



Oral Cancer The Self Made Death

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Abstract - Oral squamous cell carcinoma (OSCC) remains a significant global health concern with rising incidence rates. This project aims to elucidate potential biomarkers and therapeutic targets associated with OSCC progression. Through comprehensive genomic and proteomic analyses, we seek to identify key molecular signatures contributing to oral cancer development. Our study involves the collection of clinical samples, including tissue biopsies and saliva specimens, from a diverse patient cohort. Utilizing advanced molecular techniques such as next-generation sequencing and mass spectrometry, we aim to uncover genetic mutations, gene expression alterations, and protein aberrations specific to OSCC. Furthermore, the project explores the tumor microenvironment and immune response dynamics within oral cancers. By understanding the intricate interplay between cancer cells and their microenvironment, we aspire to identify novel immunotherapeutic strategies to enhance treatment efficacy. In conclusion, this research project aspires to provide valuable insights into the molecular underpinnings of oral cancer, paving the way for the development of targeted therapies and personalized treatment approaches to improve patient outcomes.

Keyword : Squamous cell; Oral Cancer; Cancer Etiology; Cancer Diagnosis; Cancer Treatment;

INTRODUCTION

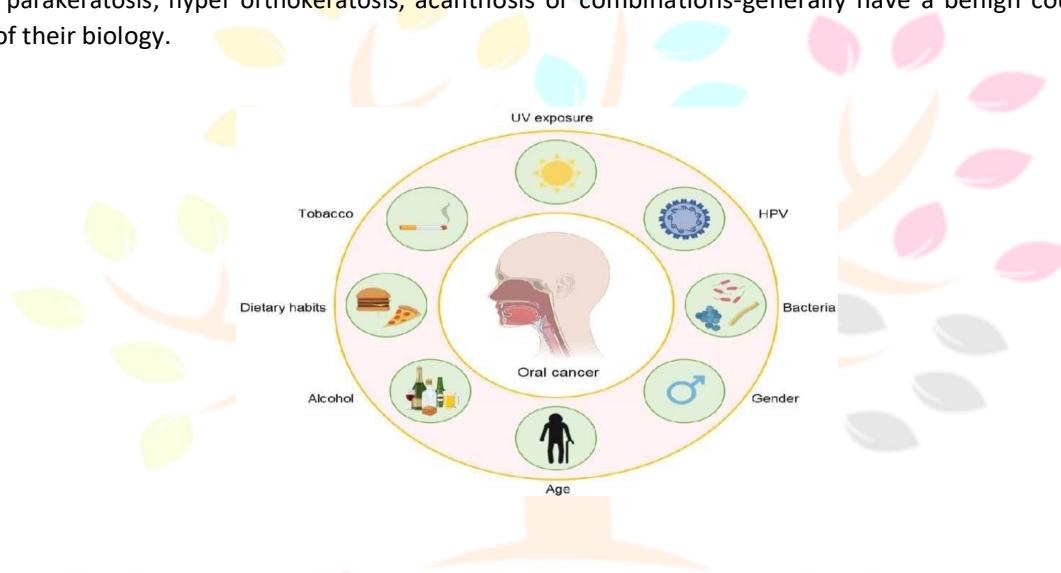
Oral cancer is one of the most common cancers and it constitutes a major health problem particularly in developing countries. It is one of the leading causes of death. Tobacco and alcohol consumption appears to be the major determinants of oral cancer. Oral cancer (OC) is the commonest cancer in India, accounting for 50–70% of total cancer mortality and accounts for highest incidence among Asian countries. OC is the sixth most common cancer worldwide. It affects anterior tongue, cheek, floor of mouth, gingiva or any other part of the oral cavity. Worldwide, there is a great variation in the incidence of cancer of the oral cavity. It accounts for less than 5% of all cancers in United States, Western Europe and Australia. India, few pockets in France, Brazil, central and eastern Europe have few of the highest rates of cancer of the oral cavity in the world. The differing social customs are likely to be responsible for regional variations in the disease incidence. The high rate of OC in France and Eastern Europe has historically been linked to the heavy consumption of alcohol and tobacco in these countries. The habit of chewing betel nut leaves rolled with lime and tobacco, a mixture known as pan, results in prolonged contact of the carcinogen with the buccal mucosa, which is thought to be the principal cause of OC in India.

