Table I. The local radioprotective effect of sodium and potassium chloride

| | | No. of animals | Protection | No protection |
|---|---|---|---|---|
| Shortly before irradiation | NaCl | 29 | 2 | 27 |
| | KCl | 29 | 26 | 3 |
| 60 min before irradiation | NaCl | 8 | – | 8 |
| | KCl | 10 | – | 10 |
| Shortly after irradiation | NaCl | 8 | – | 8 |
| | KCl | 10 | – | 10 |

the lumbo-sacral region under slight ether anaesthesia. After awaking the animals and stabilization of the electrode in the tissue, the tested solutions were injected around the tip of the electrode. The changes of oxygen tension were registered for 10 min after the injection of the solutions. As demonstrated in Table II, the potassium chloride induces, after a short-term increase, a marked drop of oxygen tension with the maximum in the 3rd min after injection. The protective effect of isotonic potassium chloride on the pilary system of young mice may be thus conditioned by the local hypoxic state.

Tabelle II. The mean values (± S.E.) of the oxygen tension in subcutaneous tissue expressed in percent of the initial value (100%) after the injection of sodium and potassium chloride

| | Minutes after the injection | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| NaCl | 90 | 94 | 101 | 99[a] | 94 | 92 | 94 | 98 | 104 | 102 |
| ($n = 4$) | ±5 | ±6 | ±8 | ±6 | ±7 | ±7 | ±7 | ±7 | ±7 | ±6 |
| KCl | 123 | 74 | 63 | 68[a] | 74 | 77 | 82 | 82 | 85 | 89 |
| ($n = 5$) | ±39 | ±41 | ±14 | ±5 | ±10 | ±18 | ±22 | ±23 | ±21 | ±18 |

[a] The values are significantly different (Wilcoxon's test of order, $P < 0.02$).

to 4 min) or 60 min before irradiation, or shortly after irradiation (up to 4 min). 8 days after irradiation the local radioprotective effects were evaluated. The complete absence of fur indicated no protection. Local protection was evidenced by the abundant fur present at the site of injection.

The results summarized in Table I indicate a highly significant protection of potassium chloride injected shortly before irradiation (when compared with sodium chloride effect, $\chi^2 = 36.5$, $P < 0.001$). Because of the known effects of potassium on the contractile state of the vascular smooth muscle[8], the mechanism of its radioprotective effect may be connected with the changes in the tissue oxygen supply. In order to test this possibility, the local oxygen tension was measured in the subcutaneous tissue. The mice were fixed and the needle of Beckman oxygen microelectrode was inserted s.c. into

*Zusammenfassung.* Wenn isotonische Kaliumchloridlösung vor einer Bestrahlung mit 550 R lokal eingespritzt wird, übt sie eine Schutzwirkung auf das Haarsystem der $C_{57}$ acht Tage alten schwarzen Mäuse aus. Dieser Effekt kann durch die vasoaktive Wirkung des Kaliums und durch die resultierende lokale Hypoxie erklärt werden.

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## Giant Histiocytes after Cyclophosphamide

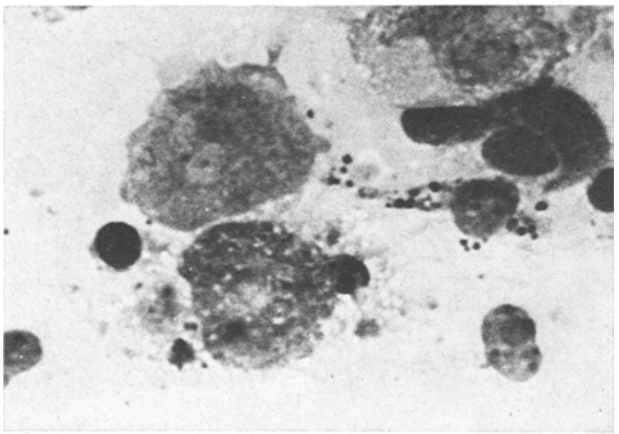
The formation of enlarged or giant cells in quickly renewing tissues following treatment with cytostatic drugs has been commonly observed in experimental[1-3] and clinical studies[4-7]. Since the reticuloendothelial system (reticulum cells, histiocytes) seems capable of cell renewal in the steady state[8,9] and even more after a suitable stimulus (antigens, particles)[10,11], we supposed that also histiocytes can present patterns of nuclear and cytoplasmic enlargement or giantism after treatment with cytostatic drugs; if this is true, the giant cells thus formed may still demonstrate phagocytic activity. The purpose of this communication is to present evidence supporting this assumption.

