Not severe &lt;1 sq cm</td>
</tr>
<tr>
<td>2</td>
<td>Erythema, ulcers, can eat solids</td>
<td>Patchy reaction &lt;1.5 cm, noncontiguous</td>
<td>Painful erythema, edema, or ulcers requiring IV hydration</td>
<td>Severe 1-3 sq cm</td>
</tr>
<tr>
<td>3</td>
<td>Ulcers, liquid diet only</td>
<td>Confluent reaction &gt;1.5 cm, contiguous</td>
<td>Painful erythema, edema, or ulcers requiring enteral nutritional support or prophylactic intubation</td>
<td>NA &gt;3 sq cm</td>
</tr>
<tr>
<td>4</td>
<td>Alimentation not possible</td>
<td>Necrosis or deep ulceration, ± bleeding</td>
<td>Severe ulcerations or requires parenteral/enteral nutritional support or prophylactic intubation</td>
<td>NA</td>
</tr>
</tbody>
</table>

OM: oral mucositis; WHO: World Health Organization; RTOG: Radiation Therapy Oncology Group; ± with or without; NCI CTC: National Cancer Institute Common Toxicity Criteria; NA: not applicable.

Sources: References 8-10, 12.
Oral mucositis stages

Mild or moderate oral mucositis = Grades 1 & 2 (WHO)

- Grade 1
  - Erythema
  - Unpleasant sensation (pain)

- Grade 2
  - Erythema
  - Ulcers
  - Pain
  - Can eat solids

Severe oral mucositis = Grades 3 & 4 (WHO)

- Grade 3
  - Ulcers
  - Significant pain
  - Only a liquid diet is possible

- Grade 4
  - Ulcers
  - Intolerable pain
  - Feeding by mouth is impossible, enteral or parenteral feeding obligatory
  - Cannot talk
• Thick, sticky saliva (mucus)
• Mucus – thicker, stringy and sticky like mucus
• Spit frequently because of mucus build up, irritating especially at night
• Mouth rinse – half a teaspoon of salt and baking soda each in 1 L of water
• Nebulizer before bedtime
STORY OF SALIVA
Functions of Saliva in Healthy Mouths

- Protects teeth from acids and dilutes sugars.
- Washes your teeth and protects them from decay.
- Protects the oral mucosa from injury and infection.
- Enables cheeks and tongue to slide easily over teeth in smiling, talking, chewing and swallowing.
- Moistens food, making it easier to move around in the mouth.
- Fights oral infections with antibiotics and antimicrobials.
With Reduced, Thickened or No Saliva

- Rampant tooth decay
- Mucosa more easily injured
- Oral and systemic infections more common
- Increased difficulty in chewing, swallowing, speaking and smiling
General Management of stomatitis

- Gargles and hygiene
- Analgesics and antiinflammatory
- Local anesthetics
- Local application gels
- Nasogastric feeding
- Gaps in treatment till stomatitis decreases
- Parenteral feeding
Gaps in the treatment lead to increase in the overall treatment time and this leads to poor results.
Table 6. Diet in oral mucositis.

<table>
<thead>
<tr>
<th>Diet that is typically acceptable</th>
<th>Things to avoid</th>
<th>Habits to avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquids</td>
<td>Rough food (potato chips, crisps, toast)</td>
<td>Smoking</td>
</tr>
<tr>
<td>Purees</td>
<td>Spices</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Ice</td>
<td>Salt</td>
<td></td>
</tr>
<tr>
<td>Custards</td>
<td>Acidic fruit (grapefruit, lemon, orange)</td>
<td></td>
</tr>
<tr>
<td>Nonacidic fruits (banana, mango, melon, peach)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft cheeses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NCCN Task Force Report

Mucositis

Xerostomia
- Sialagogues: Sugarless candy/mints, pilocarpine/cevimeline, bethanechol
- Topical fluorides: Remineralizing agents

Pain
- Bland rinses: 0.9% saline, sodium bicarbonate

Infections
- Prophylaxis: Fungal, Viral, Bacterial

Diagnosis

Treatment
- Topical
- Systemic

Moderate

Severe

Mild

Moderate

Systemic analgesics: Hydrocodone, morphine, fentanyl, oxycodone, methadone

Topical anesthetics: Lidocaine, benzocaine, dyclonine

Mucosal coating agents: Benzydamine HCl
The effectiveness of commonly used mouthwashes for the prevention of chemotherapy-induced oral mucositis: a systematic review.

