EFFECT OF MERCURIC COMPOUNDS ON THE MATERNAL TRANSMISSION OF SELENIUM IN THE PREGNANT AND LACTATING RAT

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Summary. The administration of small amounts of mercuric compounds to pregnant rats, injected with ^{75}Se in the form of selenite, markedly increased their retention of ^{75}Se and simultaneously decreased the ^{75}Se content in their foetuses. The ^{75}Se concentration in the blood and liver of foetuses from these rats was much lower than in the blood and liver of foetuses from control mothers injected with [^{75}Se]selenite only (or receiving zinc chloride instead of mercuric chloride). Retention of ^{75}Se in the maternal organs and the passage of ^{75}Se into the foetuses was partially dependent on the dose of mercury. In the doses used in these experiments, administration of mercuric salts did not result in foetal death nor in any significant effect on the weight of the offspring. In lactating rats, the administration of mercuric salts had a similar effect on the passage of ^{75}Se into the milk. This resulted in a much smaller ^{75}Se content in the newborn and suckling young of mothers exposed to small amounts of mercuric compounds during pregnancy or lactation than in control animals.

INTRODUCTION

Following the discovery that selenium is an essential nutrient (Schwarz & Foltz, 1957) and the first report revealing that prenatal myopathy in lambs can be prevented by adding a small amount of selenium to a dystrophogenic diet fed to pregnant ewes (Muth, Oldfield, Remmert & Schubert, 1958), the importance of selenium in the prevention and therapy of analogous livestock diseases affecting various animal species was confirmed by a great number of authors (see Rosenfeld & Beath, 1964; Muth, 1967).

Selenium concentrations in various organs (such as liver, kidneys or blood) of foetal or newborn lambs were reported to be markedly lower in flocks affected with congenital white muscle diseases than in those that were unaffected (Cousins & Cairney, 1961; Burton, Keeler, Swingle & Young, 1962; Hartley, 1967). Low tissue levels of selenium in the organs of young animals appear to be an essential prerequisite for the development of selenium-responsive diseases during this period of life, though some reports indicate that the incidence of these diseases may not always be connected with demonstrable

selenium deficiency in the feed (Schwarz & Mertz, 1960; Schubert, Muth, Oldfield & Remmert, 1961; Hartley & Grant, 1961). It seems reasonable to expect that during pregnancy and lactation, the interfering factors could act not only at the level of the availability of selenium for the maternal organism but also at the level of the transmission of selenium from the maternal organism into the foetuses and the milk.

The administration of small amounts of salts of certain metals such as cadmium (Ganter & Baumann, 1962; Pařízek, Ošťádalová, Beneš, Babický & Beneš, 1967; Pařízek, Beneš, Babický, Procházková & Lener, 1969b), mercury (Pařízek *et al.*, 1967, 1969b; Levander & Argrett, 1969) or thallium (Levander & Argrett, 1969) affects selenium metabolism, markedly decreasing its excretion from the organism, and it is known that some of these metals, particularly cadmium, may be present in fertilizers (Schroeder, 1963, 1967) and surprisingly large amounts of mercury compounds (see Bidstrup, 1964; Warren, Delavault & Cross, 1965) have been used in agriculture (seed dressing). It might be expected that, as a result of certain of these man-made changes in the environment connected with industrialization and agricultural development, living organisms might be exposed to significant amounts of compounds of these metals.

Earlier experiments have shown that the interrelationship between selenium and the metals, mercury, cadmium and thallium could have special implications during pregnancy and lactation, and that small amounts of selenium compounds given during pregnancy or lactation decreased the passage of mercury from the maternal organism into the offspring (Pařízek, Beneš, Ošťádalová, Babický, Beneš & Piřha, 1969d; Pařízek, Babický, Ošťádalová, Kalousková & Pavlík, 1969a). It seemed of interest, therefore, to learn if small amounts of salts of these metals given during pregnancy and lactation could have a similar effect on the passage of selenium into the offspring, changing not only the excretion of selenium from the maternal organism but also its transmission into the foetuses and the milk.

