An application of diamide alone (156 mg/kg) on gestation day 8 in mice had a teratogenic effect of 5-60%. In combined treatments diamide was injected i.p. 30 min before irradiation with 25, 50 and 100 R of different kinds of radiation.

Contrary to lucanthone as a very effective radiosensitizer (Michel, *Experientia*, 1974, 30, 1195), no synergistic effect could be observed with diamide and radiation doses of 50 or 100 R. However, with 25 R of 200 keV roentgen rays a possible synergistic effect is not to be excluded.

**ACTION OF DRUGS ON REPAIR PROCESSES.** M. C. L. Zumel, G. Cobreros and M. D. Astudillo, Instituto Química Física "Rocasolano" CSIC, Madrid.

The study of chemical compounds acting as modifiers of radiation effects requires the understanding of their ways of action. Inhibition of repair processes is one of the mechanisms by which some radiosensitizers act on living cells. In this paper the effect of chloroquine on the non-scheduled synthesis of DNA after irradiation of mice spleen cells is studied. Methyl-3H thymidine is used in order to follow the kinetics of this synthesis and 10^-2 mol hydroxyurea and 5 × 10^-4 mol chloroquine are incorporated into Hanks’ incubation medium. A 50% inhibition on the repair replication process is obtained. Ultracentrifugation studies on DNA γ-irradiated samples with and without the compound and quantitative determinations of phosphate groups and spectrophotometrical measurements on UMP and OPEA supply information about the way in which chloroquine joins at important biological molecules.

**EFFECTS OF HYDROXYUREA AND 5-FURODEOXYURIDINE ON EXCISION REPAIR IN HUMAN CELLS.** K. Erixon, B. Johansson and G. Ahnström, Wallenberg Laboratory, University of Stockholm.

Incubation of UV irradiated human cells results in the production of strand-breaks due to endonuclease attack at the site of a pyrimidine dimer. These breaks are, however, hardly detectable by the use of alkaline sucrose gradient sedimentation. By applying the rate of strand separation technique (Ahnström and Edvardsson, *Int. J. radiat. Biol.*, 1974, 26, 493) it has been possible to follow the kinetics of the enzyme reactions in which the breaks are produced and sealed. Hydroxyurea and 5-fluorodeoxyuridine, both potent inhibitors of DNA synthesis, markedly increase the number of breaks, which are detectable during the repair process. This is probably caused by a decreased polymerization rate due to lack of deoxynucleotides because addition of TdR to FUrD treated cells will drastically reduce the number of breaks observed.

Xeroderma pigmentosum cells were also investigated. Cells belonging to complementation group A showed no UV induced strand-breaks, either in the absence or presence of HU, whereas Xp-variant cells had activity like normal cells.

**ACTIONS OF SOME DRUGS ON ENZYMES INVOLVED IN DNA REPAIR AND SEMI-CONSERVATIVE DNA SYNTHESIS.** E. Wawra, W. Klein, F. Kocsis and P. Weniger, Institut für Biologie, Forschungszentrum Seibersdorf.

Different antirheumatic and cytostatic drugs had been tested by measurement of the
thymidine incorporation into DNA of spleen cells under conditions, under which either DNA synthesis or repair after γ- or UV irradiation takes place. There are substances which inhibit either only the semiconservative DNA synthesis (vinblastine, isonicotinic acid hydrazide) or only DNA repair (mixture of penicillin G and procaine penicillin G) or both (cyclophosphamide, phenylbutazone, procarbazine, nalidixic acid).

Vinceristine shows no effect on the thymidine incorporation in DNA, but by density gradient centrifugation it has been found that it influences the ligase reaction.

Two DNA polymerases had been isolated from spleen cells, one of the low molecular and one of the high molecular weight type. The influences of the described drugs on these enzymes and on a deoxyribonuclease I from beef pancreas have also been tested in in vitro systems. In all cases, it has been found that there is no effect or only a very small one, compared with the action of well-known inhibitors as e.g. ethidium bromide and p-chloromercuribenzoate, and this cannot be responsible for the suppressions found in DNA repair and semiconservative synthesis.

THE TIME RESOLUTION OF THE EFFECTS OF OXYGEN AND RADIOSENSITIZERS ON THE DNA STRAND BREAK AND REPAIR PROCESS IN E. COLI polA-. O. SAPORA and P. S. LOVEROCK, Physics Department, Institute of Cancer Research, Sutton.

By use of a rapid lysis technique the radiation induced yield of SSBs in the repair deficient strain of E. coli polA− was studied with a time resolution down to 0.2 sec. The time dependence of the repair processes including incision of base damage and polymerase III dependent strand rejoining were followed. Addition of oxygen after anoxic irradiation demonstrated that the polymerase III enzyme system and at least part of the incision process are completely inhibited under hypoxia. Oxygen or the radiosensitizer PNAP, when present during irradiation, produced the same yield of SSBs initially although the subsequent repair was different, whereas the nitroxyln NPPN produced an initial yield of breaks and similar degree of repair to that found in anoxia.

The initial (0.2 s) yield of SSBs was 0.97/krad in oxygen and 0.28/krad in nitrogen giving an OER of 3.6.

A CAFFEINE-SENSITIVE REPAIR PROCESS PREVENTING REPLICA- TION GAPS FROM OCCURRING IN UV IRRADIATED HAMSTER CELLS. G. AHNSRÖM, Wallenberg Laboratory, University of Stockholm.

DNA which is replicated immediately after the cells have been exposed to UV light contains single strand interruptions, most probably opposite unexcised pyrimidine dimers. These interruptions disappear slowly during post-label incubation. It is expected that mistakes in filling the gap opposite a remaining dimer may give rise to mutations.

After UV irradiation cells are incubated for 30 min in a medium containing 3H-thymidine and caffeine. The cells are then incubated for 2 h in medium containing only caffeine during which time control cell DNA reaches a size of 2-10⁶−5-10⁹ daltons. The closing of UV induced gaps, however, is inhibited by the presence of caffeine. The number of UV induced interruptions in the 3H-labelled DNA can then be determined by the “rate of strand separation” technique (Ahnström and Edvardsson, Int. J. radiat. Biol., 1974).

The dose response curve for UV induced replication gaps shows an initial slow rise, a threshold up to about 50 erg/mm² then the increase is more steep. If an incubation in medium is inserted between the UV irradiation and the 3H-thymidine pulse, the threshold where replication gaps start to rise steeply is moved to higher doses. This indicates a repair process which removes damage creating replication gaps. If, however, the incubation is made in the presence of caffeine no such repair takes place.

FAST MIXING STUDIES OF THE TIME SCALE OF THE OXYGEN EFFECT IN IRRADIATED BACTERIA. R. L. MAUGHAN, G. J. FISHER, B. D. MICHAEL and K. B. PATEL, CRC Gray Laboratory, Mount Vernon Hospital, Northwood.

A fast mixing technique, which combines single irradiation with rapid gas transfer, has shown that in Serratia marcescens irradiated under anoxia the lifetime of the oxygen dependent damage extends into the millisecond range.