Daily chlorhexidine mouthwash is often recommended for preventing chemotherapy-induced OM.

Povidone-iodine, NaCl 0.9%, water salt soda solution mouthwash are also recommended.

Based on study quality, 3/5 RCTS were included in a meta-analysis.

The results failed to detect any beneficial effects of chlorhexidine as compared with sterile water, or NaCl 0.9%.

**Patients complained about negative side-effects of chlorhexidine, including teeth discoloration and alteration of taste in 2/5 on chlorhexidine.**

The severity of OM was shown to be reduced by 30% using a povidone-iodine mouthwash as compared with sterile water in a single RCT.

**These results do not support the use of chlorhexidine mouthwash to prevent oral mucositis.**
Randomized Trial Of A Chlorhexidine Mouthwash For Alleviation Of Radiation-induced Mucositis.

CONCLUSION In contrast to the prestudy hypothesis that a chlorhexidine mouthwash might provide benefit for patients receiving radiation therapy to the oral mucosa, this study provides strong evidence suggesting that a chlorhexidine mouthwash is detrimental in this clinical situation.
Care of the Mouth During Cancer Treatment

• Rinse two-six times daily with half a teaspoon of baking soda dissolved in one quart water.
• If thrush becomes a problem, ask for sugar-free anti-fungal medications, rinses or lozenges.
• Dentures – either at end or proper care
Care of the Mouth During Cancer Treatment

- **Benzydamine oral rinse:** 15ml 4-8 times a day reduces frequency and severity of ulcerative oral lesions and decreases pain in oral induced mucositis
- Relieves pain when eating.
- Swish 10 minutes before meals.
- In extreme cases of pain, morphine may be prescribed.
Figure 2  Step therapy for pain management in mucositis
Courtesy of Mark Schubert, DDS, MSD.
Abbreviation: WHO, World Health Organization.
Interventions For Preventing Oral Mucositis For Patients With Cancer Receiving Treatment.

Ten interventions, showed some statistically significant evidence of a benefit (albeit sometimes weak) for either preventing or reducing the severity of mucositis, compared to either a placebo or no treatment.

– aloe vera, amifostine, cryotherapy, granulocyte-colony stimulating factor (G-CSF), intravenous glutamine, honey, keratinocyte growth factor, polymixin/tobramycin/amphotericin (PTA) antibiotic pastille/paste and sucralfate.

Cochrane Database of Systematic Reviews 2011, Issue 4
Art. No.: CD000978. DOI: 10.1002/14651858.CD000978.pub5.
Comparison of granulocyte-macrophage colony-stimulating factor and sucralfate mouthwashes in the prevention of radiation-induced mucositis: a double-blind prospective randomized phase III study

- GM-CSF mouthwashes may be moderately more effective than sucralfate mouthwashes in preventing radiation-induced mucositis and mucositis-related pain, and their use may lead to less frequent RT course interruptions from mucositis. The present findings need to be confirmed before adopting GM-CSF mouthwashes in routine clinical use.

