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THE INFLUENCE OF ENDOTOXINS AND POLYPEPTIDE IMMUNOMODULATORS ON THE IMMUNO-SUPPRESSION AND TOXIC EFFECT INDUCED BY CHEMO- AND RADIOTHERAPY

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The modulatory effects of immuno- and adjuvant endotoxin derivatives and synthetic branched polypeptides on immunosuppressed mice following chemo- or radiotherapy were studied. The immunosuppression induced by cytostatics (Adriamycin, Dianhydrogalactitol, 5-Fluorouracil, Vincristine) could be compensated by endotoxin derivatives (lipopolysaccharide from *Serratia m.08* cells; LPS and its non-toxic polysaccharide-rich fraction; PS). The immuno-potentiating effect of LPS and PS proved to be most significant in a combined treatment with Vincristine.

Immunosuppression induced by P388 tumour or cytostatics applied in therapeutic doses could be compensated by polypeptide treatment both in normal and in tumour bearing animals. However, no compensatory effect could be achieved if the inhibition of immune response exceeded 80%. Immunosuppression and the toxic effect caused by irradiation could be compensated for, or at least reduced by the immunomodulators.

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GIL

LOCAL THERMO-IMMUNOTHERAPY (MICROWAVE HYPERTHERMIA + PROPIONIBACTERIAE) OF ADVANCED RECTAL ADENOCARCINOMA.

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Treatment of advanced tumours of the gastrointestinal tract with local microwave hyperthermia (LMwH) and with non-specific immunotherapy has recently gained interest in experimental and clinical oncology. Intratumoral injection of immunomodulators results in a more pronounced anti-neoplastic effect compared with systemic administration. The combination of LMwH and intratumoral immunotherapy (Propionibacterium granulosum KP-45) has been found to act synergistically in mice bearing the Lewis lung tumour.

Patients with advanced rectal cancer were treated with a combination of LMwH and intratumoral immunotherapy. A special device was developed for intrarectal heating using LMwH with 2450 MHz microwave radiation (temperature in situ 43-44°C). Patients with rectal cancers were treated in 3 sessions with LMwH (30 min per session, twice weekly) followed by intratumoral injections of 10mg of Propionibacterium granulosum administered monthly. Fast involution of primary tumours occurred during the first two to three months of therapy. No complications or side-effects that may be related to heating the tumours or local immunotherapy were noted. The result of treatment with LMwH or immunotherapy alone was also examined.

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GOD

FACTORS INFLUENCING BINDING AND ACTIVITY OF ABRIN AND RICIN IMMUNOTOXINS

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To elucidate the factors determining the activity and specificity of immunotoxins, we have prepared conjugates of whole abrin and ricin with 3 different monoclonal antibodies and studied the interaction of the conjugates with a variety of cell lines. The abrin conjugates were obtained in higher yields than the ricin conjugates, and they consistently exhibited higher or equal activity and specificity. The sensitivity of different cell lines to the conjugates was related to the degree of expression of the specific antigens and to the sensitivity of the cells to the unconjugated, native toxins. The mechanism of the internalization and processing of the conjugate was studied by following the fate of labelled conjugate as well as that of isolated, labelled toxin and antibody.

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