scintillating solution (Spolana) were added. The total activity was measured by a liquid scintillation counter MARK I (Nuclear Chicago). An external standard was used. The radioactivity obtained was expressed in percent of activity administered – in the case of the bone marrow in percent of 1 g, in the case of the blood in percent of 1 ml, and in the other cases in percent of the total wet tissue weight. The data obtained were evaluated statistically and the mean values and the SD were computed. The statistical significance of the differences was checked by means of the Student's t-test.

Results. The distribution of ^{35}S-activity and the influence of simultaneously administered mexamine are shown in the table. A highly significant decrease in activity occurred in the kidney and bone marrow 10 min after the treatment with the mixture of cystamine-^{35}S and 5-MOT. The activity in all other tissues investigated did not differ too much as compared with the group treated with cystamine-^{35}S only. The most pronounced changes were seen at an interval of 20 min after the administration of the radioprotective mixture. The level of activity was increased markedly in the liver, small intestine and blood, whereas in the kidney and bone marrow a decrease was established. The activity in the spleen revealed a slight increase. 30 min after the treatment with the mixture, a high level of activity was found in the liver and blood. The values of activity obtained in all other tissues remained practically unchanged when compared with the animals treated with cystamine-^{35}S only. An increase of activity occurred in the bone marrow, small intestine and kidney (the difference being significant in the bone marrow) 60 min after administration of the radioprotective mixture.

Discussion. The ^{35}S-distribution in rats treated with a mixture of cystamine-^{35}S and 5-MOT has not yet been studied. However, the increased concentration of nonprotein SH-groups was described in the spleen, small intestine, muscles and the blood, whereas the decrease was noticed in the kidney 30 min after the simultaneously administered cystamine and 5-MOT[9]. In our laboratory, characteristic changes were found in the content of SH-groups in various tissues of rats under similar conditions also[10]. These findings indicated the possibility of a changed distribution of cystamine-^{35}S. Our experiments confirmed this assumption. Mexamine caused a significant increase in the ^{35}S-activity in the liver, small intestine and blood, mainly 20 min after the administration of radioprotective agents and a decrease in activity in the bone marrow and kidney at the 1st intervals followed. Our results are in good agreement with the findings of Titov and Mordukhovitch[8] who investigated the influence of 5-MOT on the distribution of cystamine-^{35}S in mice 15 and 30 min after the treatment with a mixture of both radioprotective agents. The changed ^{35}S-distribution caused by simultaneously administered mexamine was found when using other radioprotective agents than cystamine. Ayrapetyan et al.[11] described protracted penetration of cystaphos-^{35}S into various tissues of mice in the 1st 30 min. At the following intervals, an increase in ^{35}S-activity occurred. The fate of labelled sulfur of cystamine-^{35}S in the bone marrow has not yet been studied. Our findings of a decreased activity at the 1st 2 intervals could be explained by the vasoconstrictive effect of mexamine which lowered the penetration of cystamine[12]. However, this effect may not play a decisive role in the other radiosensitive tissues (spleen, small intestine). The prolonged persistence of labelled sulfur in rats treated with mexamine could be understood as a result of the increased concentration of cystamine in the kidney, which leads to a lowered elimination into the urine. This corresponds with the increased activity of labelled sulfur in the blood. The results presented indicate that at the interval during which the experimental animals are usually X-rayed (30 min after the treatment with radioprotective agents at the latest), the ^{35}S-activity of cystamine-^{35}S simultaneously administered with mexamine was increased in radiosensitive tissues (small intestine, spleen); but it was decreased in bone marrow comparing with the group treated with cystamine-^{35}S only. We could not confirm unequivocally the hypothesis of a prior role of SH-groups in the mechanism of radioprotection[13]. Our findings support the assumption of the combined effect of various biochemical mechanisms including the substantial role of hypoxic effect[14].

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Methylmercury sexual dimorphism in the mouse[1]

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Summary. 5–8 days after a single nontoxic dose of radioactive methylmercury chloride adult male mouse kidneys contain twice as much radioactive mercury per unit wet wt as do kidneys of similarly dosed adult females.

In the course of studies designed to evaluate biological variables of significance for estimating hazards of exposure of mammals, including man, to mercury compounds, we have observed that after a single, nontoxic dose of methylmercury, much more mercury is found per unit wet wt of kidney in male than in female adult mice.

Three 8-week-old C129F$_1$ hybrid (BALB/c female × 129 male) female mice were each given a single, nontoxic, i.p.

