REPORT WRITE-UP

I. **What and where is oral cancer?**
    Oral cancers are a part of a group of cancers commonly referred to as **head** and **neck** cancers, and of all head and neck cancers, they comprise about **85%** of that category.
    -   Develop on the tongue, the tissue lining the mouth and gums, under the tongue, at the base of the tongue, and the area of the throat at the back of the mouth.
    -   It can be life-threatening if not diagnosed and treated early.
    -   When it is caught early, oral cancer is much easier for doctors to treat.

   a. **Symptoms:**

    -   Velvety white, red, or speckled (white and red) patches in the mouth.

    -   Swellings/thickenings, lumps or bumps, rough spots/crusts/or eroded areas on the lips, gums, cheek, or other areas inside the mouth.
    -   Unexplained bleeding in the mouth.
    -   Unexplained numbness, loss of feeling, or pain/tenderness in any area of the face, mouth, or neck.
   -   Persistent sores on the face, neck, or mouth that bleed easily and do not heal within 2 weeks.
    -   A soreness or feeling that something is caught in the back of the throat.
    -   Difficulty chewing or swallowing, speaking, or moving the jaw or tongue.
    -   Hoarseness, chronic sore throat, or change in voice.
    -   Ear Pain.
    -   Swelling or pain in your jaw. If you wear dentures, they might be uncomfortable or hard to put in.
    -   A change in the way your teeth or dentures fit together.
   -   Dramatic weight loss.

   b. **Statistics:**

    -   Oral cancer is among the top three types of cancers in India.
    -   The incidence of oral cancer is highest in India, south and Southeast Asian countries.
    -   . In India, **90 -95%** of the oral cancers is squamous cell carcinoma.
    -   The international agency for research on cancer has predicted that India's incidence of cancer will increase from **1** million in 2012 to more than **1.7** million in 2035.

- This indicates that the death rate because of cancer will also increase from **6,80,000** to **1-2** million in the same period.
- In India, 20 per 100000 people are affected by oral cancer which accounts for about **30%** of all types of cancer.
- Over 5 people in India die every hour every day because of oral cancer and the same number of people die from cancer in oropharynx and hypopharynx.
- Most of the oral cancer cases occur between the age of **50 to 70** years, but it could also affect children as early as 10 years.
- In India, men are two to four times more affected than women due to the changes in the behavioral and lifestyle patterns.
- However, high incidence rates are seen amongst the sub populations of women in southern India because of tobacco chewing.
- Cancer in the tongue is the most common type of cancer and the common site is buccal mucosa and gingiva.
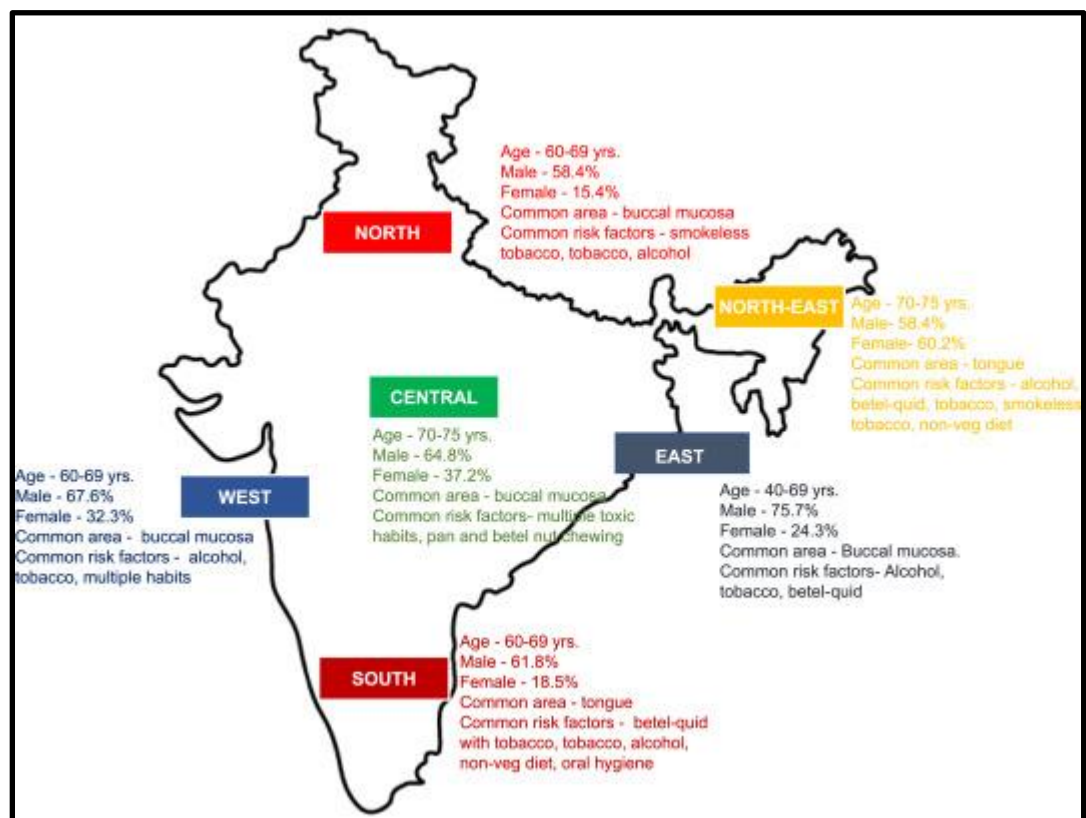
Distribution and statistics of oral cancer all over India