As cadmium salts, in contrast to those of mercury, produced serious damage in the placenta (Pařízek, 1964) and lactating mammary glands (Pařízek *et al.*, 1969d) and as mercuric compounds seem to be more potent in affecting selenium metabolism (Pařízek *et al.*, 1969b), small amounts of salts of bivalent mercury were given to pregnant or lactating rats injected with a tracer dose of [^{75}Se]selenite. In order to avoid possible interference at the level of intestinal absorption, the metallic salts were administered parenterally. The effect of the mercury on the retention of selenium in the maternal organism and on its passage into the foetuses and into the milk and sucklings was compared with the effect of salts of the chemically homologous element, zinc. A preliminary report on the results of these experiments has already appeared (Pařízek, Ošťádalová, Kalousková, Babický & Pavlík, 1969e; Pařízek, Ošťádalová, Kalousková & Babický, 1970).

MATERIALS AND METHODS

Pregnant or lactating rats (Wistar, substrain Konárovice) were kept under

constant laboratory conditions and fed a standard laboratory diet (Ošťádalová & Pařízek, 1968). The day on which sperm cells were detected in vaginal smears was taken as the 1st day of pregnancy. In the experiments on lactating rats, the number of sucklings in each litter was kept constant from the 2nd day after delivery so that eight sucklings were fed by each lactating rat.

The radioisotope of selenium was obtained as sodium [^{75}Se]selenite from the Radiochemical Centre, Amersham, and diluted with saline so that the amount of radioisotope injected per 100 g of body weight was contained in a volume of 0.1 ml.

Mercuric chloride, mercuric acetate or zinc chloride (Lachema; the highest grade of purity) were injected as 0.02 M-solutions, with the exception of the experiments in which the effects of various doses of mercury were compared and in which correspondingly more dilute solutions were used. All solutions were made isotonic with saline and injected subcutaneously 1 hr before the injection of the radioisotope of selenium. The radioisotope and the solutions of salts of the metals used were injected into different regions of the body to avoid direct contact of solutions injected into the same rat.

For the determination of radioactivity *in vivo* in pregnant rats, lactating rats and whole litters, and also for radioactivity determination of larger samples (whole maternal liver, whole non-dissected uteri, all placentae and all foetuses from each pregnant rat), a whole-body counter was used. The detectors of the whole-body counter consisted of two NaI(Tl) crystals (6 in. $\times$ 4 in. and 4 in. $\times$ 4 in.) shielded by 2 in. of steel. The electronic equipment consisted of an E.H.T. power supply, a photomultiplier balancing unit, a signal adding unit, a linear pulse amplifier and a one-channel gamma spectrometer. With the exception of the gamma spectrometer (Vacutronic), all other electronic parts and the detectors were supplied by Nuclear Enterprises (G.B.) Ltd. The measurements were taken at the photopeak of the ^{75}Se (0.40 MeV).

After determination of the radioactivity *in vivo*, the pregnant rats were killed by decapitation and maternal blood and liver samples were collected. In the experiments in which the ^{75}Se content was determined in foetal blood and liver, the foetuses were removed and also killed by decapitation immediately after the death of the mothers: foetal blood and liver samples were pooled from all the foetuses of each pregnant rat. In other experiments where the total radioactivity present in the whole uterus and in its components was determined, the uteri were removed *in toto* immediately after decapitation of the pregnant rats and the radioactivity was determined using the whole-body counter. Immediately thereafter, the uteri were dissected and all placentae and all foetuses from each pregnant rat were collected and pooled and their radioactivity was determined using the whole-body counter.

Milk samples were collected by manual expression from lactating rats from which the sucklings were removed 1 hr before the injection of the radioisotope, i.e. 25 hr before the milk collection. Immediately after the milk collection, the lactating rats were killed by decapitation and their blood and blood plasma were collected.

For the determination of radioactivity of smaller samples (1 ml of maternal blood and blood plasma or pre-weighed samples of maternal blood, foetal

blood, foetal liver and milk), a well-type NaI(Tl) crystal and a scaler (Versamatic, Tracerlab) were used.