Twenty Morini albino mice, random bred, males weight 25 g, were injected i.p. with 0.4 ml of a 1% solution of trypan blue (Merck) in saline. After 24 h, 15 of them were given an i.p. injection of 200 mg/kg of cyclophosphamide (Endoxan ®); this treatment was repeated in the following days with 24 h intervals. 5 mice injected only with trypan blue served as controls. Mice were killed under ether anaesthesia in groups of 3 animals every time at the 24th, 72nd and 96th h after the first administration of cyclophosphamide. Bone marrow smears were performed within 10 min after the beginning of ether narcosis, prepared with a fine brush, dried quickly and stained with May-Grünwald-Giemsa and neutral red.

*Results.* (1) Some reticuloendothelial cells of the bone marrow, that have phagocytized trypan blue, present patterns of nuclear and cytoplasmic giantism after treatment with cyclophosphamide (Figure); this is clearly

evident at the 48th, 72nd and 96th h after the injection of the cytostatic drug, respectively at the 72nd, 96th and 120th h after the administration of trypan blue. (2) Giant histiocytes present both nucleus and cytoplasm of increased diameter; their size is twice, three or more times larger than that of normal histiocytes. 10, 15 and 16% of the histiocytes showed, 48, 72 and 96 h respectively after the administration of cyclophosphamide, a nuclear diameter larger than 20 $\mu$. 2% of them showed a nuclear diameter larger than 30 $\mu$. According to our observations the mean nuclear diameter of the normal histiocytes of the bone marrow is $8.5 \pm 1.3$ $\mu$ large. (3) The histiocytes so transformed show still incorporated particles in their cytoplasm.

These findings support the assumption that histiocytes of the bone marrow can undergo giant cellular patterns after treatment with antimitotic drugs, likewise it has been observed by BASERGA and MARINONE[1] for myeloid cells (megamyeloid cells).



A giant histiocyte (lower, on the left) compared with a megamyeloid cell (upper, on the left) and with a normal histiocyte. Bone marrow. May-Grünwald-Giemsa stain. × 1200.

Since it is known that the reticuloendothelial system is sharing in the immunological response[12–16], it is conceivable that the antimitotic drugs may bring about an immunosuppressive effect by damaging the histiocytes too.

*Riassunto.* Nel midollo osseo di topi intossicati con dosi elevate di ciclofosfamide compaiono elementi giganti, che, per la capacità fagocitaria di cui sono dotati, appaiono appartenere al sistema istiocitario (istiociti giganti).

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## Enhancement of Haemagglutinin Production in Polyoma Virus-Infected Candida by a Defined Medium and Urethan

The transfer of polyoma virus (PyV) to *B. subtilis* with the infectious DNA was described by BAYREUTHER et al.[1]. We were not only able to verify their findings[2–4] but to propagate EMC virion[5,6] and PyV[7], as well as viral-RNA[5] and viral-DNA[4], in intact yeasts and Tetrahymena. During these assays the stimulation of virus production by Urethan was observed[3,8]. This effect can be substantially increased with further technical refinement, such as the use of the defined medium of HEALY et al.[9]. The great increase in PyV hemagglutinins is described in this communication. More details will be published separately[8].

*Materials and methods.* *C. albicans* was isolated from a patient and carried axenically in a natural medium[10,5] at 28 °C. PyV was the large plaque variant propagated in mouse embryo cells[4,7] and it went through 30 passages in yeast before being used as inoculum. 0.2 ml cell homogenate[6] containing 2048 HAU (approximately $10^3$ PFU) was added to 0.3 ml log phase yeast culture ($10^6$ cells) 1 h adsorption was allowed at 27 or 37 °C, under constant agitation in a Dubnoff water-bath at 90 rpm. To remove the unadsorbed PyV, 5 washings were made with 2 ml PBS each, followed by centrifugation. After 1 h interaction the system was brought to 50 ml with natural[10] or defined medium[9], the latter containing 0.15 *M* sucrose.

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