ETIOLOGY:-

The etiology of oral cancer in man is unknown. However, several pre-existing conditions have been found with such frequency in patients with oral cancer that they may be considered, at least in part, as contributory factors. For instance, chronic irritation seems to be related to the development of cancer, whereas a single episode of trauma does not. Other factors which may lead to the development of oral cancer include: O Ionizing radiation at therapeutic, not diagnostic, dosage levels.

Fortunately, because of stricter radiotherapeutic guidelines, few patients are today exposed to sufficient quantities of ionizing radiation to produce cancers of the oral cavity. Chronic exposure to actinic radiation. Chronic exposure to the sun is a significant factor in the development of cancer of the lower lip, the most common form of oral cancer. The high incidence of "Farmer's lip" and "Sailor's lip," as well as epidermoid carcinoma of the lip in hot climates attests to the etiologic significance of long-term exposure to sunlight. Apparently, repeated exposure to ultraviolet solar rays over a period of 15-30 years results in atrophicalterations of the exposed aspect of the lower lip, which may develop into carcinoma. The carcinogenic action of solar rays varies according to intensity and length of exposure and is probably limited by pigmentation. In black people, for example, epidermoid carcinoma

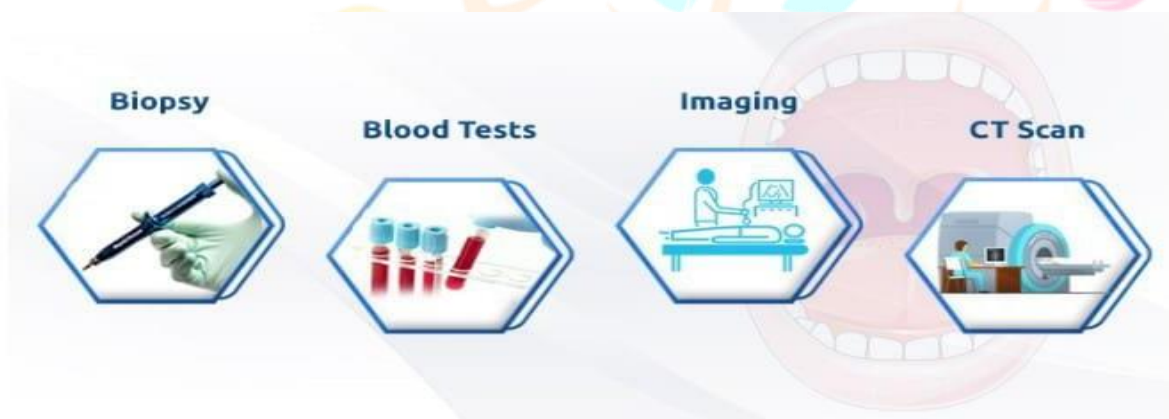
The most common type of oral cancer is epidermoid carcinoma (squamous cell carcinoma). Epidermoid carcinoma originates in abnormal mucosa as either leukoplakia, erythroplakia or speckled leukoplakia. This disease most commonly begins in a leukoplakic lesion which can be smooth or rough, flat or elevated, ulcerated or intact. Leukoplakia is manifested histologically by a thickening of the mucosa. When the thickened surface layer contains cells with retained nuclei it is termed hyperparakeratosis; if the thickened surface layer cells do not contain nuclei it is termed hyperorthokeratosis. A thickened spinous layer is called acanthosis; a thickened basal layer, basal hyperplasia. Actually, many leukoplakic lesions result from combinations of the various thickenings, for instance, hyperparakeratosis with acanthosis. These hyperplastic lesions of mucosa hyper parakeratosis, hyper orthokeratosis, acanthosis or combinations-generally have a benign course for at least some phases of their biology.