Appropriate standards were measured together with samples using the whole-body counter in addition to the well-crystal. Particular care was given to the geometry of measurement: the conditions used excluded the possibility of any significant error arising from any possible lack of homogeneity in the distribution of the isotope within the measured organism or samples. The results were expressed as a percentage of the injected dose of ^{75}Se except in Text-fig. 3, where the content of ^{75}Se in all foetuses from each rat was expressed as a percentage of the total amount of ^{75}Se retained in the whole pregnant rat at the time at which the mothers were killed and the foetuses were removed.

The mean values ($\pm$ S.E.) for the ^{75}Se content are given in Text-figs. 1 to 5 and Tables 1 and 2. Where appropriate, Fisher's *t* test or analysis of variance were used for statistical evaluation of the results, and the method of least squares for fitting the regression lines.

RESULTS

As shown in Text-fig. 1, exposure of the pregnant rats to mercuric chloride increased the ^{75}Se concentration in the maternal blood ($P < 0.01$) and liver ($P < 0.05$). In spite of the markedly increased ^{75}Se level in the blood on the maternal side of the placenta, ^{75}Se concentrations in the blood and liver of foetuses from mercuric-chloride-treated mothers were substantially decreased in comparison with the levels found in foetuses of control pregnant rats given [^{75}Se]selenite only ($P < 0.01$). Equimolar or even higher doses of zinc chloride did not have a similar effect to mercuric chloride. There was no significant effect on the ^{75}Se concentration in the maternal organs or on the level in the foetal blood, nor was there any decrease of the level in the foetal liver. On the contrary, a statistically significant ($P < 0.01$) increase of the ^{75}Se concentration was observed in the liver of foetuses of mothers treated with zinc chloride in comparison with controls receiving the tracer dose of selenite only. Further experiments are necessary to understand the mechanism of this effect of zinc.

In further experiments, a study was made of the dependence of the maternal retention of ^{75}Se (and its passage into the foetuses) on the dose of mercuric chloride given to pregnant rats. As shown in Text-fig. 2, even a small amount of mercuric chloride increased the retention of selenium in the whole maternal organism and simultaneously decreased the passage of selenium into the foetuses. As a result of this, a much smaller proportion of the whole amount of ^{75}Se retained in the pregnant rats was present in foetuses of rats given mercuric chloride (Text-fig. 3). The effect both on the retention of selenium in the pregnant rat and on its transmission into the foetuses was, within certain limits, dependent on the dose of mercury, though this dependence was not linear in character.

For a mathematical description of the relationship between the variables given in Text-figs. 2 and 3, the empirical formulae were compared with the experimental data using the method of least squares. The equations of the best-

TEXT-FIG. 1. The effect of mercuric chloride given to pregnant rats on the distribution of ^{75}Se in maternal and foetal organs. [^{75}Se]selenite (200 $\mu\text{Ci/kg}$ b.wt corresponding to 0.68 $\mu\text{mol/kg}$ b.wt) given on the 19th day of pregnancy. C: controls, ^{75}Se only ($n = 6$). Hg10: mercuric chloride 10 $\mu\text{mol/kg}$ b.wt ($n = 6$). Hg20: mercuric chloride 20 $\mu\text{mol/kg}$ b.wt ($n = 6$). Zn20: zinc chloride 20 $\mu\text{mol/kg}$ b.wt ($n = 5$). Situation 24 hr after the administration of ^{75}Se .

fit regression lines expressing the relationship between the dose of mercury given and (1) the retention of ^{75}Se in the whole pregnant rat,

(2) the ^{75}Se content in one foetus (expressed as a percentage of the injected dose of ^{75}Se), and

(3) the total ^{75}Se content in all foetuses from each pregnant rat (expressed as a percentage of the actual total amount of ^{75}Se retained in the whole pregnant rat) can be given as

