Mel 01**HISTOLOGY AND BIOLOGY OF MALIGNANT MELANOMA**
C. Schmoeckel

Histology is the most important method in evaluating melanocytic and other pigmented lesions. In most cases a clear diagnosis can be established and its metastatic potential can be assessed. However, some problems have to be pointed out:

1. The diagnosis of problem cases. Mainly the differential diagnosis between malignant melanoma and benign melanocytic and nevocytic nevi can be difficult.
2. The determination of prognosis. So far only the risk of metastases can be assessed with a certain degree of probability. A further improvement in prognostication would be useful.

New methods such as the use of specific antibodies and morphometry appear to be promising. However these methods need to be compared with histological criteria both qualitatively and quantitatively before they can be applied for routine purposes.

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Mel 02**HISTOMORPHOLOGY OF DYSPLASTIC NEVI AND MALIGNANT MELANOMAS**

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As both the benign and the malignant melanocytic lesions (nevi, melanomas) originate in the epidermis and tend to invade the dermis, the question arises if there are objective and reproducible parameters that allow the clinical pathologist to judge an intraepidermal lesion as benign or malignant. This problem is illustrated by the partly controversial discussion of the dignity of dysplastic nevi (DN) as questionable precursors of melanomas. Patients with a dysplastic nevus syndrome have a probability of 56 % developing melanoma.

In DN we found a significantly greater variability of nuclear areas indicating more anisokaryosis than in common nevi (CN). The DNA-distribution patterns of DN (Feulgen staining) revealed histographs with the signs of increased cell proliferation not being found in CN, whereas indications of malignancy like tumor cell stem lines and extremely broad distribution of DNA-content observed in melanomas could not be seen in DN. Other investigations evaluated monoclonal antibodies directed against antigens being specific for human melanoma cells and not being expressed in benign melanocytic lesions.

Histomorphologically the diagnosis of an early case of melanoma - e.g. melanoma in situ being restricted to the epidermis - is sometimes very difficult. These lesions can be compared with the intraepidermal periphery of invasive melanoma.

DNA-cytophotometrical analysis has shown in many cases already the intraepidermal part of the lesions having the potential of a malignant tumor.

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Mel 03**CYTOGENETIC STUDIES ON A GENETIC DISPOSITION TO MALIGNANT MELANOMA**

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Epidemiologic findings suggest that an exposure to UV light may largely account for the observed increased frequency of cutaneous malignant melanoma (MM). Beside this there is evidence that MM occurs on the basis of a genetic predisposition: First degree relatives of a melanoma patient have an 8- to 12fold increased risk, a lower age of manifestation and an increased risk for malignancies in general. Even more pronounced is the genetic risk to develop MM in persons who have a "dysplastic naevus syndrom"(DNS). This autosomal dominantly inherited condition is characterized by the occurrence of multiple dysplastic naevi and the lifetime risk for the development of MM approaches 100 %. The frequency of DNS in the population is 2 to 5%. About 30 % of all melanoma patients and about 90 % of patients with familial occurrence of melanoma have DNS. In order to determine the role of an individual sensitivity to the genotoxic effect of UV light, we determined the spontaneous and UV light induced chromosomal instability of 50 melanoma patients and 25 controls. Skin biopsies were taken from all probands and fibroblast cultures were initiated by standard methods. Chromosomal instability was evaluated by the determination of sister chromatid exchange and micronucleus formation. We found that MM patients have more than a 2fold increased formation of spontaneous micronuclei and - albeit to a lesser extend - an increased spontaneous formation of sister chromatid exchange. Both parameters were significantly more enhanced by an UV irradiation in vitro of the patient's cell cultures as compared to normal controls. This induction of chromosomal instability by UV irradiation is most pronounced in familial cases with melanoma and in DNS patients. From these results we conclude, that a genetic predisposition to MM can be explained at least in part by a specific chromosome instability.

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Mel 04**PROBLEMS OF CONCERNING THE CLINICAL DIAGNOSIS OF MELANOCYTIC LESIONS OF THE SKIN**

E.W.Breitbart, M.Roser and Th.Nasemann

The worldwide increase of the incidence of the malignant melanoma and its poor response to any treatment, are the reason for the necessity to diagnose clinically the malignant melanoma in its earliest stage to have the possibility of an 100% cure rate. This seems to be easy because the clinical criteria for malignancy or atypia/dysplasia are defined in literature:

- > 6 (4-5) mm in diameter
- irregular pigmentation
- irregular border
- red/white Halo
- changes of size, elevation, colour, squamation, itching and skinrelief etc.
- occurrence after the age of 35.

To test the validity of these criteria we investigated 69 non-selected patients excising 236 melanocytic lesions. 50% of the excised lesions were clinically suspect in order to the described criteria, 50% were clinically unsuspect. After comparison to the histological diagnosis and the statistical evaluation we came to the following conclusions:

- critical diameter is > 3 mm
- the highest percentage (50%) of malignancies we found (in correspondence between clinical and histological diagnosis) if two of the described criteria were fulfilled
- a lower (15%) percentage of malignancies we found (in correspondence between clinical and histological diagnosis) if all of the described criteria were fulfilled.

That means: In the moment the clinical recognition of the earliest stage of the malignant melanoma is a lucky chance. To have in future a higher security in the early recognition we need objective criteria for the clinical, the histomorphological, the immunological and the genetic findings. This presupposed a close interdisciplinary co-working like we have in the "Arbeitsgemeinschaft Malignes Melanom Eppendorf (AMME)".

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