*International Journal of Radiation Oncology*Biology*Physics
*Volume 54, Issue 2, 1 October 2002, Pages 479–485*
Supersaturated Calcium Phosphate

• Mouth rinse that is rich in both calcium and phosphate ions

• Designed to moisten, lubricate and clean the oral cavity including the mouth, tongue and oropharynx

• Making food easier to swallow

• Helps maintain the integrity of the oral cavity

• Mouth rinse that is scientifically proven to help prevent, reduce the duration and the pain of oral mucositis
Supersaturated Calcium Phosphate

- Reduction of painful oral mucositis by supersaturated calcium phosphate oral rinse in head and neck cancer patients receiving chemotherapy and radiation

- Haas M et al. 50th ASTRO congress 2008; abstract 2530
Supersaturated Calcium Phosphate

- A Retrospective Match Controlled study of Supersaturated Calcium Phosphate Rinse vs. Supportive Care for Radiation Induced Mucositis

_Curtis et al. Journal of cancer therapy; 2012, 3, 630-636_

**Conclusion:** The reduction in the occurrence of OM has been proven to be statistically significant in SCPR treated group of patients
Flow chart: Management

Identification of Patient at Risk to Develop Mucositis

Patient Related Factors
- Age
- Nutritional status
- Therapy

Flow Chart for the prevention and treatment of mucositis

Prophylactic Intervention

Assessment of Mucosal Injury using standard rating scales and pathological investigations.

Oral Mucositis Develops

Patients Counseling
- Oral Care
- Nutritional Support

Symptoms of secondary infection

Obtain appropriate cultures and treat with suitable agents.

Topical coating agents
- Local anesthetics
- Laser Therapy
- Topical Analgesics.

Type, Dose and Duration of Chemotherapeutic Agents/Radiation

Cryotherapy, Allopurinol, Pilocarpine, Cytokines, Investigational agents

Oral Hygiene
- Usage of Mouth washes and dental care.
Conclusions for Mucositis

No clear guidelines for prevention of oral mucositis with CT+RT as on today

Constant Oral rinsing & salivary substitutes, proper nutrition and supportive care, taking care of infection and good use of opioid analgesics and steroids specially in last two weeks specially is the key to phase off the menace from so called and mostly ignored symptom - mucositis.

Mucositis affects outcomes in many ways and increases workload and requires adaptation requiring replanning, admissions, treatment delays with incomplete treatments, increasing costs directly or indirectly & affecting outcomes.

Multidisciplinary team approach by physiotherapist, occupational therapist, dietician, Psychologist, pain management team with oral care specialists is the need.

Oral Care Protocols should be strictly implemented with the institutional guidelines and changed as per the needs
Grading of Early skin reactions

• Grade 0  No change

• Grade I  Follicular, faint/dull erythema, Epilation, Dry desquamation, Decreased sweating

• Grade II Tender or bright erythema Patchy Moist desquamation Moderate edema

• Grade III Confluent moist desquamation

• Grade IV Ulceration, hemorrhage, Necrosis
Care to be taken during RT

- Gentle washing
- Avoidance of friction
- Loose cotton clothing
- Avoid wet shaving
- Protect from sun, irritants and extremes of temperature
- Abstain from smoking (damage caused by cutaneous vasoconstriction)
Management Of Skin reactions

• Keep part open in air if possible

• Use of gentian violet or povidone iodine solution or spray

• Aqueous creams like hydro-gels and hydrocolloids

• Steroid and antibiotic combination creams

• Homeopathic creams (e.g. Calamine) have been used for treatment of acute skin reactions in many centers
Dysgeusia

- abnormal or impaired sense of taste, an unpleasant alteration of taste sensation, or a distortion or perversion of the sense of taste.
- Zinc gluconate and amifostine not routinely recommended
- Dietary and educational counseling

Fungal and Viral infections

Hoarseness

Dysphagia – nutritional deficiencies

Malaise, Nausea, Bad breath (changes in saliva, improper hygiene, infection)
DRY MOUTH
Xerostomia can take form of thick saliva

Or total lack of salivation

Radiation Caries
History & Symptoms of Dry Mouth

History: the subjective complaint of dry mouth
1. Feel dry mouth while eating
2. Need Frequent Sips of Liquids While Eating
3. Difficulties in Swallowing Food