The stage following hyperplasia in the pathogenesis of oral cancer is dysplasia. This is evidenced histologically by cytologically atypical cells and an alteration in the sequence of maturation and organization of the epithelium. It is not proven if the removal of the cause of dysplasia in the oral cavity will result in resolution of the disease; therefore, dysplastic areas are considered irreversible precancerous lesions. Carcinoma in situ, cancer confined to the surface epithelium, shows all of the histological criteria of cancer. However, this process has not spread beyond the boundaries of the surface epithelium. Therefore, invasion and metastasis are not present in carcinoma in situ. In other sites of the body (uterine cervix, for example), and perhaps the oral cavity, carcinoma in situ can persist for some time, even years, before progressing into invasive epidermoid carcinoma. Epidermoid carcinoma can be of varying levels of differentiation which exhibit all the clinical and histologic features of cancer. The sequence in the development of carcinoma seems to be similar regardless of origin (leukoplakia, erythroplakia or speckled leukoplakia). This disease shows invasion and later metastasis. Metastases, which generally occur via the lymphatics of the neck, produce neck metastases. These neck metastases can obtain considerable size, produce fistulation and cause marked discomfort. When the disease spreads beyond the neck, target organs are usually the lungs. Metastases to the oral cavity from other sites of the body-generally from cancers of the breast, lung or prostate frequently present as a non-symptomatic radiolucency of the posterior aspect of the mandible often associated with the teeth. These radiolucencies are irregular, with a "moth eaten" pattern. Although the patient is usually aware of his disease, cases of unsuspected cancers have been diagnosed as a result of "periapical granulomas" or "atypical periodontitis" submitted for histopathologic examination. The differential diagnosis of white lesions relies on an adequate history and thorough physical examination, as well as histopathological investigation. Some of the more common diseases which may present as a white or whitish lesion are listed below. Ectopic sebaceous glands (Fordyce's disease) presents as yellowish, small elevations which, when clustered, may resemble a white patch and occur on the lips, buccal mucosa or vestibular mucosa; Leukoedema appears

as a filmy, bluish-white lesion which is usually bilateral, confined to the buccal mucosa and most frequently observed in black patients; Chemical burns (Fig. 1.) produce a lesion with necrotic surface epithelial cells which can, at least in part, be scraped clean, leaving a raw red surface, and, in most instances, are associated with a history of topical application of some medication, often acetyl salicylic acid.

DIGNOSIS : Tests and procedures used to diagnose mouth cancer include: Physical exam. Your doctor or dentist will examine your lips and mouth to look for abnormalities—areas of irritation, such as sores and white patches. Removal of tissue for testing (biopsy). If a suspicious area is found, your doctor or dentist may remove a sample of cells for laboratory testing in a procedure called a biopsy. The doctor might use a cutting tool to cut away a sample of tissue or use a needle to remove a sample. In the laboratory, the cells for cancer or precancerous changes that indicate a risk of future cancer. Determining the extent of the cancer Once mouth cancer is diagnosed, your doctor works to determine the extent (stage) of your cancer. Mouth cancer staging tests may include: Using a small camera to inspect your throat. During a procedure called endoscopy, your doctor may pass a small, flexible camera equipped with a light down your throat to look for signs that cancer has spread beyond your mouth. Imaging tests. A variety of imaging tests may help determine whether cancer has spread beyond your mouth. Imaging tests may include X-ray, CT, MRI and positron emission tomography (PET)scans, among others. Not everyone needs each test. Your doctor will determine which tests are appropriate based on your condition. Mouth cancer stages are indicated using Roman numerals I through IV. A lower stage, such as stage I, indicates a smaller cancer confined to one area. A higher stage, such as stage IV



Prevention :- There's no proven way to prevent mouth cancer. However, you can reduce your risk of mouthcancer if you: Stop using tobacco or don'tstart.If you use tobacco,stop. If you don't use tobacco, don'tstart. Using tobacco, whether smoked or chewed, exposes the cells in your mouth to dangerous cancercausingchemicals. Drink alcohol only in moderation, if at all. Chronic excessive alcohol use can irritate the cells in your mouth, making them vulnerable to mouth cancer. If you choose to drink alcohol, do so in moderation. For healthy adults, that means up to one drink a day for women of all ages and men older than age 65, and up to two drinks a day for men age 65 and younger. Avoid excessive sun exposure to your lips. Protect the skin on your lips from the sun by staying in the shade when possible. Wear a broadbrimmed hat that effectively shades your entire face, including your mouth. Apply a sunscreen lip product as part of your routine sun protection regimen. See your dentist regularly. As part of a routine dental exam, ask your dentist to inspect your entire mouth for abnormal are as that may indicate mouth cancer or precancerous changes.

TREATMENT .: Treatment for mouth cancer depends on your cancer's location and stage, as well as your overall health and personal preferences. You may have just one type of treatment, or you may undergo a combination of cancer treatments. Treatment options include surgery, radiation and chemotherapy. Discuss your options with yourdoctor.

