Oral and oropharyngeal cancer

Important research into oral and oropharyngeal cancer is underway in many university hospitals, medical centres and other institutions around the world. Researchers are constantly looking at causes of the disease, how to prevent it and how to improve treatment.

An abundance of research is being conducted to learn what DNA changes are responsible for causing cells of the oral cavity and oropharynx to become cancerous. One alteration often found in DNA of oral cancer cells is a mutation of the p53 gene. The protein produced by this gene normally works to prevent cells from growing excessively and helps to destroy cells with DNA damage too extensive for the cells to repair. Damage to p53 DNA can lead to increased growth of abnormal cells and development of a malignancy (1). Recent studies suggest that tests to detect these p53 gene alterations may allow very early detection of oral and oropharyngeal tumours (2). These tests may also be used to better define surgical margins and to determine which tumours are most likely to respond to surgery or radiation therapy. Another DNA change found in some oral cancers is that DNA from a papillomavirus (HPV) becomes mixed together with the patient's own DNA (3). Some parts of the HPV DNA instruct the cells to produce proteins that inactivate the p53 protein. Studies are underway to determine whether tests to detect HPV DNA may help in diagnosing these cancers.

Researchers have discovered naturally occurring substances in the body that promote cell growth. These hormone-like substances are called growth factors. Growth factors activate cells by attaching to growth factor receptors, which are present on the outer surface of the cells. Some cancer cells grow particularly fast as they contain more growth factor receptors than normal cells do. One of the growth factors that has been linked to oral and oropharyngeal cancers is called epidermal growth factor (EGF) (4). Oral and oropharyngeal cancers with too many EGF receptors are apt to be especially aggressive. New drugs that specifically recognize cells with too many EGF receptors are now being tested in clinical trials. These drugs are effective by preventing EGF from promoting reproduction of cancer cells, and may also aid the patient's immune system distinguish and attack the cancer. Preliminary studies indicate that at least one such drug, C225, makes radiation therapy more effective in killing head and neck squamous cell cancers (5).

New chemotherapy drugs continue to be developed that may be more successful against advanced oral and oropharyngeal cancer. Intra-arterial chemotherapy (injection of drugs into arteries feeding the cancer) is being tested in combination with radiation therapy in an attempt to improve their effectiveness (6). Another new advance in treating head and neck cancers is intra-lesional chemotherapy (injecting the drug directly into the tumour) (7, 8). Success with this approach has limited because the drug is apt to spread to adjacent tissues and others parts of the body somewhat rapidly. Recent advances in preparation of the drug solution keeping it confined to a small area in the tumour have renewed the interest in intra-lesional chemotherapy, and preliminary results shows potential for success.

Clinical trials have been conducted to test the effectiveness of new radiation regimens delivering twice-a-day irradiation in the treatment of oropharyngeal cancer, as superior treatment results have been achieved with some of these new regimens (9). As well, new studies suggest that amifostine can help reduce xerostomia by limiting radiation damage to salivary glands (10). The drug is administered intravenously shortly before each radiation treatment. Side effects of amifostine include low blood pressure, nausea and vomiting. Moreover, a new protocol for radiating an area from multiple angles, and controlled by new software and blocking shutters, seems to be useful in avoiding the radiation-induced destruction of the salivary glands by targeting multiple beams around them, removing the gland from the radiation field.

Vaccines are being studied as a way to treat people with cancer by aiding their immune system to recognize and attack the cancer cells. As some oral and oropharyngeal cancers contain DNA from HPVs, vaccines against these viruses are being studied as a treatment for these cancers (11). Special attention is being paid to gene therapy, and how changes in the DNA of cells in the oral cavity and oropharynx cause these cells to become cancerous. This knowledge is being applied to experimental treatments intended to reverse these changes. Clinical trials are testing whether it is possible to replace abnormal tumour suppressor genes (such as the p53 gene) of oral cancer cells with a normal copy, to restore normal growth control.

Gene therapies to interfere with growth-stimulating effect of certain papillomaviruses are being developed. Another type of gene therapy adds new genes to the cancer cells to make them more susceptible to being killed by certain drugs (12).

As with all diseases, prevention is the best way to approach oral cancer (13). As such, there is a new organization dedicated to Prevention called 'IL CHIRONE, *Accademia di studi e ricerche di odontostomatologia e prevenzione odontostomatologica* or *Academy of studies and searches of odontostomatologia and odontostomatologica prevention*'(14). The website is under construction, but the first meeting of the Accademia-IlChirone will be September 2008, and the focus will be on Prevention of Oral Cancer. For further information, e-mail to: accademiachirone@libero.it or telephone (tele fax: +39 080 9641172). The main objective is the management of the oral care of the patient, based on prevention and promotion of oral and total health. The principle behind this objective is based on the definition of the concept of health supplied from the World Health Organization (WHO) and applies to the physical, social and psychical well-being of the patient.

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