COMPARATIVE EFFECTS OF CYTOTOXIC AGENTS ON LYMPHOMYELOID TISSUES IN MICE. J. G. SHARP and D. K. NELSON, University of Nebraska Medical Center, Omaha.

The effects of x-irradiation, nitrogen mustard, vincristine and busulphan on the lymphomyeloid tissues have been compared in 2 strains of mice. The initial damaging effects of these agents on whole tissues are remarkably similar, even though their known modes of action and effects on stem cells are very different. Altered nutrition and the removal of damaged cells by the immune system appear to be implicated. The patterns and duration of the recovery phases show considerable differences between various lymphomyeloid tissues and strains of mice. These differences not only result from the differing effects of the various drugs on the precursor cell populations with differing kinetic properties, but also from the influence of systemic and local humoral (microenvironmental) factors which regulate the patterns of stem cell differentiation during the recovery phase. The differences between 2 strains of mice appear to result from the differing size of their stem cell compartments.

INTERACTION OF TETRACYCLINE AND LUCANTHONE ON RADIATION DAMAGE IN MAMMALIAN EMBRYOS AS DEPENDENT ON LET (EXPERIMENTS WITH PIONS). H. FRITZ-NIGGLI and CH. MICHEL, Strahlenbiologisches Institut der Universität Zürich.

The very high sensitizing effects of iodoacetamide, tetracyclines and lucanthone for embryonic systems of rat and mouse are presented. In comparison, we studied the effect of tetracyclines and lucanthone on malignant tumours and tissue cultures (Fritz-Niggli, Michel and Rao, *Agents and Actions*, 1974, **4**, 54). Interesting differences in response are shown. The sensitizing effects of the drugs mentioned are studied in relation to LET. Data with the pions of 590 MeV proton accelerator of SIN are represented as well as experiments with 31 MeV photons and 15 MeV electrons. Although the relative biological effectiveness of pions on embryonic damage seems to be extremely high, a radiosensitizing effect of lucanthone can still be demonstrated. The results agree with our working hypothesis of the important action of sensitizers on energy metabolism (membranic systems), (Fritz-Niggli and Michel, *Atomkernenergie*, 1971, **18**, 105).

INVESTIGATIONS ON SERUM PROTEIN CHANGES IN MICE AFTER WHOLE-BODY X-IRRADIATION COMBINED WITH OPEN SKIN WOUNDS. R. HENNEBERG and O. MESSERSCHMIDT, 8-München 22, Schackstr. 5.

Changes in the serum protein composition of mice after irradiation with 600 R only or after additional infliction of a skin wound 2 days after irradiation (600 R) were investigated using Sephadex G-200. In animals burdened with radiation as well as mechanical skin injury, the acute phase of serum protein alterations appeared much earlier and was more distinct. In spite of a striking decrease of albumin (60%) a slight increase of the relative area of the third peak compared with the total peak was found. Analysis of single eluates of the third peak by disc electrophoresis in polyacrylamide gel revealed that the decrease of albumin results in an increase of a protein of similar molecular weight, situated between the albumin and α_2-macroglobulin ranges. B. J. Davis assigns this to transferrin. The increase of this protein seems to be correlated with the decrease of albumin. The extent of the change seems to depend on the radiation dose, the second trauma (skin wound) and on the time interval between the 2 traumata.

IDENTIFICATION OF HYPOXIC MOUSE BONE MARROW CFU *IN VIVO*. H. J. KEIZER and L. M. VAN PUTTEN, Radiobiological Institute TNO, Rijswijk.

Immobilization of mice during whole body irradiation, both by anaesthesia and restraint without anaesthesia, decreases the radiosensitivity of mouse bone marrow CFU (Keizer *et al.*, *Int. J. radiat. Biol.*, 1971, **20**, 192).

Compound Ro-07–0582 (1 g/kg i.p. 1 h before irradiation), a 2-nitroimidazole, radiosensitizes hypoxic bone marrow CFU *in vivo* (animals killed 10 min before irradiation), as shown by a decrease of the D_0 from 281 to 161 rad γ-rays. The radiosensitivity of well oxygenated bone marrow CFU *in vivo* was

not changed significantly. By means of this agent, hypoxic CFU could be identified in the bone marrow of restrained mice but not in pentobarbitone anaesthetized mice, indicating that the radioprotective effect of pentobarbitone anaesthesia is caused by some mechanism other than hypoxia. We also showed that pentobarbitone prevents the recruitment of resting mouse bone marrow CFU into S phase following x-irradiation. Evidence for a higher radiosensitivity of mouse bone marrow CFU in S phase compared with resting CFU was presented by Duplan and Feinendegen (*Proc. Soc. exp. Biol. Med.*, 1970, **134**, 319). This might explain the radioprotective effect of pentobarbitone anaesthesia during irradiation.

