

Save lives: do a HPV-detection test!

Worldwide, cancer is today the second most common cause of morbidity (after cardiovascular diseases). By 2020, more than 15 million new cancer cases will be reported every year. Cancer, also known as malignant tumor or malignant neoplasm, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body, ultimately causing death. There are over 100 different known cancers that can affect humans. Causes of cancer can be chemicals (e.g. tobacco), diet and exercise (e.g. obesity), infection (e.g. viruses), radiation, heredity, immune conditions, physical agents (e.g. asbestos) or hormones (e.g. insulin-like growth factors).

Epidemiology

Cancers in the oral cavity are mostly oral squamous cell carcinomas. In 2012, oral cancers were ranked 15th in the list of most common cancers (2.1% of all cancer cases). In men, the prevalence is higher than in women (2.7% vs 1.5%). In the black population it occurs twice as often as in the whites. Survival rates over 5 years are much poorer for blacks than for whites (33% vs 55%).

In the US, yearly 45,000 to 50,000 people are diagnosed with oral or pharyngeal cancer, leading to nearly 8750 deaths per annum. So oral cancer kills 1 American per hour, 24 hours a day, 365 days a year... The death rate is not particularly high because it is a hard to discover or to diagnose type of cancer; it is that high because this cancer is being routinely discovered (too) late in its development.

Worldwide there is no specific program for screening this disease; therefore a late discovery is common. Since the HPV16 (Human Papilloma Virus 16) has a strong contribution to this cancer and causes specifically a high incidence rate of cancers in the posterior part of the oral cavity (tongue base, tonsils and oropharynx); this pathology stays often undetected. After all, the lesions are frequently producing no pain or other symptoms. Moreover, in these areas they are much less visible. Therefore this type of cancer is often only discovered when it is metastasized to other locations like the lymph nodes of the neck. At this stage, the prognosis is significantly worse moreover, the primary tumor has had time to invade deep into local tissues.

Origin

Cancers result from mutations in genes, which control cell behaviors. Mutated genes may result in cells, which grow and proliferate at an uncontrolled rate, which are unable to repair DNA damage within their self, or which refuse to self-destruct or die. When a cell does become mutated, it is capable of passing on the mutations to all of its progeny, when it divides itself. Besides random occurrences, genetic errors can be inherited, be caused by viruses, or develop as a result of exposure to chemicals or radiation. Our bodies normally have mechanisms that destroy these abnormal cells. When the latter fails to take place, cancers may occur.

In general, oral cancer is caused by excessive tobacco, alcohol or betel use. The majority of the cases develop over the age of 40; but more recently also younger people are diagnosed due to the use of chewing tobacco.

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Also the encroachment of HPV16 plays a significant role in this group. This virus is sexually transmitted between partners (causing also 90% of all cervical cancers). The human *Papilloma* virus is a double-stranded DNA virus that infects the epithelial cells of skin and mucosa. The moist epithelial surfaces include all areas covered by skin and/or mucosa. Transmission of the virus occurs when these areas come into contact with a virus, allowing it to transfer between epithelial cells. While it is established that sexual contacts are means of transferring the HPV virus through skin-to-skin contact, it is still poorly understood what other transfer pathways may exist.

There are 200 strains of HPV, of which most are quite harmless. Most people will have some contact with a HPV in their lifetimes (even be exposed to the oncogenic versions of it). Approximately 1% of those infected have a lack of immune response to the HPV16 strain, now known as a cause of oral cancer. So infection with even a high risk HPV virus does not mean that oral cancer will develop: most people's immune systems will clear the infection before malignancy can occur.

There are other risk factors, which have been associated with oral cancers: lichen planus, inflammatory diseases of the oral soft tissues and genetic predispositions.

Symptoms

As possible sign or symptom a white or red patch appears in the oral cavity, or a small indurated ulcer, which looks like a common canker sore. Because there are many benign tissue changes that occur normally in the mouth, it is important to have any sore or discolored area of the mouth, which does not heal within 14 days, looked at by a professional.

