1 Introduction: Epidemiology, Risk Factors, Pathology, and Natural History of Head and Neck Neoplasms

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The most frequent malignant head and neck neoplasms can be grouped under two major headings. The most abundant are the epithelial malignancies of the mucous membranes of the upper aerodigestive tract, so-called head and neck squamous cell carcinoma (HNSCC), accounting for about 90% of all head and neck neoplasms (Greenlee et al. 2001). The second largest group of neoplasms can be described as “glandular neoplasms”, the majority arising in the thyroid, a minority in the salivary glands.

Skin cancer is generally considered a separate entity, and so is skin cancer of the head and neck, mainly including squamous cell carcinoma and basal cell carcinoma. Less frequent head and neck neoplasia includes localized lymphoma, soft tissue and bone tumours (sarcomas), and neuroectodermal tissue tumours (paraganglioma, olfactory neuroblastoma, neuroendocrine carcinoma, malignant melanoma). For information on these tumour types, the reader is referred to specific head and neck oncology literature.

In this introductory chapter the first paragraph deals with epidemiology and risk factors of head and neck neoplasms. An overview of the pathology and natural history of the most frequent benign and malignant head and neck neoplasms will be outlined in the second paragraph.

1.1 Epidemiology and Risk Factors

1.1.1 Epidemiology: Incidence

Head and neck cancer, excluding skin cancer and Hodgkin and non-Hodgkin lymphoma, is the sixth most frequent cancer worldwide. The world incidence of epithelial malignancies of the mucous membranes is about 500,000 cases per year (laryngeal cancer: 136,000 new cases and 73,500 deaths yearly; oral and pharyngeal cancer: 363,000 new cases and 200,000 deaths yearly) (Parkin et al. 1999). Thus 6% of the global world incidence of cancer can be attributed to these neoplasms. Likewise, in the European Union 5% of the global cancer burden encountered in 1997 was caused by oral, pharyngeal and laryngeal cancer, and 1% by thyroid cancer (IARC CancerBase N°4 1999). Comparing these two largest groups, HNSCC and thyroid cancer, a definite gender difference is apparent regarding the incidence. As an example, the incidence of laryngeal SCC shows a male:female ratio of 10:1 (Boffetta and Trichopoulos 2002), whereas for incidence of thyroid cancer, the odds are in the opposite direction with a male:female ratio of 1:3. The incidence of salivary gland cancer is at the subpercentage level when looking at cancer in general, but is responsible for between 1% and 7% of head and neck cancer incidence (Kane et al. 1991; Spiro and Spiro 2001).

There is an important geographical variation in incidence of head and neck cancer. The incidence of hypopharyngeal cancer is typically very high.
in Northern France (10/100,000 males per year) as compared to e.g. the US (2/100,000 males per year). The incidence of laryngeal cancer in Northern Spain (20/100,000/year) is about 200 times as high as compared to certain regions is China (0.1/100,000/year) (IARC 1997). Besides probable differences in genetic susceptibility, a different prevalence of strong risk factors (e.g. Calvados drinking, smoking habits) is undoubtedly a large part of the explanation of these differences for HNSCC. In the same way differences in incidence among races can be observed [higher incidence in African versus Caucasian Americans (Day et al. 1993), and among men and women, largely attributable to differences in risk factor exposure (De Rienzo et al. 1991)].

1.1.2 Risk Factors for the Development of Head and Neck Malignancies

1.1.2.1 Risk Factors for Development of HNSCC

The most important established risk factor is chronic use of tobacco and alcohol (Fig. 1.1). The reason why these two factors are so important is twofold: there is a strong association with the disease on the one hand, and a very high prevalence of the factors among the population on the other. They are two independent risk factors that have been shown clearly to act in a multiplicative way when used in combination. Figure 1.2 shows that a 5.8-fold increased risk for development of oral and pharyngeal cancer is observed in non-smokers who consume 30 or more units of alcohol per week, a 7.4-fold increased risk is associated with smokers not consuming alcohol but with a history of 40 or more pack-years (smoking 20 cigarettes per day over a period of 40 years), whereas the person combining these two has a 38-fold increased risk (Blot et al. 1988). Conversely, after cessation of the use of tobacco, the risk of oral mucosal dysplasia and cancer falls to the level in the population that never smoked after 15 years (Morse et al. 1996).

The carcinogens in tobacco are nitrosamines, polycyclic aromatic hydrocarbons and aldehydes. Nitrosamines are alkylating agents that induce mutational events. Alcohol acts as a solvent and thus enhances permeability of the mucosa for the toxic substances in tobacco. A direct effect of alcohol is ascribed to mucosal enzymatic formation (alcohol dehydrogenase) of the carcinogenic acetaldehyde. The sites that are most at risk for alcohol induced carcinogenesis are the oro- and hypopharyngeal mucosal surfaces (Brugere et al. 1986), much more than the glottic larynx, for example, where only very high alcohol intakes can be shown to independently increase HNSCC risk.

Indirectly alcohol over consumption is associated with intake of non-alcoholic carcinogenic compounds contained in alcoholic drinks, e.g. nitroso dimethylamine in beer and tannin in wine. Furthermore, high intake of these beverages goes along with nutritional deficiencies, which in turn also confer an increased risk of HNSCC development. With poor nutrition, the proven protective effect of high intake of fruits and vegetables is lost. Indeed, a diet rich in fresh fruit and vegetables is associated with a 50%–70% reduction in the incidence of HNSCC (De Stefani et al. 1999). Especially dark yellow vegetables, citrus fruits (rich in vitamin C) and the carotene-rich vegetables (fresh tomatoes, carrots, pumpkins) are strongly protective. A crucial role is ascribed to antioxidant micronutrients in these vegetables such as vitamin C, vitamin E, beta carotene, and flavonoids (La Vecchia et al. 1997). Less proven but also suggested protective effects have been ascribed to use of olive oil (Franceschi et al. 1996) and high fibre intake (De Stefani et al. 1999).

Given the factors enumerated above, it is understandable that socioeconomic status is strongly associated with the development of HNSCC. Of this patient group, 75% live in the lower social classes, in terms of level of education and income. One in three patients has no partner and one in six patients is unemployed at the time of diagnosis. This social situation is a risk factor for having the combination of the direct risk factors tobacco, alcohol and poor dietary

Fig. 1.1. Smoking is the most prevalent and most powerful risk factor for the development of HNSCC. A doubled incidence of Warthin's tumor of the parotid gland has also been observed.