INCIDENCE AND MORTALITY OF ORAL CANCER IN INDIA
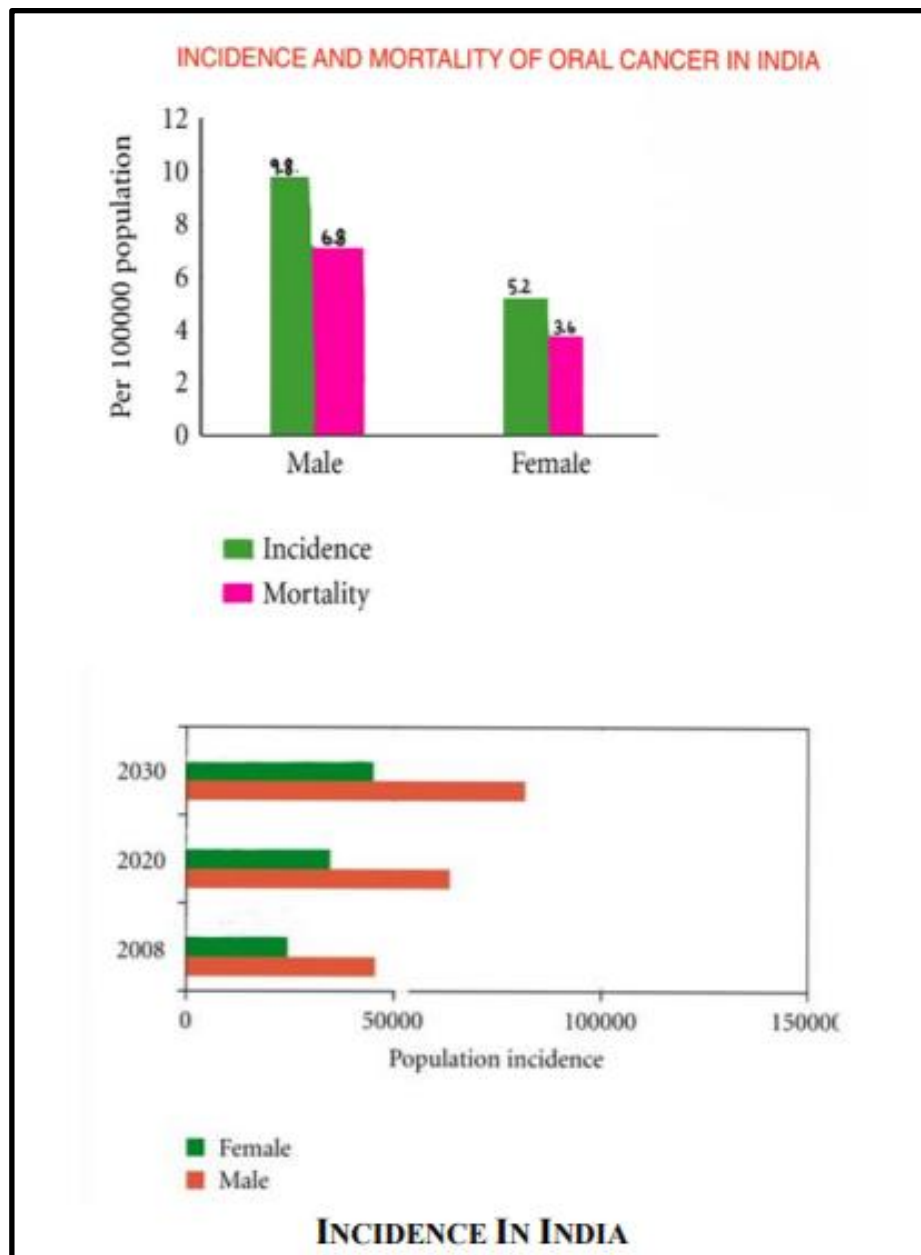
INCIDENCE IN INDIA

c. Regional Variation:

- The burdens imposed by cancer vary greatly between the regions of India. Oral cancer incidence and mortality is generally high in affluent States.
- Oral cancer mortality relate is high due to the mortality in rural areas where cancer treatment facilities are scarce.
- Indian States like **Tamil Nadu** and **Kerala** achieve relatively good health outcomes, future health developments will be integrally linked to the nation's economic fortunes and collective commitment to equity and universal health care provision.
- The use of smokeless tobacco (pan parag, zarda etc) is on rise in north India and especially in states like Uttar Pradesh. The impact of habit lead to high incidence of oral cancer in this region.

- The population is still fighting for relatively high rates of parasitic, bacterial and viral diseases, while encountering increasing levels of illness caused by cancer.

II. Causes of oral cancer?

a. **Tobacco Use:**
Statistics indicate that **57% of men** and **11% of women** between 15-49 years of age use some form of tobacco.

Types of tobacco used-
i. Smokeless tobacco
ii. Use of betel liquid
iii. Pan (pieces of Areca nut)
iv. Processed or unprocessed tobacco
v. Aqueous calcium hydroxide (slaked lime) and some pieces of are a nut wrapped in the leaf of piper betel vine leaf.
vi. Gutka, panparag, zarda,mawa, kharra and khainni. These are dry mixture of powdered tobacco, lime and Areca nut flakes which are chewed or sucked orally.

