

intestinal diamine oxidase activity, both being associated with the tumour growth.

#### THE EPIDEMIOLOGY OF ENDOGENOUS NITROSATION IN MAN

D.Forman(1), T.Knight(1), D.Palli(2), P.Cocco(2), R.Pirastu(2), P.Tosi(2) and S.Leach(3)

(1)Imperial Cancer Research Fund, Oxford, U.K.; (2)ISS, Rome, Italy; (3)PHLS, Porton Down, U.K.

Epidemiological investigations designed to study the role of endogenous N-nitroso compounds in human cancer have produced inconclusive results. The development of the N-nitrosoproline (NPRO) test (1) has made possible the quantitative estimation of endogenous nitrosation. We have used this test to study nitrosating ability in relation to the risk of gastric cancer.

Healthy males aged 20 to 35 years, resident in two regions of Italy with contrasting mortality from gastric cancer have been compared using the test. NPRO is measured in 12-hour urine samples following a dose of 500 mg proline. In a separate study, patient groups with precursor lesions for gastric cancer were compared with those having normal gastric epithelia. In this case 24-hour urine samples were analysed following proline and nitrate doses.

The results of these studies have been evaluated in relation to dietary characteristics of the groups.

(1) Ohshima H. and Bartsch H. Cancer Res. 41: 3658-3662, 1981.

#### THERAPEUTIC EFFECT OF CHEMOIMMUNOTHERAPY ON LYMPHOMA BEARING MICE

F.Fornelli, C.Rossi, M.Sensi and G.Parmiani

Istituto Nazionale Tumori, Divisione OSB, Via Venezian 1, 20133 Milan, Italy

The therapeutic effect of a combination therapy employing anti-tumour immune lymphocytes and either doxorubicin (DX) or cis-diamminedichloroplatinum II (DDP) was tested on BALB/c mice bearing YC-8, a weakly immunogenic lymphoma. Mice inoculated with  $10^4$  YC-8 tumour cells given i.v. all died with liver metastasis. Therapy with immune lymphocytes alone ( $30 \times 10^6$  i.v. every 2 days x 3) gave an 80% cure rate when started 3 days after tumour inoculation; when treatment was delayed (5 days) only 20% of the mice were cured. Given at 7 days, immune lymphocytes were ineffective. DX (10 mg/kg) and DDP (6 mg/kg) i.p. gave a

significant increase in survival time at all days tested but no cures were obtained. DDP was slightly more active than DX. The association of DDP (day 5) with immunotherapy (day 7) was more effective (54% cures) than DDP alone and day 5 or 7 immunotherapy alone. Only a slight increase in life span was found by combining immunotherapy with DX. The results suggest that combination of chemotherapy and immunotherapy may improve the effects of each treatment alone.

#### BINDING FOR cis-DIAMMINEDICHLOROPLATINUM (II) TO DINUCLEOTIDES

A.Försti, R.Laatikainen(1) and K.Hemminki

Institute of Occupational Health, Helsinki, Finland; (1)University of Kuopio, Kuopio, Finland

Cis-diamminedichloroplatinum (II) (cis-Pt) is a widely used anticancer agent, whose main target is thought to be DNA. In this study, we have incubated cis-Pt with four homodinucleotides (GpG, ApA, CpC, and UpU) and six heterodinucleotides (GpC, CpG, GpU, UpG, GpA, and ApG) at pH 6 at 37°C. The reaction products were purified by HPLC. Cis-Pt reacted equally well with all guanosine-containing dinucleotides, while the reaction with ApA was much slower. With CpC and UpU no reaction products were formed. The most important products were characterised by  $^1\text{H}$  NMR spectra. In all the heterodinucleotides except the ones containing uridine, the main Pt-adduct was an intramolecular cross-link, in which the other binding site of cis-Pt was the N-7 atom of guanosine. The other products were intermolecular cross-links and monofunctional Pt-adducts. In the case of homodinucleotides GpG gave almost entirely intramolecular cross-links, and ApA gave both monofunctional and bifunctional Pt-adducts. These results suggest that in DNA cis-Pt is first bound to the N-7 atom of guanine, and then to another base, which may be either guanine or adenine, or even cytosine or thymine.

#### ISOLATION OF LYMPHOCYTE CLONES REACTING AGAINST AUTOLOGOUS HUMAN MELANOMA

G.Fossati, A.Anichini, P.Squarcina, S.Cerasoli and G.Parmiani

Istituto Nazionale per lo Studio e la Cura dei Tumori, 20133 Milan, Italy

Peripheral blood lymphocytes (PBL) of a melanoma patient were cultivated with autologous melanoma cells (Auto-Me) and recombinant interleukin 2 (RIL-2, Biogen)