radiation and with a number of chemotherapeutic agents. The hypoxic fraction of the B16 melanoma was not modified by prior treatment with cyclophosphamide but it was increased when BCNU was given. Treatment with 1000 rad of γ-irradiation rendered the tumour cells more resistant to drugs.

HILL, R. P. & STANLEY, J. A. (1975) The Response of Hypoxic B16 Melanoma Cells to *in vivo* Treatment with Chemotherapeutic Agents. *Cancer Res.*, **35**, 1147.

INTERACTION OF ACTINOMYCIN D, RADIATION AND YEAST CELL SURVIVAL. E. VAN DUYSE, A. DUNJIC and P. LIPNIK, Laboratoire de Radiobiologie, Institut du Cancer, Université Catholique de Louvain, Leuven.

The survival of yeast cells after irradiation and the use of actinomycin D in the culture medium were further investigated (Van Duyse and Dunjic, European Society for Radiation Biology, Tenth Annual Meeting, Madrid 1973).

Additional data concern dose-response relationship of both radiation and drug effects. Based on 66 individual observations, the parameters of cell survival curve for actinomycin D are:

$$\tilde{N} = 1{\cdot}07\ (0{\cdot}83\text{–}1{\cdot}38),$$
$$\hat{D}_0 = 228\ (155\text{–}432)\ \mu g/ml$$

The potentiation of radiation effects with actinomycin D was studied following concentration in culture medium from 12·5 μg/ml to 125 μg/ml. The significant differences are obtained only with concentrations of actinomycin D (above 75 μg/ml) which already alone impair the cell proliferation.

Following on, three-dimensional data analyses indicate that the enhanced effects of radiation and AMD treatment are additive in nature.

Analyses of cell survival data were performed by using gamma function model (Lipnik and Dunjic, 6th L. H. Gray conference, London 1974).

COMPARISON OF THE RESULTS OF DETAILED ANALYSIS OF CHROMOSOMAL ABERRATIONS IN HUMAN LYMPHOCYTES AFTER EXPOSURE TO RADIATION AND CHEMICALS *IN VITRO*. M. KUČEROVÁ, Genetic Laboratory, Institute of Hygiene and Epidemiology, Prague.

Human peripheral blood samples from 2 healthy donors were exposed *in vitro* to 200 R of x-rays and/or to 10^{-4} mol solution of TEPA or 10^{-6} mol solution of Epichlorhydrin in different phases of cell cycle. Using the trypsin banding method, detailed cytogenetic analysis revealed different types of chromosomal aberrations induced by radiation and by chemicals, even if the cells were exposed to mutagens in the same phase of cell cycle. Non-random distribution of breaks of individual chromosomes as well as especially fragile or resistant bands were found, but differently after irradiation and after exposure to chemicals tested. Most probably the differences could be explained by a different mutagenic mechanism of these 2 types of mutagens.

COMBINED EFFECTS OF BLEOMYCIN AND X-RAYS ON DNA SYNTHESIS IN ASCITES TUMOUR CELLS. I. V. CHAPMAN and F. A. ALALAWI, Department of Medical Biophysics, The University, Dundee.

The separate effects of each agent on DNA synthesis have been investigated using ^{14}C-thymidine tracer techniques and Ehrlich tetraploid ascites tumour cells in predominantly stationary phase suspensions. The studies reveal that whilst the effect on intracellular pool size is markedly different for each agent, inhibition of the rate of incorporation of the tracer into DNA is observed in both cases.

A number of schedules involving drug treatment and irradiation of the same suspensions were studied to investigate the combined effects of bleomycin and x-rays on DNA synthesis. Single doses of bleomycin (20 μg/ml) given before or after or simultaneously with exposure to x-rays (2·5 krad) have an additive or less than additive effect. However, split bleomycin schedules in combination with x-rays have a significantly greater than additive effect on DNA synthesis rates.

INTERACTION OF BLEOMYCIN WITH UNIRRADIATED AND IRRADIATED DNA. J. DIRS, W. KÖHNLEIN, R. SEIDLER, I. TOBÜREN-BOTS and W.

WÜBKER, Institut für Strahlenbiologie, Universitat Münster.