Factors	Cases (350) n (%)	Controls (350) n (%)	OR*	95% CI of OR	p-value
Tobacco Use (overall)	328 (93.7)	200 (57.1)	11.2	7.0-18.0	0.001
Active smoking (overall)	125 (35.7)	61 (17.4)	2.6	1.8-3.7	0.001
Filtered cigarette	44 (12.6)	33 (9.4)	1.4	0.9-2.3	0.149
Non filtered cigarette	15 (4.3)	6 (1.7)	2.5	1.0-6.7	0.046
Bidi (Hand rolled cigarette)	70 (20.0)	20 (5.7)	4.1	2.4-6.9	0.001
Passive smoking	75 (21.4)	19 (5.4)	1.7	1.6-2.2	0.001
Smokeless tobacco (overall)	303 (86.6)	158 (45.1)	7.8	5.4-11.4	0.001
Tobacco flakes	175 (50.0)	55 (15.7)	5.3	3.7-7.6	0.001
Betel leaf (Paan)	44 (12.6)	31 (8.9)	1.4	0.9-2.4	0.112
Pan parag	21 (6.0)	18 (5.1)	1.1	0.6-2.2	0.621
Gutkha	112 (32.0)	21 (6.0)	7.3	4.5-12.0	0.001
Supari	32 (9.1)	12 (3.4)	2.8	1.4-5.6	0.002
Mishri	118 (33.7)	65 (18.6)	2.2	1.5-3.1	0.001
Alcohol (overall)	106 (30.3)	48 (13.7)	2.7	1.8-3.9	0.001

Univariate analysis diagram of oral dipping products

Here the OR relates to the risk factor for each form of consumption. We can see the risk was **7.3** for consumption of gutka, **5.3** for consumption of tobacco flakes and **2.8** for consumption of supari (pure areca nut). However, the lower risk was found for mishri.

Smoking includes use of cigarettes, bidi and hookah. These tobacco products are commercially available in sachets or packets and it is very popular among young adults which leads to oral cancer in young age.

Bidi smokers are 4 times at risk of developing oral cancer compared to non-smokers. This could be due to poor combustibility as well as the nicotine and tar content of bidi which exceeds that of cigarette. The number of bidis smoked per day, a longer duration of smoking and a younger age at starting to smoke was associated with oral cancer.

b. Alcohol Consumption:
Drinking alcohol is an important risk factor for oral cancer. Risk increases with number of drinks consumed in a week.

A prospective study in India has found that alcohol consumption increases the incidence of oral cancer by **49%** among current users and **90%** in past drinkers. This could be due to residual effect of alcohol consumption or them having quit the habit due to serious illness.

Consumption of alcoholic beverages was associated with increased risk for Oral cancer in men but it was not observed in women because very few women consumed alcohol as per statistics.

c. Poor Oral Hygiene:
In one study, more than **85%** of oral cancer patients had poor oral hygiene.

Poor oral hygiene related attributable risk is around **32% for men** and **64% for women** in India.

Patients wearing dentures for more than 15 years and not visiting a dentist regularly was highly associated with Oral cancer.

d. HPV (Human Papillomavirus):
Infection with the sexually transmitted (STI) human papillomavirus (specifically the HPV 16 type) has been linked to oral cancers.

e. Age:
Risk increases with age. Oral cancers most often occur in people over the age of **40**.

f. Sun Exposure:
Cancer of the lip can be caused by prolonged sun exposure.

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III. Current screening methods?

a. Visual oral cancer exam:
   i. Method- It's a 8-step methodical clinical examination of the oral cavity and surrounding structures of the head and neck.
   Intraorally a dental mirror is used with good lighting and a gauze for thorough examination. The tongue and floor of the mouth (a common location for oral cancer) and other intraoral structures are examined. Gloved hands and good lighting are used to examine the skin and palpate muscles, TMJ and lymph nodes.
   ii. It's good for monitoring all patients. Should be performed at every dental visit.