Symptoms
- Thirst
- Difficulty eating, speaking, wearing denture
- Need sips of water while eating
- Burning sensation of mouth
- Abnormal taste
- Cracked Lips & Soreness of Corners of Mouth

Definition: Salivary gland hypofunction is a decrease in salivary secretion, with pathological low saliva secretion as ≤ 0.1 ml/min for unstimulated whole salivary flow and ≤ 0.5 ml/min for stimulated whole salivary flow.
Dry Mouth or Xerostomia Can Affect

- Ability to eat, swallow, speak and smile
- Nourishment/food choices
- Ulcerations of oral tissues
- Tooth decay
Tips to Alleviate Dry Mouth

• Drink frequent sips of water
• Suck ice chips
• Use sugar-free gum, mints and hard candies
• Avoid alcoholic drinks
• Moisturize lips
• Humidifier in home
Tips to Alleviate Dry Mouth

- Rinse at least twice daily with a half teaspoon baking soda dissolved in one cup of warm water.

- Ask for salivary substitutes

- Try mouthwash, toothpaste and chewing gum, found in the dental aisle, made especially for Dry Mouth.
Tips to Alleviate Dry Mouth

• Take small bites, moist foods with gravy

• Chew slowly

• Sip liquids while eating
Tips to Combat Rampant Caries

- After eating, brush teeth with soft brush and small dab of fluoride toothpaste.
- Floss gently, yet thoroughly, between teeth once daily.
- Chew gum sweetened with xylitol 3-5 times a day for 3-5 minutes.
- Consider alternate anti-fungal regimens.
AMIFOSTINE-FREE RADICAL SCAVenger

Phase III Trial of RT ± Amifostine in Patients With H&N Cancer:

**STRATIFY**
- Treatment center
- 1º tumor site
- Definitive vs postoperative adjunctive radiation
- N¹ vs N₀
- Karnofsky performance status

**RANDOMIZE**

**ARM I (n = 150)**
- Amifostine: 200 mg/m² IV over 3 min, 15 - 30 min before RT
- RT: 1.8 - 2.0 Gy/d Total: 50 - 70 Gy x 5 d/wk

**ARM II (n = 153)**
- RT: 1.8 - 2.0 Gy/d Total: 50 - 70 Gy x 5 d/wk

Min. 40 Gy to 75% of total parotid

AMIFOSTINE

**RT ± Amifostine**

*Randomized Phase III Trial*

Grade ≥2 Xerostomia

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>RT + Amifostine</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>32%</td>
<td>29%</td>
</tr>
<tr>
<td>18</td>
<td>56%</td>
<td>51%</td>
</tr>
<tr>
<td>24</td>
<td>51%</td>
<td>20%</td>
</tr>
</tbody>
</table>

*P* = 0.002*

Mucositis: No Difference

<table>
<thead>
<tr>
<th>Site of mucositis</th>
<th>Cancer treatment</th>
<th>References</th>
<th>Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Mucositis (stomatitis)</td>
<td>Head and neck (radiation)</td>
<td>[12]</td>
<td>No benefit: no guideline possible</td>
</tr>
<tr>
<td></td>
<td>Head and neck (chemoradiation)</td>
<td>[2, 13, 24, 37, 41, 42]</td>
<td>Inconsistent benefit: no guideline possible</td>
</tr>
<tr>
<td></td>
<td>Transplant</td>
<td>[7, 15, 16, 34, 35, 38]</td>
<td>Inconsistent benefit: no guideline possible</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>Lung cancer (chemoradiation)</td>
<td>[1, 3, 4, 17, 22, 31, 43]</td>
<td>Amifostine should be recommended for the prevention of esophagitis (level of evidence III, grade of recommendation C)</td>
</tr>
<tr>
<td>Proctitis</td>
<td>Rectal carcinoma (radiation)</td>
<td>[5, 21, 26, 27]</td>
<td>Amifostine in a dose of at least 340 mg/m² should prevent proctitis in patients receiving standard dose radiotherapy (level of evidence III, grade of recommendation B)</td>
</tr>
<tr>
<td></td>
<td>Colorectal carcinoma (chemotherapy)</td>
<td>[40]</td>
<td>Inconsistent benefit: no guideline possible</td>
</tr>
<tr>
<td></td>
<td>Other pelvic cancers</td>
<td>[5, 23]</td>
<td>Inconsistent benefit: no guideline possible</td>
</tr>
<tr>
<td></td>
<td>Intrarectal route</td>
<td>[8, 9]</td>
<td>Pilot studies: no guideline possible</td>
</tr>
</tbody>
</table>
ETHYOL-CONCLUDING REMARKS