Other symptoms include: a lump or mass felt inside the mouth or neck, pain or difficulty in swallowing, speaking or chewing, any wart like masses, hoarseness which lasts for a long time, or numbness in the oral/facial region.

Common areas for oral cancer to develop are on the tongue and the floor of the mouth. Individuals that use chewing tobacco are likely to

have them in the sulcus between the lip and cheek where the tobacco is held mostly. The base of the tongue, the oropharynx, the pillars of the tonsils, the tonsillar crypts and the tonsils itself; are other sites where cancers are commonly found.

Examinations

The protocol for dental professionals ensures a complete assessment of the patient. A conventional oral examination (visual inspection of the oral cavity + tactile examination of head and neck lymph's) has 93% sensitivity, but only a poor 31% specificity.

Oral examination & palpation

Oral cavity: The mouth should be examined with both hands free for bimanual palpation or to hold gauze or tongue blade(s) for improved visualization. Dental appliances should be removed. When examining mucosal surfaces, it is important to gently dry them with a gauze or air syringe, so that color or texture changes will become more obvious. Studies have shown that the earliest manifestation of many oral cancers is a persistent erythroplastic lesion. Clinicians must therefore be on the lookout for both red and white (leukoplakia) lesions on the oral mucosa.

Lips: They can be involved with squamous cell carcinoma of the aero digestive tract or with basal cell carcinomas of the skin. The lips should be evaluated with the mouth open and closed noting any abnormalities in symmetry, contour, color or texture. The lips are retracted and their inner surface is inspected. The labial mucosa should be smooth and uniform in color. Signs of smokeless tobacco use (ulcers, red or white discolorations, texture variations) on the labial mucosa can be detected. With the lip retracted, one can also inspect the gingivolabial sulcus and the gingival mucosa. Palpation of the lip, notes any firm or nodular submucosal areas.

Buccal mucosa: The buccal mucosa must be spread away from the teeth and gums to visualize the sulcus, which connects this area to the gingiva. It is not uncommon to see a white line here from a habit of biting the inside of the cheek. Any irregularity in texture or color or other signs listed above should be noted. Stenson's duct is a small protrusion in this area opposite the upper second molar and should secrete clear saliva from both sides when the parotid gland is pressed. The cheek should be pinched between fingers and thumb; allowing palpation for hidden masses.

Tongue: While opening the mouth and relaxing the tongue; any ulcerations, swellings, or other abnormalities should be noted. The tongue should move easily and completely too both sides without spasm or asymmetry. Observation of the dorsum of the tongue, noting any discolorations, irregularities, or limitations to movement, has to be performed. One of the most common sites of oral cancer is on the lateral aspect of the tongue. Examination requires using gauze to pull the tongue out and roll it from side to side while retracting the cheek with a tongue blade. A dental mirror is used to visualize the base of the tongue. This area is best viewed by pulling the tongue forward while holding it with gauze. Next, palpation of the dorsum and lateral margins of the tongue should be performed.

Floor of the mouth: This area is inspected while the tongue is elevated. The frenulum in the midline and the ducts from the submandibular glands are noticed, even as the sublingual glands. It is helpful to first dry this area with gauze before looking for any

surface abnormalities. Next, a gloved finger is inserted beneath the tongue, and another under the chin on the exterior skin. Bimanually palpation of the submandibular glands and the entire submental region is performed.

Palate: The patient opens widely and tilts his or her head backward to provide an adequate view of the hard and soft palate. The base of the tongue is depressed with a tongue blade to provide a better view of the soft palate. Red spots, white spots, ulcerations, rough areas, asymmetry, growths, or other masses may be a sign of a cancer. The uvula should hang down in the midline. Some patients have a torus palatinus, or bony outgrowth from the midline of their hard palate, which is no sign for malignancy.