iii.   It's the easiest and least invasive way to screen for tissue changes.
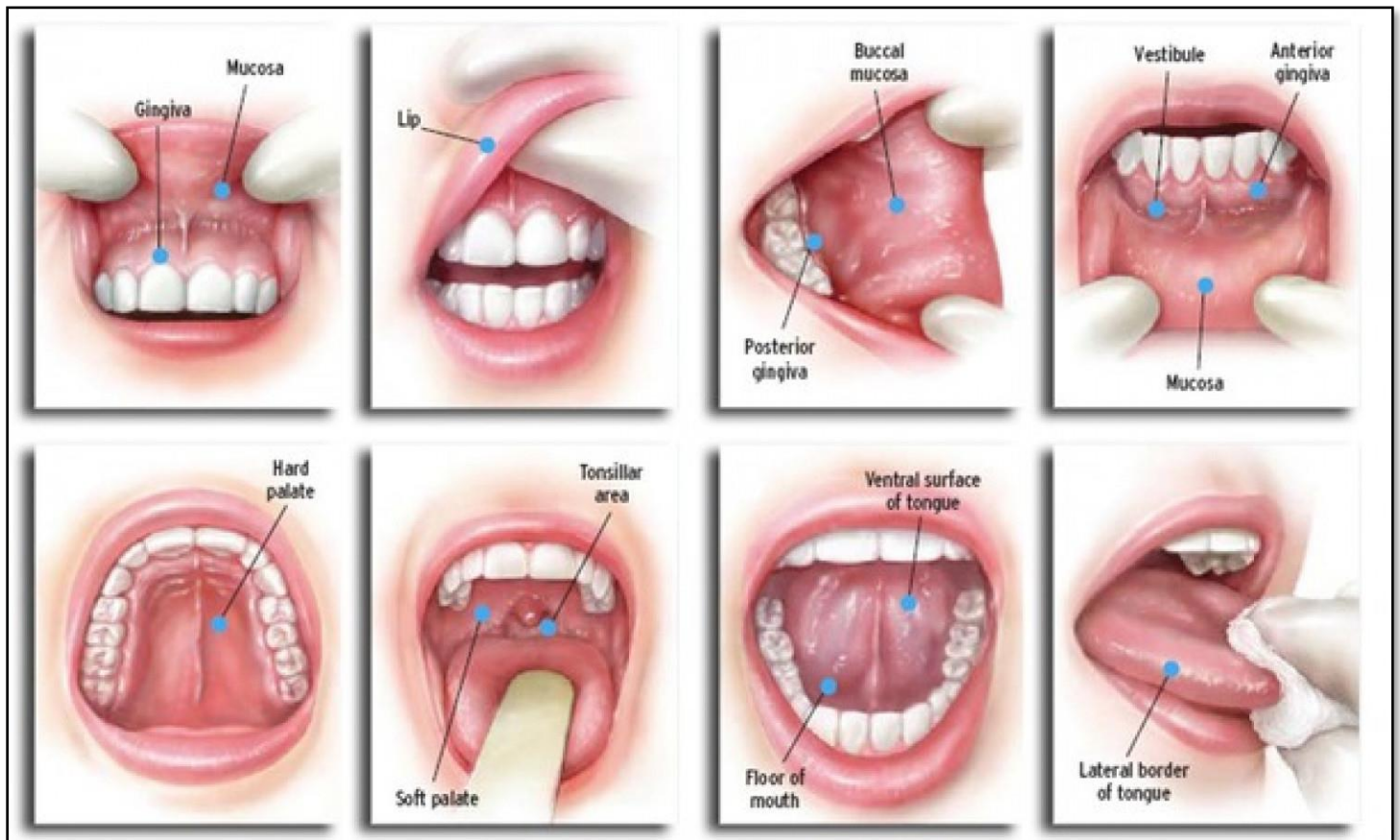
b. **Direct Visualization using Tissue Fluorescence:**
    i.   **Method-** A blue light is used to illuminate the tissues of the oral cavity, decreased tissue fluorescence can indicate tissue changes.
    ii.   Can be used as a screening tool. Can also be used to help aid in determining margins when surgical removal of a lesion is needed.
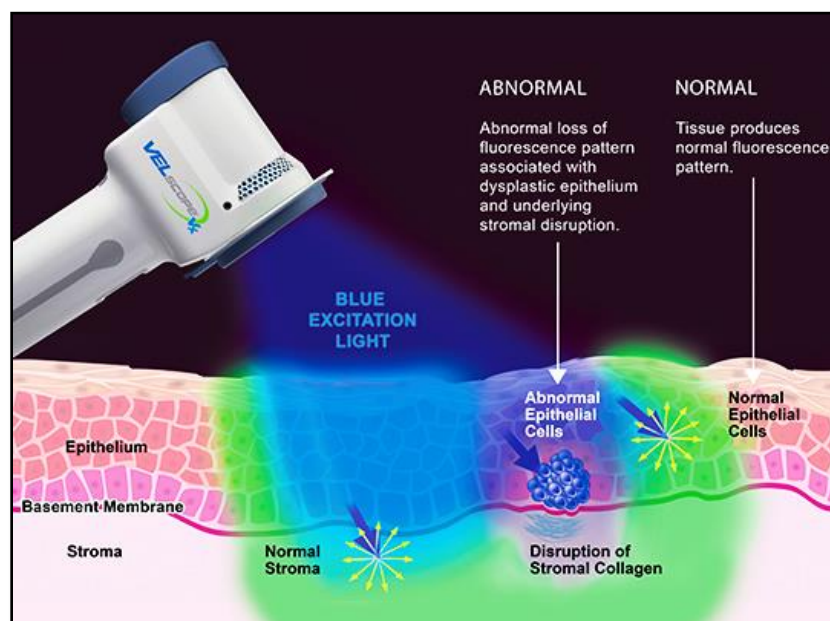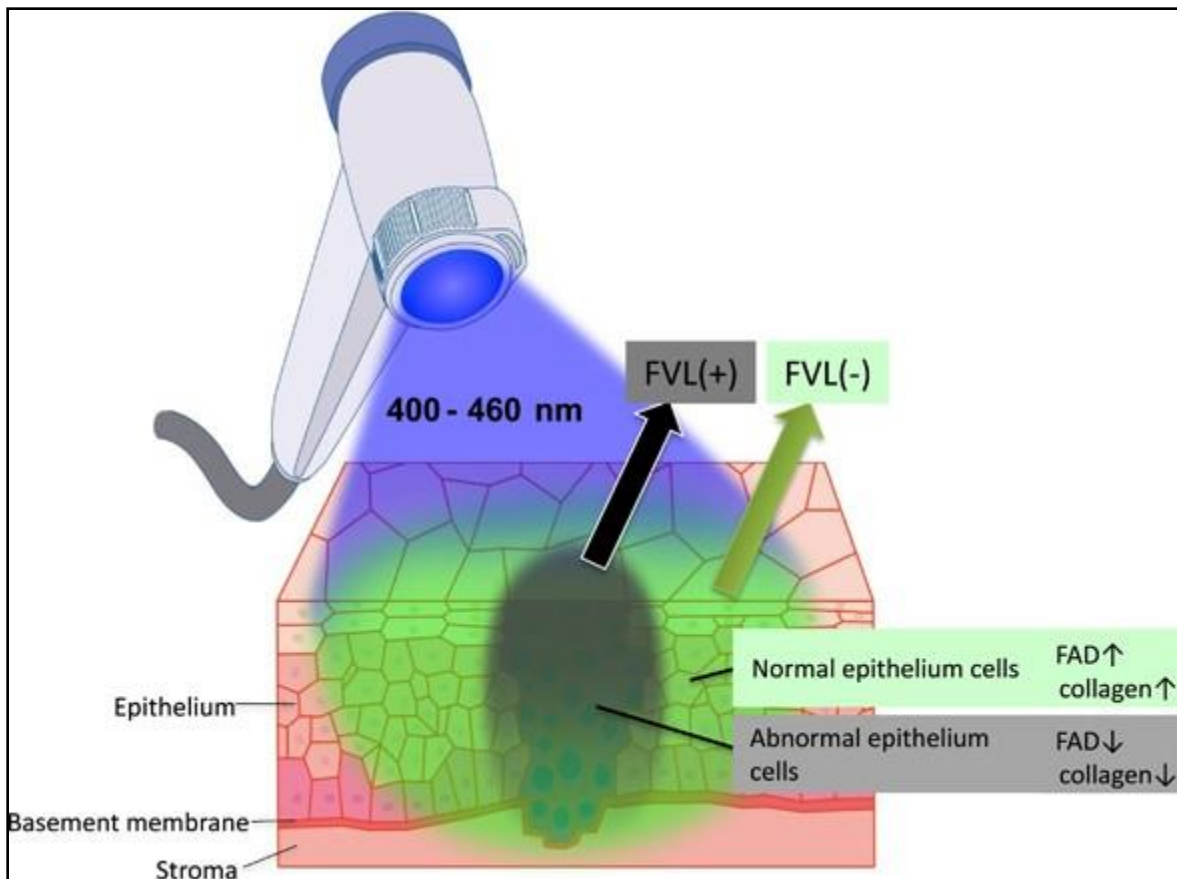