• US FDA approved indication for ethyol use: *Xerostomia* prevention in the setting of *RT alone*.

• Only small studies indicate effectiveness of ethyol in prevention of mucositis in concurrent chemoradiation setting.

• Ethyol use along with IMRT not yet adequately studied.
Pilocarpine: * A Muscarinic Receptor Agonist Available as 5 mg tab.
- Shown to improve symptoms of RT induced xerostomia
* A Maximum Dose of 30 mg/day in divided doses.
- Effects of Pilocarpine are usually immediate;

* In RT-induced Xerostomia, Pilocarpine can take up to 12 weeks to Produce Effects
* Increase in Saliva Production Generally Lasts 4 hrs
- Undesirable Side Effects of Pilocarpine: Perspiration, Flushing, Lacrimation, Urinary Frequency and GI Disturbances.

Pilocarpine

• Pilocarpine Pills Useful in Increasing Saliva Flow & Providing Relief of Dry Mouth.

• Since Pilocarpine May Cause Fluctuations in the Blood Pressure or Heart Rate, the Patient Needs to be Closely Supervised
Xylitol Strengths & Limitations

When Salivary Function is Preserved, Stimulation of Salivary Glands with Xylitol is Aimed to increase the Salivary output.

Naturally Xylitol/SST Would Work Only in Patients Whose (at least) Partial Salivary Function has been Conserved.

Saliva Substitute suitable Option for Patients With Damaged Salivary Function Due to Radiation Therapy
Sugar Vs Xylitol

- Sugars, when in mouth, stimulate Saliva Flow to flush the content
- Sugars Get Converted in Lactic Acid
- The Bacterial Colony Shifts to Acidophilic Bacteria
- Result: Erosion, Caries Formation

- Xylitol is Anti-Cariogenic
- It does not get degraded in Mouth by the Acidophilic Bacteria
- Being Sweeter, it Stimulates Salivation
What is Xylitol?

• Xylitol is a White Crystalline powder
• Synthesized in Germany, Known Since 1891
• Xylitol is a Sugar Alcohol Sweeter than Sucrose
• Xylitol Chemical Formula is $\text{C}_5\text{H}_{12}\text{O}_5$ (not $2:1$)
• Glucose Chemical Formula is $\text{C}_6\text{H}_{12}\text{O}_6$ ($2:1$)
• In Classical Sense Xylitol is Not a Sugar

• Hence it is Not Metabolized like Sugars

This has Relevance to Sugars Versus Xylitol in Xerostomia & Overall Dental Care
Outcome versus Toxicity

Toxicity

Local Control

Survival

What can improve the outcome
Without increase in complications
The Evolution of Radiation Therapy

- **1960s**
  - First Linac and Basic Collimator

- **1970s**
  - Cerrobend Blocking
  - Electron Blocking
  - Computerized 3D Treatment Planning
  - Multileaf Collimator

- **1980s**
  - Dynamic MLC
  - IMRT

- **1990s**
  - High-Resolution IMRT

- **2000s**
  - High-Resolution IMRT
IMRT - Target volume

- IMRT requires a thorough understanding of target delineation in the complex H&N
- IMRT is a process
  - Planning
  - Information Transfer
  - Delivery
  - Verification
- IMRT allows you to customize your treatment delivery based on a specific planning objective
IMRT Clinical Studies

August 2002 Review of the Literature

Arno Mundt MD, University of Chicago
Isodose – Ca Tongue
DVH
PET Scores over others!