The production of single strand breaks (SSBs) and double strand breaks (DSBs) in T_2 DNA (16 μg/ml) by bleomycin (Bl) (40 μg/ml) was investigated quantitatively. At 5°C 0·11 SSB/min per T_2 genom were found. The addition of 1 mmol cysteamine (SH) enhances the single strand breakage rate by a factor of 25. DSBs were found at a rate of 0·5/min only in the presence of SH and Bl. Since the accidental DSB rate due to SSBs in opposite DNA strands is less than 10^{-3}/min per T_2 genom DSBs must be produced directly by the action of Bl. The obtained DNA profiles did not follow a random distribution; thus bleomycin apparently acts at specific sites along the T_2 genom. X-irradiation followed by Bl–SH treatment resulted in an increased DNA degradation. The number of SSBs is at least 3 times larger than expected if the effect of both treatments is just additive.

MODIFICATION OF THE RESPONSE OF MOUSE SKIN TO X-IRRADIATION BY BLEOMYCIN TREATMENT. J. T. LEITH and B. S. LEWINSKY, Lawrence Berkeley Laboratory, University of California.

Skin reactions occurring on the legs of mice after 230 kV x-irradiation were used to investigate the combined effects of x-irradiation and bleomycin. Bleomycin was given daily for 5 days (5 mg/kg/day), either preceding or following graded single doses of x-rays. Skin reactions occurring after combined treatment were compared with skin reactions produced by x-irradiation alone. Both bleomycin schemes yielded average 1–30 day post-irradiation skin reactions greater than skin reactions seen after x-irradiation alone. Dose-response curves for the combined treatments were parallel to the x-irradiation alone treatment, but were displaced upwards. The responses obtained in the 2 bleomycin schemes were not significantly different. The dose modifying effect of the bleomycin treatments ranged from 1·5 at low levels of effect to 1·2 at higher levels of effect. It is concluded that the combined effects of bleomycin and x-irradiation in this design were additive. In a second series of experiments, the ability of bleomycin to affect the ability of mouse skin to recovery from radiation injury in a fractionated experiment (3F/4D) was studied. Bleomycin was found to apparently decrease, by about 30%, the repair of sublethal radiation damage when given simultaneously with the radiation exposure (5 mg/kg).

RADIATION AND ANTI-TUMOUR DRUGS. M. BARKER-GRIMSHAW, K. HELLMANN and G. E. MURKIN, Chemotherapy Department, Imperial Cancer Research Fund, London.

Growth inhibitory effects of the anti-tumour drugs 5-flourouracil, adriamycin, hydroxyurea, bleomycin, cyclophosphamide, methotrexate, ICRF 159 and 593A and the radiosensitizer Ro–07–0582 combined with a standard dose of radiation was tested on the radiosensitive sarcoma 180. The most effective potentiators were 593A and ICRF 159. They were then examined against the relatively radioresistant Lewis lung carcinoma and melanoma B16 using either single doses of drug and radiotherapy or the same total dose given in fractions over 5 days. 593A was equally potent whether given as a single maximum tolerated dose or in divided doses; ICRF 159 was ineffective when given as a single low dose (though it was effective given in a single high dose), but highly effective in divided low doses. Clinical trials with ICRF 159 in combination with radiotherapy are in progress.

EFFECT OF LUCANTHONE ON THE RADIOSENSITIVITY OF A MOUSE TUMOUR. K. R. RAO and H. FRITZ-NIGGLI, Radiobiology Institute of Zürich University.

Lucanthone is reported to be carcinostatic (Hirschberg *et al.*, *J. natn. Cancer Inst.*, 1959, **22**, 567) and a radiosensitizer (Bases, *Cancer Res.*, 1970, **30**, 2007). But in our study lucanthone alone (70 mg/kg body weight) had no lasting effect on the Ehrlich carcinoma in mice. Based on mitotic studies, 4-day old ascites tumour was not sensitized to x-rays when pretreated with lucanthone. Tumour growth, evaluated as the average weight of solid tumours or the number of tumour cells in ascites bearing mice, was not significantly different between the group treated with x-rays only and the one treated with lucanthone plus x-rays. Thus, lucanthone seems to enhance the radiosensitivity of normal cell