c. Oral Cytology (aka "Brush Biopsy "):
   i.   **Method-** Oral brush cytology; the brush is rotated 5-10 times with firm pressure.
   ii. Good for monitoring patients with history of mucosal changes. Quick chairside tool for screening suspicious lesions.
   iii. It's very precise. Causes minimal discomfort to patient. Patients with atypical or positive results should have scalpel biopsy.
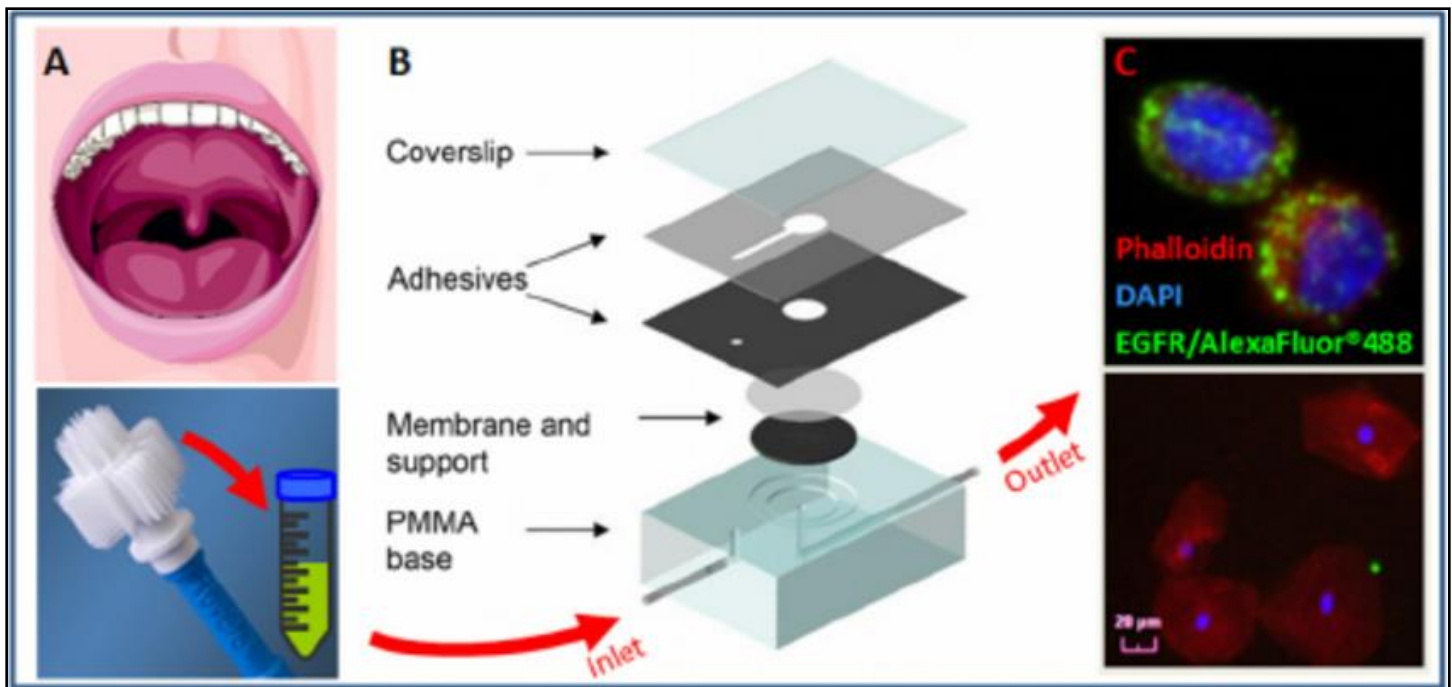
Experimental setup of oral cytology test