CT, MRI
Anatomical imaging

PET is functional imaging
Active viable tumor
Newer Techniques in Radiation Therapy
Image Guided Radiation Therapy

WHY ??
- Set up error
- Intra & Inter fraction organ movement
- Daily verification
- Accurate Treatment Delivery
Types of IGRT

- Portal Imaging
- EPID – Electronic Portal Imaging Device
- USG guided RT
- In room CT
- KV Cone beam CT
- MRI guided RT
- Tomotherapy
Tomotherapy

Cyber Knife
**Trismus**
- 2º to fibrosis of muscles, exacerbated by pre-XRT trauma (ie. Sx)
  - TM joint
- impaired nutrition if severe
- very limited access for dental treatment
  - Physiotherapy for trismus

**Edema**
- 2º to decreased lymphatic drainage from fibrosis
- not usually a functional problem but cosmetic

**Speech and language therapist**

**Radiation Caries**

**Craniofunctional disturbances**
Osteoradionecrosis

- Inci- 5%, hypoxic injury, 0%- 3 weeks for healing after extraction
- ORN is characterized by a nonhealing area of exposed mandibular and maxillary bone of at least 6 months duration in a patient who has been treated with radiation therapy (RT) for cancer.
- Mandibular molar area most affected precipitated by dental extraction
- Higher doses of RT and concurrent CT increases risk
- Management depends on severity and range from local irrigation, antibiotic treatment, local sequestrectomy or wide segmental excision with or without reconstruction.
- Controversial role of HBOT - helps to promote vascularity, growth of new blood vessels, aiding healing process
HN SCC.. Are we ready to tame the bull?
The philosophy

- The success of HNC treatment only partly lies in improving the 5yrs survival.

- The true challenge lies in restoring function and anatomy.

- There cannot be any fixed protocol as all cases need tailormade treatment.

- While planning treatment …..
Combined modality treatment for Head and Neck Cancers: Acute Toxicities

- Acute Grade 3/4 toxicity can be as high as 90% with CT+RT
- Such high toxicities leads to treatment breaks offsetting benefit from aggressive Rx
- Many agents have seen to be promising: ice chips, benzydamine
- Many agents have seen to be disappointing: Sucralfate
- Efforts still needed to decrease acute mucosal reactions
Combined modality treatment for Head and Neck Cancers: Late Toxicities

- Patients complaint of xerostomia

- Patients can be on long term feeding tube because of stricture formation

- Conformal techniques to reduce toxicity

- Dental care even after treatment – non invasive 3 and invasive 6 months
BASIC GUIDELINES

- **PSYCHOEDUCATION:** comprehensive patient education to prepare them for the expected course of events and methods to cope with them.
- Family and staff education.
- Regular & timely evaluation of these protocols.
- Quality improvement.
GOOD CLINICAL PRACTICE

- Use of validated tools to **regularly assess** oral pain & hygiene.

- **Interdisciplinary approach** (nurse, dentist, dietician, physician, dental hygienist).

- **Tumor board meetings**

- **Dental professionals:** vital before initiation of therapy as well as throughout treatment & follow up.

- Technique of RT

- **Benzydamine:** anti-inflammatory with analgesic, anesthetic & anti-microbial properties reduces frequency & severity of ulcerative lesions.

- Amifostine, Pilocarpine....

- Occupational Speech Therapist

- **Palliation of acute oral pain:** most important component of patient care.
Our View Multidisciplinary team
Head & Neck Multidisciplinary Team
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A Cure for all Head and Neck Cancers
“What matters is just not the machine, but also the man behind the machine.”