Early diagnosis Early diagnosis is critically important to decrease oral cancer mortality. Most oral cancers develop in areas that can be seen and/or palpated, meaning that early detection should bepossible²³. Key signs are ulcer ation, in duration, infiltration, bleeding, and nodes. Unfortunately, patients are most often identified after the development ofsymptomsassociated with advanced stages of the disease, such as discomfort, dysphagia, otalgia, odynophagia, limited movement of the tongue, limited ability to open the mouth, cervical and submandibular nodes, weight lesion is unilateral. In contrast, some cancer may be asymptomatic, which further contributes to late diagnosis.

Opportunistic oral cancer screening examinations conducted by OHPs therefore remain an important meansfor early identification and diagnosis. In early stages, the lesionmay be flat or elevated andmay beminimally palpable orindurated.

Diagnosis based on clinical examination and biopsy, which is the gold standard procedure. Biopsy layer should be conducted between sound and pathologic tissues to the depth of the basal.

Positive diagnosis: Pre-malignant disorders : leukoplakia, erythroplakia, Lichen planus Oral Cancer: oral intraepithelial neoplasia, in-situ carcinoma, micro-invasive or invasive Carcinoma The management of patients with Oral cancer is complex . Manifestation of cancer therapy may include infections, mucositis and oral ulceration, xerostomia, bleeding, pain, osteoradionecrosis, Taste loss, trismus, and caries. These require prevention and management . Treatment strategies vary based on the stage of oral cancer at the time of diagnosis. Depending on the stage , treatment may include surgery and/or radiotherapy, leading to a high probability of long term survival but often with considerable morbidity 24. Chemotherapy, including targeted therapy, may be combined with radiation in initial treatment or used to treat recurrent cancer. Immunotherapy is a newer option for advanced or recurrent cancer²⁵. The choice of treatment also depends on the comorbidities presented by the patient and his / her nutritional status, ability to tolerate treatment, and wishes to undergo therapy Multi disciplinary treatment is crucial to improve the oncologic results and minimize the impact on function and quality of life.

Before treatment :- Before treatment is initiated, it is recommended that dentists perform a systematic dental assessment and establish an oral care programme to improve treatment compliance by decreasing infection risk. Upon diagnosis, the majority of patients present associated dental Pathologies (caries, periodontal disease). Dentists should conduct oral rehabilitation, non-invasive treatment, fluoride dental tray, and maxillofacial prosthesis as appropriate. In addition, radiotherapy (with or without chemotherapy) often induces oral complications, and surgical treatment frequently required bone resection with dental extractions. Clinical and radiological examination (panoramic) should be performed to repair and remove infectious dental foci. This involves the elimination of dental caries(endodontic management and restorative treatment) and extraction of at risk teeth with primary wound closure 7 to 10 days before initiation of radiotherapy to minimize the risk of osteoradionecrosis associated with post radiation dental extraction and elimination of all causes of mucosal trauma 15. Depending on the irradiated field, provision should be made for definitive dental prosthodontic trays. An oral care programme which includes oral health instruction (tooth cleaning by toothbrush, interdental brush, and dental floss, followed by gargling three times per day), removal of dental calculus (scaling), professional mechanical tooth cleaning, removal of tongue coating with a tooth brush, and denture cleaning should be established.

During treatment : Dentists should minimize the side effects of radiotherapy and recommend a basic oral self care programme , which is a combination of toothbrushing, flossing, and rinsing to improve treatment compliance by decreasing infection risk as follows Post-radiotherapy mucositis: local antiseptic, anesthetic gel use, non-alco Caries: brush twice-daily with a soft toothbrush and with fluoride toothpaste between 2800ppm and 5000ppm and/or application of fluoride dental tray; Xerostomia: sugar-free chewing gum and salivary substitutes.