d. **Aspiration:**
   i.   **Method-** 18-gauge needle with a 5-10 mL syringe inserted to depth of mass.
   ii. **Indications-**

   - Any lesion that may contain fluid.
   - Intraosseous lesions prior to surgical exploration, to rule out a vascular lesion.

   iii. Pus may indicate infectious or inflammatory lesion. If it's straw colored, it's often cystic lesion.
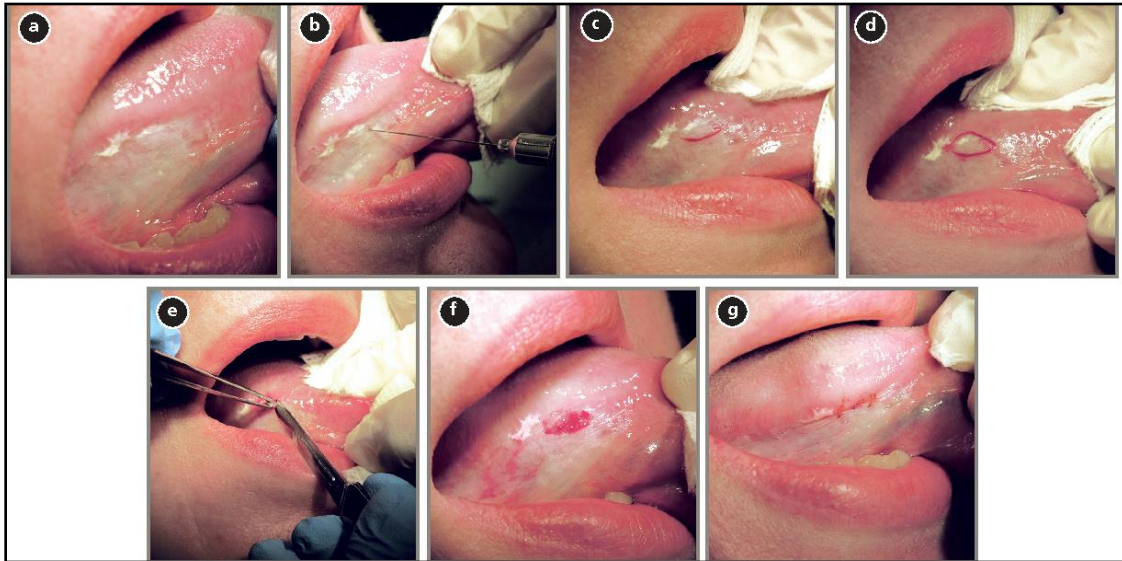

e. **Incisional Biopsy:**
   i.   **Method-** Involves taking a sample of a representative part of the lesion. Using a scalpel blade, make two incisions forming an ellipse at the surface and a V at the base including normal tissue.
   ii. **Indications-**

- Lesions >1 cm in diameter.
- The lesions are in a location that makes them difficult to remove.
- When malignancy or an aggressive benign lesion is suspected.
iii. The incision is made at the edge of the lesion so as to include both normal and abnormal tissue. Necrotic tissue is avoided in the specimen. If the lesion varies from one area to another, more than one biopsy may be necessary.

f. Excisional Biopsy:
   i. **Method-** It involves removing the entire lesion during the surgical diagnostic procedure. Using a scalpel and blade, two incisions are made forming an ellipse at the surface and a V at the base. If the lesion appears benign, 2-3 mm of normal tissue is included in the periphery. If the lesion appears malignant, 5 mm of normal tissue is included in the periphery.
   ii. **Indications-**

   - Lesions <1 cm in diameter
   - Lesions that appear benign
   - Lesions in locations that facilitate removal
   - Pigmented and small vascular lesions.

g. Risks of oral exams-

   i.   Oral cancer screening could lead to additional tests-

   -   Many people have sores in their mouths, with the great majority of these sores being
       noncancerous. An oral exam can't determine which sores are cancerous and which
       are not.
   -   If your dentist finds an unusual sore, you may go through further testing to
       determine its cause. The only way to definitively determine whether you have oral
       cancer is to remove some abnormal cells and test them for cancer with a procedure
       called a biopsy.

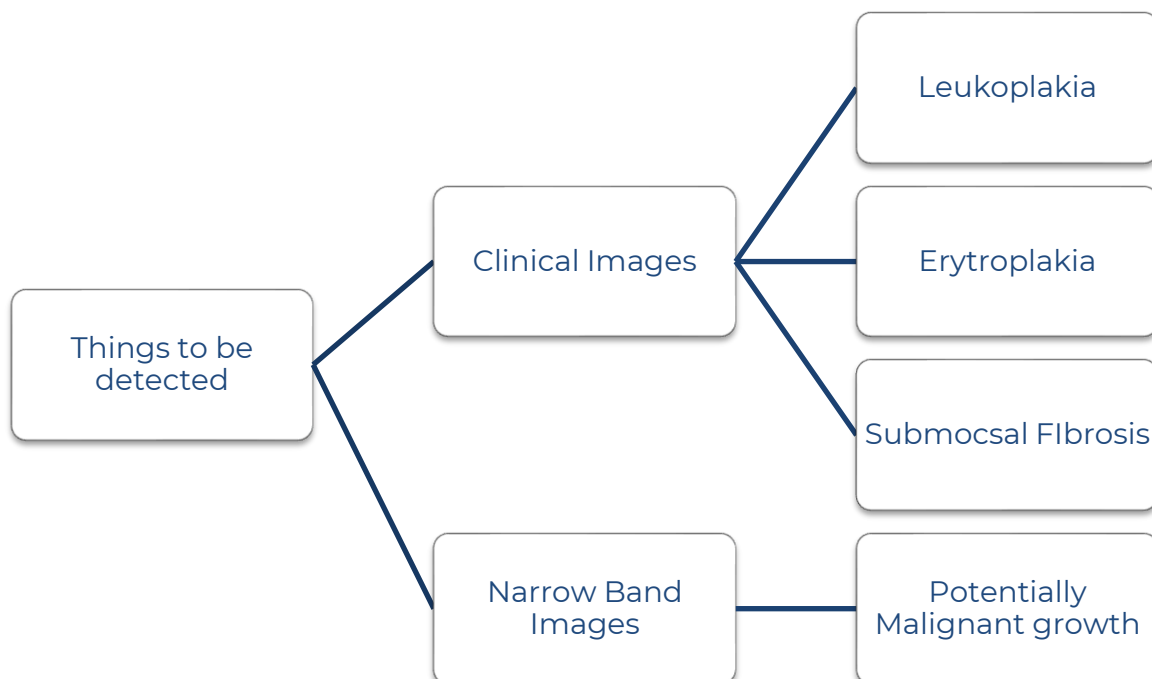   ii.   Oral cancer screening can't detect all mouth cancers-

