of the hereditary susceptibility is supported by the finding of multiple primaries in three of eight offspring of the affected mother, while branch B is free of the malignancies. The occurrence of malignancies in the three other organs will be left undiscussed for the time being. We will, however, mention 1 female patient in our clientele belonging to a breast cancer family. This woman had breast cancer at the age of 61, renal cell carcinoma (clear cell type) age 67 as well as transitional cell cancer of the lower ureter discovered at the same age.

High incidence of colorectal cancer and urinary tract tumours, including renal cell carcinoma has been reported in families [6]. Urothelial tumours are also recognised as part of the Lynch II cancer family syndrome [7].

With this report we add evidence to the growing body of information suggesting a hereditary factor in the aetiology of urothelial tumours. Clustering of four members from the same nuclear family is unlikely to be caused by environmental factors alone.

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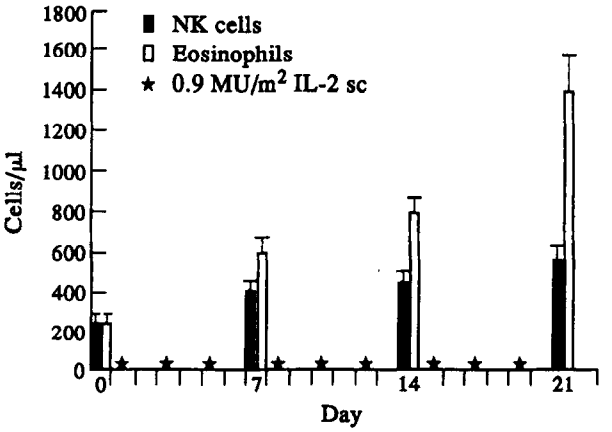

Fig. 1. Numbers of peripheral blood natural killer (NK) cells ($CD56^+CD3^-$) and eosinophils in cancer patients treated with 0.9 MU/m² IL-2 subcutaneously (sc) thrice weekly (nine doses). The values represent means of 5 patients ± S.E.M.

Scheduling of Ultra Low Dose Interleukin-2 in Immunotherapy

Albrecht Lindemann and Roland Mertelsmann

THE THERAPEUTIC use of ultra low dose interleukin-2 (IL-2) is currently based on the view that "IL-2 can best be used to stimulate immunoreactivity by maintaining IL-2R saturating concentrations for a long time" [1]. In keeping with this notion, ultra low dose IL-2 (<100 µg/m²/day half life *in vivo*: $t_{1/2}\alpha \sim 20$ min, $t_{1/2}\beta = 4{,}5$ h) has been administered as a continuous infusion [1, 2]. The development of polyethylene glycol (PEG)-derived IL-2 was also based on these considerations [3]. However, we find that subcutaneous administration of 50 µg/m²/day IL-2 (specific activity 1.8×10^7 U/mg of protein, Euro-Cetus, Amsterdam, The Netherlands) every other day thrice weekly (nine doses) is highly effective as well. Delayed type hypersensitivity responses of the skin, measured 8 days after discontinuation of therapy [sum of the total induration (in mm) of all positive responses to the Multitest CMI (Merieux, Lyon, France)], increased 2.7 ± 0.3-fold (relative to pretreatment ± S.E.M.) in 5 patients studied [4]. This therapy also induced a progressive increase of natural killer cells ($CD56^+CD3^-$) and eosinophils (Fig. 1). Thus, intermittent subcutaneous administration of ultra low dose IL-2 at 50 µg/m²/day may well induce prolonged immunological effects despite its short half life.

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