After Treatment: Specific attention should be given to the healing process and possible recurrence of oral cancer. Follow-up with recall should be done at least twice per year and adapted as required. Any traumatic dental procedures following radiotherapy should be performed under antibiotic cover. Non-traumatic prosthetics for rehabilitation should be performed within 6 to 12 months. Surgery Surgery for mouth cancer may include:

Surgery to remove the tumour. Your surgeon may cut away the tumour and a margin of healthy tissue that surrounds it to ensure all of the cancer cells have been removed. Smaller cancers may be removed through minor surgery. Larger tumours may require more-extensive procedures. For instance, removing a larger tumour may involve removing a section of your jawbone or a portion of your tongue. Surgery to remove cancer that has spread to the neck. If cancer cells have spread to the lymph nodes in your neck or if there's a high risk that this has happened based on the size or depth of your cancer, your surgeon may recommend a procedure to remove lymph nodes and related tissue in your neck (neck dissection). Neck dissection removes any cancer cells that may have spread to your lymph nodes. It's also useful for determining whether you will need additional treatment after surgery Surgery to reconstruct the mouth. After an operation to remove your cancer, your surgeon may recommend reconstructive surgery to rebuild your mouth to help you regain the ability to talk and eat. Your surgeon may transplant grafts of skin, muscle or bone from other parts of your body to reconstruct your mouth. Dental implants also may be used to replace your natural teeth. Surgery carries a risk of bleeding and infection. Surgery for mouth cancer often affects your appearance, as well as your ability to speak, eat and swallow. You may need a tube to help you eat, drink and take medicine. For short-term use, the tube may be inserted through your nose and into your stomach. Longer term, a tube may be inserted through your skin and into your stomach. Your doctor may refer you to specialists who can help you cope with these changes

Radiation therapy

Radiation therapy uses high-energy beams, such as X-rays and protons, to kill cancer cells. Radiation therapy is most often delivered from a machine outside of your body (external beam radiation), though it can also come from radioactive seeds and wires placed near your cancer (brachytherapy). Radiation therapy is often used after surgery. But sometimes it might be used alone if you have an early stage mouth cancer. In other situations, radiation therapy may be combined with chemotherapy. This combination increases the effectiveness of radiation therapy, but it also increases the side effects you may experience. In cases of advanced mouth cancer, radiation therapy may help relieve signs and symptoms caused by the cancer, such as pain. The side effects of radiation therapy to your mouth may include dry mouth, tooth decay and damage to your jawbone. Your doctor will recommend that you visit a dentist before beginning radiation therapy to be sure your teeth are as healthy as possible. Any unhealthy teeth may need treatment or removal. A dentist can also help you understand how best to care for your teeth during and after radiation therapy to reduce your risk of complications.

MODERN TECHNIQUES OF ORAL CANCER:

Chemotherapy

Chemotherapy is a treatment that uses chemicals to kill cancer cells. Chemotherapy drugs can be given alone, in combination with other chemotherapy drugs or in combination with other cancer treatments. Chemotherapy may increase the effectiveness of radiation therapy, so the two are often combined. Common side effects include nausea, vomiting and hair loss. Ask your doctor which side effects are likely for the chemotherapy drugs you'll receive. Targeted drug therapy Targeted drugs treat mouth cancer by altering specific aspects of cancer cells that fuel their growth. Targeted drugs can be used alone or in combination with chemotherapy or radiation therapy. Cetuximab (Erbix) is one targeted therapy used to treat mouth cancer in certain situations. Cetuximab stops the action of a protein that's found in many types of healthy cells, but is more prevalent in certain types of cancer cells. Side effects include skin rash, itching, headache, diarrhea and infections. Other targeted drugs might be an option if standard treatments aren't working.

Immunotherapy

Immunotherapy uses your immune system to fight cancer. Your body's disease fighting immune system may not attack your cancer because the cancer cells produce proteins that blind their immune system cells. Immunotherapy works by interfering with that process. Immunotherapy treatments are generally reserved for people with advanced mouth cancer that's not responding to standard treatment

APPROACH TO THE ORAL CAVITY :

1. Per-oral: This approach has the following prerequisites (Figure 1) adequate mouth opening Small size Anteriorly located lesions All resection margins accessible Noncontiguous lymph nodal spread Upper cheek flap: This approach allows access to the maxilla, upper alveolus, hard palate. Care should be exercised while raising the flap superolaterally to avoid injury to the infra-orbital nerve and to anticipate subcutaneous/cutaneous soft tissue extent of the tumor while deciding the thickness of the flap. Extensions of the flap such as the lateral rhinotomy, Weber Ferguson with or without Dieffenbach extension can be used to excise sinonasal tumors. Lateral subciliary, or supra-orbital incisions can be combined to perform orbital exenteration depending upon the extent of the tumor Lower cheek flap: This approach allows access to the mandible, lower gingiva-buccal complex, retromolar trigone and tonsil. Depending upon the location and extent of the tumor, the decision to preserve the mental nerve and the lateral mandibular periosteum is made.