   -   It can be difficult to detect areas of abnormal cells just by looking at your mouth, so
       it's possible that a small cancer or precancerous lesion could go undetected.

   iii.   Oral cancer screening hasn't been proved to save lives -

   -   There's no evidence that routine oral examinations to look for signs of oral cancer
       can reduce the number of deaths caused by oral cancer. However, screening for oral
       cancer may help find cancers early — when cure is more likely.

IV.   What are we going to do in the project?

a. Our basic plan is to devise a **Computer Vision** and **Image Processing** based system to help
   in the detection of cancerous lesions and growth from various images.

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                                                    │   Leukoplakia    │
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                              │  Clinical Images │──│   Erytroplakia   │
                              └──────────────────┘  └──────────────────┘
  ┌──────────────────┐                              ┌──────────────────┐
  │  Things to be    │                              │ Submocsal FIbrosis│
  │   detected       │                              └──────────────────┘
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                              │   Narrow Band    │──│   Potentially    │
                              │     Images       │  │ Malignant growth │
                              └──────────────────┘  └──────────────────┘
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Detection from Clinical Images-
- Clinical images can be a helpful tool for the quick diagnosis of disorders.
- They are relatively easier take and do not require heavy equipment like Xray or CT machines.
- The primary focus here will be to detect the 3 major **pre-cancerous lesions.**
- The detection and identification of these lesions can help the health worker get a better understanding about could be the possibility of a future malignancy.
- This helps speed up the process of advising further tests/treatments even by those with lack of experience and training to identify the lesions manually.

b. Information about each lesion-

i. Leukoplakia-
- Leukoplakia is defined as a whitish patch or plaque mainly associated with **tobacco** use.
- Roughly **2%** patients with oral (homogenous i.e., most common) leukoplakia develop invasive and malignant oral cancer.
- Lesions present particularly in the floor of the mouth, tongue, lip and vermilion have a high risk of malignant potential.
- The malignancy rates of other kinds of Leukoplakia are:

Type of Leukoplakia	Malignancy Rate
Thin	N/A
Homogenous	1 – 7 %
Verruciform	4 – 15 %
Speckled	18 – 47 %

- Clinical Criteria for classifying Leukoplakia lesions as malignant.
  - The high risk is considered to be the verrucous type.
  - If the lesion is associated with erosion or ulceration then, the lesion is suggested to have high malignant potential.
  - The presence of a nodule in the lesion indicates higher malignant potential.
  - A lesion that is hard and indurative in its periphery is predictive of malignant change.
  - Oral leukoplakia seen in the anterior floor of the mouth and undersurface of the tongue is strongly linked to malignant potential.

- The **Proliferative verrucous leukoplakia** is the one with highest malignancy rate of around 63 to 100%. The transformation usually starts after 8 years post the initial diagnosis.

Thin Leukoplakia
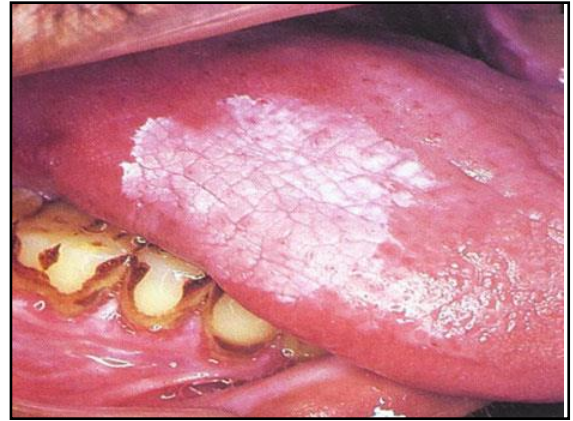
Homogenous Leukoplakia

Verruciform Leukoplakia

Speckled Leukoplakia

ii.   Erythroplakia-
- It is Far less common than leukoplakia.
- Erythroplakia has a **much greater probability** (91 %) of showing signs of dysplasia or malignancy at the time of diagnosis.
- Such lesions have a flat, red, macular, velvety appearance and may be speckled with white spots. They are present as singular lone specks.

iii.   Sub Mucosal Fibrosis-
   - OSF is a disease of the oral cavity resulting from **inflammation** and **progressive fibrosis** of the submucosal tissue (connective tissue) resulting in significant rigidity and inability to open the mouth.
   - It also li it's the wound healing capacities of the affected and nearby areas.
   - OSF is predominantly found in Southeast Asia and caused by chewing areca nut, which is the predominant component of betel quid.
   - It has a malignancy conversion rate of roughly **9%.**

c. Narrow Band Imaging (NBI)-

   - Narrow Band Imaging (NBI) is an endoscopic optical imaging enhancement technology that improves the contrast of mucosal surface texture, and enhances visualisation of mucosal and submucosal vasculature.

   - White light is filtered to emit two 30-nm narrow bands of blue (415 nm) and green light (540 nm) light simultaneously, the former corresponding to the main peak absorption spectrum of haemoglobin, and the latter allowing visualisation of blood vessels in the deeper mucosal and submucosal layers.