Neck: The patient should sit so that his face is at the examiners eye level (head supported with a headrest). Bimanually palpation the neck, comparing both sides simultaneously for signs of enlargement is done, including a carefully palpation for enlarged lymph nodes. Examination is performed: on the jugular chain, along the course of the sternomastoid muscles, underneath the mandible and down to the clavicle. Afterwards there is palpation of the supraclavicular spaces, the parotid groups lying anterior and inferior to the ears, the submental, the submaxillary chain and finally along the course of the larynx for signs of immobility or enlargement. Enlarged nodes that are painless are seldom the result of an infectious process.

Biopsy

This technique is incontestably the gold standard. If an area is decided to be suspicious, the only way to know for sure if it is something dangerous is to do a biopsy of the area. This is a not painful, inexpensive procedure that takes little time. It is important to have a firm diagnosis as early as possible. Referring to a specialist to have the biopsy performed is advisable.

Fluorescence inspection-OralID®

This is an effective, easy and rapid method for screening oral cancers. It is a light based technology that helps to shine a blue light that potentially identifies oral cancer, pre-cancer or other abnormal lesions at an earlier stage.

Fluorescence is a unique property where a material produces a longer wavelength and a lower energy light than the absorbed light. Fluorophores within the oral epithelium and stroma absorb UV and visible light at longer wavelengths in the form of fluorescence. When the reflected illumination light is blocked with an absorbing filter, it is possible to visualize the longer wavelength fluorescence even with the naked eye. Auto fluorescence originates from a variety of Fluorophores in the oral cavity, and is sensitive to alterations in both tissue morphology and biochemistry associated with neoplasia.

The OralID® device (Forward Science LLC, Stafford - USA) is a commercial available lamp to visualize loss of tissue auto fluorescence associated with pre-cancer and cancer in the mouth. The blue light of this device (435-460nm) helps to identify abnormal lesions at an early stage. It is always used adjunctive too mucosal screening. Healthy tissues shine green, abnormal tissues remain black. The incorporation of the OralID® in daily practice would help to detected premalignant and malignant lesions in an early stage. Using histology as the gold standard, the device demonstrated 98% sensitivity and 100% specificity for discriminating dysplasia and cancers from normal oral mucosa.

Hpv detection - prevo-check®

The Prevo-Check® (Abviris, Hünfelden-Germany) is an in-vitro diagnostic medical device and represents the first commercially available, highly specific screening method for HPV-induced oral cancer worldwide. This immunoassay detects antibodies against HPV16 in whole blood samples and therefore allows important insights regarding HPV-induced neoplasia in mucous membranes.

The Prevo-Check® is easy to use and can be performed in any professional environment. Test results are available in 15 minutes. Recent studies showed 100% specificity and 70% sensitivity for this test.

Others

Other detection methods are: brush cytology, toluidine blue staining and chemiluminescence.

Treatment

After a definitive diagnosis has been made and the cancer has been staged, treatment may begin. Treatment of this type of cancers is preferably a multidisciplinary approach involving the efforts of surgeons, radiation oncologists, chemotherapy oncologists, dental practitioners, nutritionists, and rehabilitation and restorative specialists.

The actual curative treatment modalities are usually surgery and radiation, with chemotherapy added to decrease the possibility of metastasis, to sensitize the malignant cells to radiation, or for those patients who have confirmed distant metastasis.

Prior to the start of these treatments, it is likely that other oral health needs will be addressed. The purpose is to decrease the likelihood of post therapeutic complications. Teeth with poor prognosis from periodontal problems or caries are extracted. This avoidance of post radiotherapy surgery is important as it can induce osteonecrosis. The bone, which has lost its ability to efficiently repair itself due to reduced blood supply, yields a chronic and difficult to treat situation. A thorough prophylaxis or cleaning will likely be done as well. Regular recalls are of utmost importance.

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Conflicts of interest

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