

Dissertations

A Clinical and Experimental Study of Basal Cell Carcinoma.

Aspects on Epidemiology, Genetics and Microphysiology

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The literature constantly reports increasing incidence of basal cell carcinoma (BCC) in the western world. Information from Sweden in this matter has been scarce, likely because BCC has not been registered in the national cancer register. It is common that patients with BCC develop more than one BCC in life, but the risk factors are unknown. Associations with human leukocyte antigen, using serological technique on patients with multiple BCCs, have been reported from different parts of the world.

The BCC tumour grows slowly, and rarely metastasises like other cancer tumours. The microphysiology of the BCC, the subject for our study with energy dispersive X-ray microanalysis is unknown in contrast to other cancer tumours.

In our paper the incidence was studied during two periods 1971-1980 and 1996-1997, with a mean number of inhabitants of 320,000 and 500,000 respectively in approximately the same area of southern Stockholm. The incidence of cases with BCC increased between the two periods 6.8 times among the male population and



Peter Wallberg (*No. 3 from the left*) defended his thesis on February 4, 2000, at Södersjukhuset, Stockholm. Professor Olle Larkö (Faculty Opponent), Department of Dermatology, Sahlgrenska University Hospital, Göteborg (*No. 2 from the left*), Dr Magnus Lindberg (Supervisor), University Hospital, Uppsala (*left*) and Taavi Kaaman (Faculty Chairman) (*right*), Södersjukhuset, Stockholm.

6.6 times among women.

A follow-up study of patients with the primary BCC 1971-1980 in 1997, found only 76 patients possible to assess of 1,032. The limited number of patients effects the power of the results. However, 51% of the patients got a second BCC. The median time to a second BCC was 21 years.

Since a large part of patients with one BCC will develop a second or even several BCCs, this influence statistics. Interest in community and among colleges has increasingly focused on skin cancer and its associated risks. Consequently, today we examine more patients concerned about skin cancer than twenty years ago.

To assess risk factors associated with multiple BCC we investigated 110 patients with two or more BCCs in life. No phenotypic markers for patients with two or more BCC was found except for skin tumours in family with a relative risk of 10, and burned by the sun after the age of 60. To investigate the associations between multiple BCC and skin tumour in family, blood was analysed from patients with four or more BCC with high resolution sequence specific primers for any association to HLA class II antigens. No association with the HLA class II antigens could be found.

In cancer tumours the intracellular Na/K ratio is usually increased

whereas in hyperproliferating tissues, like psoriasis, it is decreased. We investigated the elemental composition in ten nodular basal cell carcinomas with the patient's buttock skin as control. A scanning electron microscope with an energy dispersive X-ray device (EDX) was used on frozen thick sectioned BCCs. In all 80 analysis times seven elements were performed. The intracellular ratio of Na/K in BCC decreased. Considering the clinical picture and the findings in our study inevitably raises the question; whether BCC is a malignant tumour or more related to hyperproliferative tissues.

To summarise the findings:

1. A significant increase of BCC has occurred during the last two

decades in southern Stockholm. This is probably representative of the development in the whole country.

2. Half of the patients with one primary BCC will develop a second BCC in life.
3. Risk factors associated with risk of developing multiple BCC are: skin tumour in family and burned by the sun after the age of 60 years.
4. No associations with HLA-DRB, HLA-DQA1 or HLA-DQB1 was found in Swedish patients with four or more BCCs.
5. The elemental composition of BCC has more in common with hyperproliferating tissues rather than the elemental composition of other cancer tumours.

List of original publications

- I. Wallberg P, Skog E. The incidence of basal cell carcinoma in an area of Stockholm county during the period 1971-1980. *Acta Derm Venereol* 1991; 71: 134-137.
- II. Wallberg P, Kaaman T, Alsterborg E, Lindberg M. Two decades of basal cell carcinoma. A retrospective follow-up study and the incidence 1996-1997 in Stockholm. In manuscript.
- III. Wallberg P, Kaaman T, Lindberg M. Multiple basal cell carcinoma. A clinical evaluation of risk factors. *Acta Derm Venereol* 1998; 78: 127-129.
- IV. Emtestam L, Wallberg P, Aldener A, Olerup O. Multiple basal cell carcinomas: no association with HLA-DRB, HLA-DQA1 or HLA-DQB1 in Swedish patients. *Br J Dermatol* 1996; 134: 886-891.
- V. Wallberg P, Lindberg M, Alsterborg E., Roomalns GM, Wróblewski R. Elemental changes in skin from patients with basal cell carcinoma. Submitted.

Regulation of the Expression of Human Collagenase-3 (MMP-13) - Implications for Wound Repair and Dermal Fibrosis

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Controlled degradation of extracellular matrix (ECM) is required for several aspects of wound healing, including keratinocyte migration,



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