   - NBI has been used to better assess oral potentially malignant disorders (OPMD), identify oral and oropharyngeal squamous cell carcinoma (SCC), and to define surgical margins of head and neck malignancies.

   - The pattern/orientation of blood vessels varies drastically in health, pre-cancerous and cancerous stages. Using NBI is boon because the images generated by it are already in monochrome and can hence be quickly preprocessed without the need of a lot data cleaning.

   - What we aim to do here is to find the spot of suspected growth to help the physician narrow down to a spot for biopsy/surgery. A process which would have otherwise been time consuming due to the multitude of frames from a single endoscopy session.
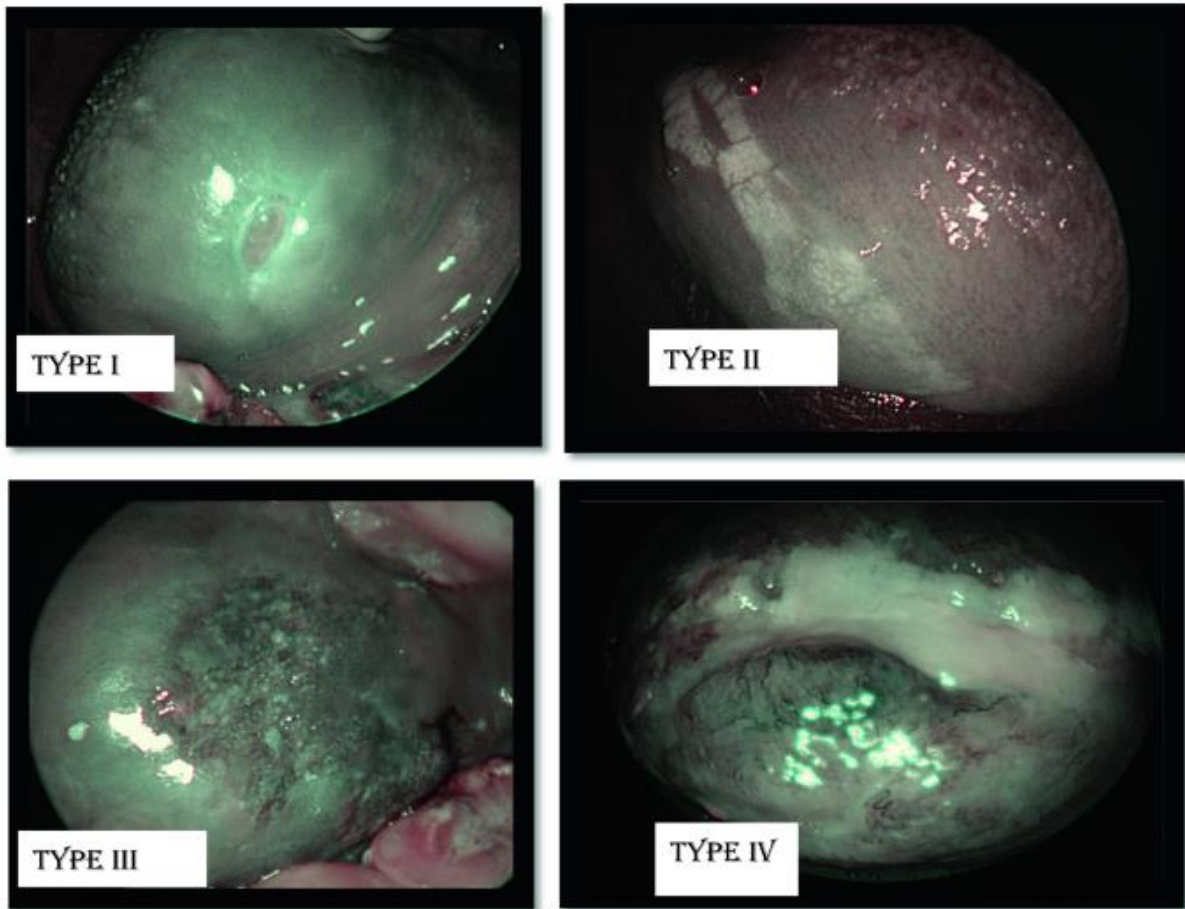
Figure 1- https://link.springer.com/article/10.1007/s00405-020-06578-4

- Type 1 is near healthy whereas Type 4 is a cancerous lesion as seen under NBI.

- The orientation of the blood vessels is a vital indicator of the spread of malignant growth.

- Straight, organized vessels imply normal mucosa whereas haphazard and crisscross vessels indicate the presence of a cancerous growth.

Erythroplakia under Normal Endoscope (left) and NBI (right)

V.   Impact of the Project

-   Cancer, like any other disease, becomes potentially lethal if left untreated for a long period of time. Early detection of cancer could be the key to personalized, faster and more effective treatment and rehabilitation processes.

-   The use of AI will be making the whole process faster and doable by even those who do not have enough experience to distinguish good mucosa from bad.

-   We aim to track down cancer causing regions in its early stages itself so that the patient can then be sent to a specialist for further treatment.

-   This could prevent more 30% of all oral cancers from ever happening since the potentially malignant lesions are identified and treated din the pre-cancerous stage itself.

-   Another very crucial impact of this project will be to detect secondary cancers. Due to increased rate of cancer detection, the health worker can examine more sites during inspection thus revealing other potentially malignant growths as well.

-   People returning for post treatment check-ups can also have faster and easier diagnosis about any secondary cancers or relapses if there.

-   Since the visits are less of returning patients, it is crucial to examine as much as possible as any delay can cause the secondary cancer to become potentially harmful.

VI.   References

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