DISTRIBUTION AND RADIOSENSITIZATION *IN VIVO* OF PIROMELITIC ACID. F. Sanz Sanchez, A. Anadon Navarro, A. Goicoechea Mayo, R. Martinez Larrañaga and M. D. Astudillo, Department of Pharmacology, Madrid, Veterinary Faculty and Co-ordinated Center of Pharmacology, CSIC.

To test piromelitic anhidride as a radiosensitizer *in vivo* and with acute and subacute toxicity established, a preparatory study was conducted of tissue distribution and blood levels.

The LD_{50} was 1 gr/kg administered intravenously. The oral dosage of 1 gr/kg during 3 weeks did not cause noticeable variations in weight, food consumption and other parameters.

To calculate the distribution kinetics of piromelitic acid-^{3}H at pH 7, using oral doses 1/5-LD_{50}, animals were killed at intervals of 15 min, 30 min, 1, 2, 3, 6, 9, 24 and 48 h and blood samples taken; later brain, heart, lung, liver, kidney, intestine, muscle and skin samples were examined to determine the relation between per cent activity/mg min at time intervals and ratios of fresh organ to dry organ weight; maximum activity was reached in 30 min.

This study of a radiosensitizer was conducted using Swiss/D mice as controls, irradiated and non-irradiated, inoculated with ascitic Ehrlich tumour cells.

RADIATION CHEMISTRY OF GLUTATHIONE AND ITS POSSIBLE ROLE IN AFFECTING RADIOSENSITIVITY OF BIOLOGICAL SYSTEMS. M. Tamba, R. Badiello, M. Quintiliani and G. Gorin, Laboratorio di Fotochimica e Radiazioni d'Alta Energia (CNR), Bologna.

It has been postulated that intracellular sulphydryl affects radiation sensitivity of living cells. Accordingly, glutathione being the main low molecular weight intracellular SH compound, the study of its radiolysis is relevant.

Steady-state radiolysis of reduced glutathione (GSH) in oxygen containing solutions at pH 7 shows that G(-SH) is about 20 at 3 mmol concentration. As the GSH concentration is increased from 2 to 20 mmol the value changes gradually but constantly. Pulse radiolysis studies of interactions of OH radicals with GSH were carried out at different pH's. The primary product of such reactions appears to be the thiyl radical GS', with a λ_{max} at 330 nm. In oxidized glutathione (GSSG) the primary product of the reaction with e^{-}_{aq} is the well known radical anion $GSSG^{-}$ absorbing at 420 nm. The $GSSG^{-}$ radical decays with first-order kinetics ($k = 2{\cdot}4 \times 10^{5}\ sec^{-1}$) producing the thiyl radical. The reaction of hydroxyl radicals with oxidized glutathione ($k = 9{\cdot}9 \times 10^{9} M^{-1} sec^{-1}$) leads to the formation of a transient species with λ_{max} at 330 nm ($k_{form} = 9{\cdot}3 \times 10^{9} M^{-1}\ sec^{-1}$), which we identify as GS.

When experimental solutions are saturated with N_2O containing different amounts of oxygen, reactions between the radical species GS, $GSSG^{-}$ and O_2 are observed.

STUDIES ON $tRNA^{Val}$ ISOLATED FROM CHICK EMBRYO LIVER IRRADIATED *IN OVO*. L. Gyenge, E. Bölöni, A. Benkó and L. D. Szabó, F. Joliot-Curie National Research Institute for Radiobiology & Radiohygiene, Budapest.

Estimation of the *in vitro* effect of ^{60}Co irradiation on $tRNA^{Val}$ and $tRNA^{Phe}$ isolated from chick liver has been previously reported (Abstracts of 9th FEBS meeting). In our recent experiments 15- and 18-day old chick embryos (Leghorn) were irradiated *in ovo* with 400, 500 and 700 R respectively (dose rate 96 R/min); 96 h and 24 h after irradiation the mortality of the embryos was estimated and tRNA was isolated from liver of surviving embryos. UV absorption spectra and amino acid acceptance activity of $tRNA^{Val}$