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N-nitrosamine acids (e.g. nitrosoproline) excreted per 24 hr urine, represent an index for endogenous nitrosation. Formation of endogenous N-nitroso compounds was assessed by this method in the following subjects: subjects living in high/low incidence areas (a) for stomach cancer in northern Japan and (b) for oesophageal cancer in China; (c) subjects from 26 provinces in China with different mortality for cancer of the oesophagus, stomach and liver; (d) subjects from India with different chewing habits of betel quid; and (e) patients with urinary bladder infection.

In general, higher exposures in endogenous N-nitroso compounds were found in high risk subjects, but individual exposure was greatly affected by dietary components, modifying chemicals or disease state. Vitamin C lowered the body burden of intragastrically formed N-nitroso compounds. Mechanisms by which these nitrosamines are formed in vivo have been evaluated.

ANTIMETASTATIC EFFECT OF IL-2 AND DIFFERENT LYMPHOID CELLS

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We have studied the effect of systematically administered lymphoid cells given in conjunction with IL-2 on established lung metastases. Tumours were an anaplastic carcinoma (ACA) of Y59 rat and a mammary carcinoma (MCA) of CBA mouse. IL-2 was prepared by allosensitation of rat spleen cells with mitomycin C treated mouse splenocytes. Metastases in the lung were generated by i.v. injection of tumour cells. Five days after inoculation of tumour cells, animals were injected i.v. with 10^7 spleen cells from normal or specifically immunized donors or with those cells which were expanded in vitro with IL-2. Following this and every 24 hr thereafter during the 3 consecutive days recipients were given an i.p. injection of 0.5 ml of IL-2. Results indicate that in vivo administration of IL-2 in conjunction with immune lymphocytes in adoptive immunotherapy is effective in controlling metastatic growth in the lungs. In vitro expanded lymphocyte cultures however were less effective than entire splenocyte population.

DEMONSTRATION OF THE POTENTIATION OF ENDOCYTOSIS OF AN ANTI-CEA ANTIBODY BY A COLON CARCINOMA CELL LINE USING ANTI-CEA/NCA ANTIBODIES

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Carcinoembryonic antigen (CEA) may be a suitable target for immunotherapy of carcinoma of the G.I. tract, and factors which influence the cytotoxic effect of toxin-conjugated anti-CEA antibodies are important. In this study, factors influencing the endocytosis of an anti-CEA antibody by a gastric carcinoma cell line, MKN-45, have been investigated.

MKN cells were incubated on ice for 30 min with an anti-CEA antibody labelled with TRITC whose fluorescence was quenched by conjugation to HSA. After washing, the cells were incubated at 37° C for 2 to 6 hr. As endocytosis of the antibody occurred, the TRITC-HSA was degraded and the increase in fluorescence was quantitated by flow cytometry.

Endocytosis of anti-CEA-TRITC by MKN-45 cells was demonstrated after 2 hr and increased up to 6 hr. This was potentiated, in a dose-dependent manner, by the addition of certain antibodies defining epitopes common to CEA and normal cross reacting antigen (NCA), to the initial incubation mixture. After 6 hr, the value of fluorescence after potentiation was 1.8 times that of unpotentiated endocytosis.

PREVENTION OF EXPERIMENTAL LIVER METASTASES BY LECTIN BLOCKAGE

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According to recent results, our hypothesis that organ-specific lectins (e.g. the D-galactose specific Hepatic-Binding Protein) play an important role in the organ location of metastatic malignant cells, has been evaluated. In Balb/c mice, pre-injection (1 hr) and regular application (for 3 days after tumour cell inoculation) of the lectin blocking agents D-galactose (2 mg/g body weight) or arabinogalactan (0.5 mg/g body weight) completely prevented the establishment of sarcoma L-1 tumour in the liver but did not influence the localization into other organs. Non-specific, galactose-free polysaccharides showed no