(1)
$$\frac{1}{y_1} = 0.01462e^{-0.446x} + 0.01130$$
 where x is the dose of mercury injected ($\mu\text{mol/kg}$ b.wt) and y_1 is the amount of ^{75}Se retained in the whole

TEXT-FIG. 2. The effect of mercuric chloride on the retention of the ^{75}Se in pregnant rats and on the passage of ^{75}Se from the maternal organism into foetuses: the dependence on the dose of mercury. [^{75}Se]selenite ($100 \mu\text{Ci/kg b.wt}$ corresponding to $3.6 \mu\text{mol/kg b.wt}$) given on the 19th day of pregnancy. Situation 20 hr after the ^{75}Se administration. Experimental data (means $\pm$ S.E.) for the ^{75}Se content in one foetus (○) and in the pregnant rat (●) as well as the corresponding best-fit curves are represented. The numbers in parentheses are of pregnant rats.

pregnant rat (expressed as a percentage of the dose of ^{75}Se injected). In that case,

$$\lim_{x \rightarrow \infty} y_1 = 88.5\%.$$

$$(2) \quad y_2 = 0.377e^{-0.126x} + 0.104,$$

where x is the dose of mercury ($\mu\text{mol/kg b.wt}$) injected into a pregnant rat and y_2 is the amount of ^{75}Se present in one foetus (expressed as a percentage of the dose of ^{75}Se injected). In that case,

$$\lim_{x \rightarrow \infty} y_2 = 0.104\%.$$

$$(3) \quad y_3 = 8.24e^{-0.245x} + 1.30,$$

where x is the dose of mercury ($\mu\text{mol/kg b.wt}$) injected into a pregnant rat and y_3 is the total ^{75}Se content in all foetuses from each pregnant rat (expressed as a percentage of the actual amount of the ^{75}Se retained in the whole pregnant rat). In that case,

$$\lim_{x \rightarrow \infty} y_3 = 1.30\%.$$

The organ distribution of ^{75}Se in pregnant rats treated with various doses of mercuric chloride is given in Table 1. By increasing the dose of mercuric chloride, the concentration of ^{75}Se increased in all the maternal organs studied and decreased in the foetuses. When the ^{75}Se content was determined in samples containing both maternal and foetal components (whole non-dissected uteri, placentae), the dependence of the ^{75}Se content on the dose of mercury had a different character than in the case of maternal blood and liver (Table 1).

TEXT-FIG. 3. The effect of mercuric chloride given to the mother on the ^{75}Se content of foetuses (expressed as a percentage of the total amount of ^{75}Se retained in the pregnant rat). The same conditions as in the Text-fig. 2, but here the total ^{75}Se content in all foetuses from each rat is given and expressed as a percentage of the total amount of ^{75}Se retained in the whole pregnant rat.

All foetuses were found alive at the time when the pregnant rats were killed and no significant difference was observed in the weight of the placentae and foetuses in controls and in pregnant rats given various doses of mercuric chloride.

A similar effect of bivalent mercury was observed when mercuric acetate was given to pregnant rats and the ^{75}Se content in newborn animals was determined after delivery (Table 2). Even here, the administration of mercuric acetate resulted in an increase in the ^{75}Se retention by the mother ($P < 0.01$). In spite of the much higher ^{75}Se content in the mercury-treated mothers, the content in their newborn young was much lower than in those of mothers treated with selenite only ($P < 0.01$). No significant difference was observed in the body weight of the newborn in the two groups.

