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**EFFECT OF HYPERTHERMIA ON
THE CYTOTOXICITY OF 4
CHEMOTHERAPEUTIC AGENTS
CURRENTLY USED FOR THE
TREATMENT OF
TRANSITIONAL CELL
CARCINOMA OF THE
BLADDER:
AN IN VITRO STUDY**

ANTOINE G. VAN DER HEIJDEN,
GERALD VERHAEGH, CORNELIUS F. J.
JANSEN, JACK A. SCHALKEN AND J.
ALFRED WITJES*

From the Department of Urology,
University Medical Centre Nijmegen,
Nijmegen, The Netherlands

Purpose: Hyperthermia combined with chemotherapy is not a novel cancer treatment. However, the working mechanism of this combination therapy is not fully understood. In the current in vitro study we investigated the differences in cytotoxicity of 4 chemotherapeutic agents at 37C or 43C.

Materials and Methods: The human transitional cell carcinoma cell lines used were RT4, RT112, 253J and T24. Cells were seeded in 96-well microtiter plates. After 24 hours cells were treated for 60 minutes with increasing concentrations of mitomycin C, epirubicin, gemcitabine and EO9 at a temperature of 37C or 43C. After treatment cells were rinsed 3 times and left for 24 hours in the incubator at 37C. The influence of chemotherapy and temperature on cell survival was determined by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide) assay.

Results: Decreased cell proliferation with increasing concentrations of chemotherapeutic agents was demonstrated. EO9 proved to be the most potent agent at each temperature.

Hyperthermia alone did not demonstrate decreased cell proliferation. However, a synergistic effect on decreased cell proliferation was demonstrated in all cell lines and chemotherapeutic agents used, although each had a maximum at a different chemotherapy concentration and to a different extent. Synergism was most obvious in cell lines treated with low dose epirubicin.

Conclusions: Synergism with hyperthermia and chemotherapy was clearly demonstrated for epirubicin, EO9, mitomycin C and to a lesser extent gemcitabine. Hyperthermia alone did not cause decreased cell proliferation. Synergism was most prominent with low drug doses and the most potent drug used in this in vitro study was EO9.