injection (0.1 ml per 25 g mouse) of $CH_3{}^{203}HgCl$ (0.4 mg Hg/kg) in 5 mM Na_2CO_3 on day 0. Three 8-week-old $C129F_1$ male mice were similarly dosed (0.4 mg Hg/kg). $CH_3{}^{203}HgCl$ (specific activity 1.55 mCi/mg Hg, purity >92%) was purchased from New England Nuclear and was mixed with nonradioactive (ethanol-recrystalized, purity >99%) methylmercuric chloride (K&K Labs, Plainfield, NJ). Total body radioactive mercury was determined immediately after dosing, and again on day 8 before autopsy, with a whole body gamma counter, by placing each mouse in the 70×130 mm center well of a 135 mm diameter × 160 mm deep thallium activated sodium iodide crystal. Kidneys were counted in a Packard Series 5000 autogamma spectrometer. Mercury body burdens and kidney mercury concentrations were calculated after correction for radioactive decay and are expressed as nanograms of mercury, Fractions of Initial Dose (F.I.D.) or Fractions of Initial Concentration (F.I.C.):

$$\text{F.I.D.} = B_t \div B_0 \quad \text{F.I.C.} = \frac{B_t \div W_t}{B_0 \div W_0} \quad \text{(or)} \quad \frac{K_t \div KW_t}{B_0 \div W_0}.$$

B_0 and B_t = total body radioactivity on day 0 or day t; W_0 and W_t = body wt on day 0 or day t; K_t = total radioactivity of kidneys on day t; KW_t = total weight of kidneys on day t. Results are recorded in the table and show that 8 days after the methylmercury dose, adult male mouse kidneys contain approximately twice as much radioactive mercury per g wet wt as do kidneys of similarly dosed adult females.

To confirm this observation using another stock of mice, 4 female and 4 male 16-week-old strain 129 mice were each similarly dosed i.p. with $CH_3{}^{203}HgCl$ (0.4 mg Hg/kg; specific activity, 1.71 mCi/mg; purity >99%). Total body counts were determined on day 0 and on day 5 before the mice were autopsied. Kidneys were counted as described for the previous experiment. Results are shown in the table. t-tests were performed to test the hypothesis that there were no significant differences in kidney mercury concentration between males and females in terms of retained whole body total mercury content (F.I.D.), whole body mercury concentrations (F.I.C.) or kidney mercury concentrations (F.I.C.). Probability values for the stated hypothesis are listed in the table. It can be seen that though no significant sexual differences were observed in terms of whole body mercury content (F.I.D.), and whole body mercury concentrations (F.I.C.), highly significant differences were found between male and female kidney mercury concentrations (F.I.C.).

A 2fold sex difference has been observed in the amount of alcohol dehydrogenase contained in kidneys of adult male mice compared to those of adult females[2]. Sex differences in activities of mouse kidney glucuronidase have also been reported[3]. Our results reveal that adult male and female mouse kineys concentrate mercury differently.

We are currently examining sex correlated differences in metabolic processing of mercury compounds in terms of mouse strain, stage of development, cellular localization and hormonal stimulation. These observations could help in defining biochemical details of renal excretion of different forms of mercury. A better understanding of factors influencing excretion of mercury compounds is expected to aid in evaluation of hazards of exposure to different mercury compounds and in design of treatment methods for accelerating excretion of mercury compounds.

Whole body retention and kidney concentrations of mercury in adult male and female mice

Mouse strain	Sex	F.I.D. Whole body $\bar{x}$ (SE)	F.I.C. Whole body $\bar{x}$ (SE)	F.I.C. Kidney $\bar{x}$ (SE)
$C129F_1$ (day 8)	Male	0.495 (0.031)	0.481 (0.021)	5.33 (0.40)
	Female	0.507 (0.019)	0.507 (0.020)	3.34 (0.20)
t-test result (p)		(0.76)	(0.42)	(0.011)
129 (day 5)	Male	0.704 (0.013)	0.683 (0.019)	7.47 (0.16)
	Female	0.691 (0.006)	0.691 (0.001)	3.57 (0.15)
t-test result (p)		(0.39)	(0.68)	(0.000002)

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Free radical intermediates produced by autoxidation of 1,8-dihydroxy-9-anthrone (dithranol) in pyridine

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Summary. The autoxidation of the antipsoriatic agent dithranol, monitored by an ESR-spectrometer, proceeds through several free radical intermediates. The initial radical, attacking a bulky spin trapping agent in a sterically comparatively hindered constellation, may be the active therapeutic form of dithranol.

Dithranol (anthralin, anthranol, Cignolin®) has been the mainstay in the topical treatment of psoriasis since 1916[1,2]. Indirect evidence has accumulated that dithranol has to be activated before its final oxidation to the therapeutically inactive anthraquinone and dimeric products[3], and it has been postulated that a free radical mechanism is involved[4]. We have proved this by electron spin resonance (ESR) and spin trapping techniques.

The autoxidation of dithranol (~1 mmole/l) in pyridine solution in the presence of 2,4,6-tri-tert-butylnitrosobenzene (TBNB) (~3 mmoles/l), known as an effective difunctional spin trapping agent[5,6], gave the ESR spectrum shown in the figure. It indicates the presence of one TBNB adduct with the g-value 2.0066 and the hyperfine splitting constants $a_N = 1{,}20$ mT (1 N), $a_{H(\beta)} = 1{,}36$ mT (1 H), and $a_{H(m)} = 0.075$ mT (2 H), as verified by computer simulation. These data are in accordance with literature[5,6] values for a nitroxyl-type adduct so that the illustrated spectrum is assignable to a trapped 1,8-dihydroxy-9-anthrone radical in which the attacked site is the 10-position (see figure). It is