BAR THE ASSAY OF CIRCULATING IMMUNE COMPLEXES IN HUMAN MALIGNANT TUMOURS BY THREE DIFFERENT NEPHELOMETRIC TECHNIQUES

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Immune complexes (IC) have been found to be elevated in large populations of patients with metastatic cancer employing several assays. No definitive conclusions, however, could be drawn as far as identifying a single "unique" method, showing a clearly superior utility. We assayed serum IC in a wide group of cancer patients divided according to clinical stage of disease by three different nephelometric techniques: a direct assay, the evaluation of 3.5% PEG precipitable IgG and complement factors and a method that measures the agglutination of latex particles coated with Clq (Behring). The neoplasms studied were mainly breast, lung, gastrointestinal and genito-urinary tract cancers. Differences were observed among the three different assays suggesting that such data could be helpful in understanding the mechanisms of IC formation in cancer patients as well as during the follow-up period.

BAR INTRAGASTRIC FORMATION OF N-NITROSO COMPOUNDS (NOC): TESTING OF AN ETIOLOGICAL HYPOTHESIS

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Subjects with an achlorhydric stomach may have an increased intragastric formation of NOC due to a large number of bacteria in their stomach that convert $NO_3^- \rightarrow NO_2^-$ and catalyse nitrosation. To test this hypothesis, patients with chronic atrophic gastritis (CAG), pernicious anaemia and who have undergone gastrectomy are being analysed for the levels of nitrosated amino acids in urine after application of the N-nitrosoproline (NPRO) test. NPRO levels in CAG-patients were found to depend on gastric pH (max. yield at pH 1.7 with large inter-individual variations (0-120 µg/day) of NOC excreted). CAG patients, as compared to controls, excreted no excess of NPRO, but their gastric juice contained higher NO_2^- levels. We now found 25 out of 35 bacterial strains (isolated from human sources) that exhibited nitrosation activity at pH 7 in vitro. The formation of N-nitrosomorpholine followed a Michaelis-Menten kinetics and substrate specificity for several amines was found (PRO being a poor substrate), suggesting a nitrosation catalysis by bacterial enzyme(s). These data clearly indicate that endogenous nitrosation does occur in the human stomach, but its relation to the induction of upper gastrointestinal cancer remains to be proven.

BAS EFFECT OF OXYGEN ON IN VITRO TUMOUR CELL GROWTH AND INTERACTION OF MACROPHAGES AND TUMOUR CELLS

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The effect of O_2 on the in vitro growth rate and colony forming ability of both primary and early passage tumour cell cultures was tested. The effect of O_2 on the interaction between tumour cells and macrophages was also studied. Primary cultures of 6 murine sarcomas and carcinomas were grown in an atmosphere of either 5% CO_2 in air or 2% O_2, 5% CO_2, and N_2 to balance. The lower O_2 levels (2%) greatly enhanced clonogenicity of cells and reduced the growth lag period, but only slightly increased the growth rate. In contrast, low O_2 did not influence the growth of established cells lines (CHO, V-79, and human glioma 87MG). Tumour cells in 2% O_2 grew similarly to primary cultures throughout 10 passages, while cells grown for 10 passages in 20% O_2 showed no preference for either environment. When tumour cells were plated onto monolayers containing syngeneic peritoneal macrophages, both the growth rate and clonogenicity of cells grown in 2% O_2 were inhibited. However, in 20% O_2, macrophages had either no effect or a stimulatory one. These data show that primary cultures of tumour cells grow better under 2% O_2 in vitro compared to 20% O_2. The presence of macrophages, however, diminish the enhancement of both the growth and clonogenicity of tumour cells in low O_2. Therefore, the in vivo hypoxic environment present in many solid tumours may stimulate tumour cell proliferation, but macrophages may modify that effect.