DISSICATION:-

Conventional examination has limited efficacy in discriminating oral mucosal lesions and assessing the deep extension of the disease. Biopsy remains the gold standard confirmatory test. Genomics-based approaches could identify tumor-specific biomarkers for helping in early diagnosis. The advent of qMIDS has enabled objective diagnosis based on biopsy samples. Despite these technological advancements, biopsy is limited by its invasiveness, sampling bias, time, and resource requirements. Adjunctive approaches are needed to assist in screening asymptomatic patients, enabling effective diagnosis, and reducing unnecessary biopsies. However, none of the currently available adjunctive aids provide sufficient accuracy for the early detection of PMLs. Although some diagnostic imaging techniques appear promising, approaches are needed to enable early detection, improve diagnostic efficacy, and reduce unnecessary exceptional circumstances. Diagnostic imaging modalities show promise in examining the deep extension of oral lesions. CT has been proven effective in detecting bony involvement in malignancy, but has limited utility in soft tissue characterization, especially in the early stages. MRI helps assess soft tissue invasion and identify tumor locations. PET

offers a functional imaging approach, but should be considered only if results from CT and MRI are inconclusive. CT, MRI, and PET are useful for diagnosing the advanced stages of the disease. Ultrasound can be used to delineate boundaries and measure sizes of tumors as small as 1 mm thick and up to 20 mm in depth with high accuracy. A handful of studies have demonstrated the potential of ultrasound colour Doppler, strain imaging, and shear wave elastography for oral cancer staging. PAI can provide functional information of tumor vascularity, complementing the structural information obtained from ultrasound and OCT. OCT is effective in diagnosing oral cancer progression up to only a depth of 3 mm. However, further studies are needed to assess the efficacy of the imaging techniques.

CONCLUSION:-

Many Ayurvedic herbal plants, which are reviewed, possess antimicrobial, anti-inflammatory, analgesic, antiulcerogenic activities when screened according to the modern parameters. However, among them very negligible amount of herbals extracts are used in clinical practice and the rest of others are not practiced because of their unknown toxicological effects. The clinical studies should be encouraged to assess the efficacy as well as toxicity of herbal drugs. The traditional knowledge of Ayurveda should be integrated with the modern.

REFERENCES:-

1. Ettleton S. The Sociology of health and illness. Cambridge: Polity Press; 1995.
2. Dotiwala AK, Samra NS. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Apr 14, 2022. Anatomy, Head and Neck, Tongue. [PubMed].
3. Mouth anatomy Alternate titles: buccal cavity, mouthparts, oral cavity By The Editors of Encyclopaedia Britannica <https://www.britannica.com/science/mouth-anatomy>
4. Jackson SL, Vann WF, Jr., Kotch JB, Pahel BT, Lee JY. Impact of poor oral health on children's school attendance and performance. 2011;101(10):1900–1906 [https://my.clevelandclinic.org/health/body/22845-tongue#:~:text=Your%20tongue%20is%20mostly%20made,\(bumps\)%20and%20taste%20buds.](https://my.clevelandclinic.org/health/body/22845-tongue#:~:text=Your%20tongue%20is%20mostly%20made,(bumps)%20and%20taste%20buds.)
5. Sosmitha Girisa, Aviral Kumar, Varsha Rana, Dey Parama, Uzini Devi Daimary, Saman Warnakulasuriya, Alan Prem Kumar, Ajaikumar B. Kunnumakkara <https://www.cancerjournal.net/article.asp?issn=0973-1482;year=2016;volume=12;issue=2;spage=458;epage=463;aulast=Kumar>
6. ACS Pharmacology & Translational Science. 2021; 4(2): 647 [PubMed] | [DOI] <https://www.bu.edu/dental-research/2013/11/22/history-of-oral-cancer-research-initiative/>
7. Oral Cavity, Pharyngeal, and Laryngeal Cancer Prevention". National Cancer Institute. 1 January 1980. Retrieved 5 June 2019. https://en.m.wikipedia.org/wiki/Mouth_ulcer
8. World Health Organization Oral Health. [(accessed on 11 March 2020)]; 2018 Available online: <https://gco.iarc.fr/today/data/factsheets/cancers/1-Lip-oral-cavity-factsheet.pdf>