Skin Cancer (Non-Melanoma)

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Skin cancer is currently of interest because of the increasing incidence of tumors diagnosed by dermatologists. Because these cancers are not generally reported in tumor registries, the numbers are likely to be underestimated. About 600,000 new cases, representing one third of all new cancers, are diagnosed annually in the USA (reviewed in Corona, 1996), making non-melanoma skin cancer the most frequent type of cancer. The increased incidence is probably due to the depletion of the ozone layer, the shield protecting us against UV-C and most UV-B, in addition to an increase in outdoor activities. Based on data from a health plan in the Portland area (Oregon, USA), the incidence of skin carcinomas increased 2.6 fold in men and 3.1 fold in women from 1960 to 1980 (for review see Mortimer, 1991).

The increasing incidence applies to both types of skin cancer, squamous cell carcinomas (SCC) and basal cell carcinomas (BCC). However, the number of BCC far exceeds that of SCC. Mortality from skin cancers is low and mostly due to SCC. The number of metastasizing SCC is estimated at 3 to 10%. Metastatic BCC are hardly ever seen (less than 1 per 4000 cases). The recurrence rate, on the other hand, is high, approximately 35% at three years and approximately 50% at five years following first diagnosis (for review see Corona, 1996). Furthermore, the occasionally widespread local damage, particularly with BCC, remains a serious problem.

The incidence of skin cancer in the white population is strongly associated with UV exposure, with the highest incidence rate reported for Australia, particularly for British-born migrants who went to Australia before the age of 18. An increase in both the incidence and mortality rates, particularly of SCC, is being seen in renal transplant recipients (for review see Mortimer, 1991) and a Dutch study reported an overall incidence of SCC 250 times higher in
renal transplant patients than that in the general population (Harteelt et al., 1990). Both BCC and SCC develop predominantly in sun-exposed parts of the body such as head and neck, hands and legs. However, an increasing number of trunk lesions have also been reported (see Corona, 1996). In addition to the epidemiological evidence, molecular evidence is accumulating that UV radiation is the cause of skin cancer. Brash and coworkers demonstrated that a high proportion of BCC and SCC carry mutations in the p53 tumor suppressor gene which are C to T transitions in CC sites. Of these mutations, 10% are CC to TT double base changes, indicative of UV-B-induced mutations (Brash et al., 1991; Ziegler et al, 1994).

SCCs usually arise from the interfollicular epidermis as infiltrating sheets of islands of squamous epithelium with variable degrees of differentiation, dysplasia and proliferative activity. Classification was originally based on the degree of differentiation as shown by the degree of keratinization (horn pearl formation and single dyskeratotic cells). However, to predict the malignant potential of the tumor other features are important, including the degree of pleomorphism, the number of mitotic figures and the growth pattern (depth of penetration, way of spreading). In well-differentiated tumors the tissue architecture is quite regular with mitotic cells mainly located basally with horn pearls in the center of the epithelial islands. BCCs, on the other hand, are believed to be derived from hair follicles and typically consist of lobules of basal-like epithelial cells with limited peripheral palisading, surrounded by a characteristic fibrous stroma. Five subtypes are described with a classification depending on the clinical behavior and general growth pattern. Approximately 75% of all BCCs are of the nodular type in which large lobules form a circumscribed tumor mass (for review see McKee, 1996). The lobules can be of various shapes and sizes and are generally interconnected and do not usually differentiate.

1. CULTURE CONDITIONS

Few skin cancer cell lines exist. Most lines were established in the early 1980s and all these were derived from SCC (see Table 1). A limiting factor is the low success rate of establishment of skin cancer cell lines, and this applies to both SCC and BCC (Rheinwald, personal communication and own unpublished results). For skin cancers there is no magic formula, either for a successful primary culture (explant culture versus enzymatically dispersed cells) or for continuous cultivation (medium, trypsinization protocol or feeder support) (Rheinwald and Beckett, 1981; Wu et al., 1982; Tilgen et al., 1983). This low success rate is strange as normal keratinocytes from human skin easily adapt to culture conditions.