TABLE I
THE EFFECT OF MERCURIC CHLORIDE ADMINISTRATION ON THE DISTRIBUTION OF ^{75}Se IN THE PREGNANT RAT

Mercuric chloride ($\mu\text{mol/kg}$) <i>b.wt</i>	No.	^{75}Se content (% of injected dose)							
		Mothers			Organs with maternal and foetal components			Foetuses	
		Blood (1 ml)	Liver (whole organ)	Whole non-dissected uteri (with placentae and foetuses)	All placentae from each pregnant rat	One placenta (whole organ)	100 mg of placenta	All foetuses from each pregnant rat	One foetus
0	5	0.26 ± 0.01	5.93 ± 0.46	6.46 ± 0.74	1.25 ± 0.14	0.15 ± 0.02	0.030 ± 0.002	3.83 ± 0.47	0.457 ± 0.036
2.5	5	0.63 ± 0.04	9.01 ± 0.59	12.18 ± 0.63	3.54 ± 0.58	0.39 ± 0.05	0.090 ± 0.013	3.46 ± 0.22	0.384 ± 0.008
5.0	6	0.82 ± 0.03	13.37 ± 0.39	13.57 ± 0.64	3.84 ± 0.29	0.43 ± 0.04	0.091 ± 0.005	2.75 ± 0.22	0.304 ± 0.015
10.0	5	0.94 ± 0.07	15.22 ± 1.10	13.11 ± 0.30	4.29 ± 0.55	0.50 ± 0.08	0.109 ± 0.013	1.73 ± 0.08	0.199 ± 0.014
20.0	5	1.18 ± 0.16	16.73 ± 0.53	11.81 ± 0.34	3.56 ± 0.93	0.36 ± 0.03	0.079 ± 0.008	1.39 ± 0.12	0.139 ± 0.005
									0.0127 ± 0.0005 0.0114 ± 0.0001 0.0084 ± 0.0004 0.0069 ± 0.0007 0.0039 ± 0.0001

The same experimental conditions as in Text-fig. 2.

The administration of mercuric chloride to lactating rats had a similar effect on the passage of ^{75}Se across the mammary gland (Text-fig. 4). In spite of an increased ^{75}Se level in the blood ($P<0.01$) and blood plasma ($P<0.01$) of lactating rats treated with mercuric chloride and given [^{75}Se]selenite, the

TABLE 2
THE EFFECT OF MERCURIC ACETATE GIVEN DURING PREGNANCY
ON THE ^{75}Se CONTENT OF THE NEWBORN YOUNG

Group	⁷⁵ Se content (% of injected dose)			Average b.wt of sucklings (g)
	Mothers	Newborns		
		Whole litter	One suckling	
Se	45.23 ± 0.75	16.66 ± 1.00	1.83 ± 0.13	6.4 ± 0.3
Hg-Se	81.00 ± 3.34	5.11 ± 0.54	0.60 ± 0.03	6.2 ± 0.6

The radioisotope of ^{75}Se in the form of sodium selenite (100 $\mu\text{Ci/kg}$ b.wt corresponding to 3.6 $\mu\text{mol/kg}$ b.wt) injected subcutaneously into pregnant rats on the 21st day of pregnancy. Se: [^{75}Se]selenite only. Hg-Se: mercuric acetate (5 $\mu\text{mol/kg}$ b.wt) given subcutaneously 1 hr before the injection of [^{75}Se]selenite. Four pregnant rats in each group. The ^{75}Se content in the mothers and sucklings determined within 24 hr of delivery, 51 hr after the injection of ^{75}Se .

TEXT-FIG. 4. The effect of mercuric chloride on the passage of ^{75}Se into milk. [^{75}Se]selenite (200 $\mu\text{Ci/kg}$ b.wt corresponding to 1.3 $\mu\text{mol/kg}$ b.wt) given to lactating rats 15 to 16 days after delivery. C: controls, ^{75}Se only. Hg: mercuric chloride 5 $\mu\text{mol/kg}$ b.wt. Zn: zinc chloride 5 $\mu\text{mol/kg}$ b.wt. Seven lactating rats in each group.

^{75}Se concentration in the milk of these rats was lower ($P<0.01$) than in the milk of control rats treated with selenite only. The analogous injection of zinc chloride given to lactating rats apparently did not affect the ^{75}Se concentration in the blood and blood plasma and did not decrease the ^{75}Se level in the milk.

An increased ^{75}Se level was, in fact, found in the milk of these rats when compared with controls injected with [^{75}Se]selenite only ($P < 0.05$).

Mercuric chloride given to lactating rats markedly decreased the passage of ^{75}Se from the mother to the sucklings. As shown in Text-fig. 5, the administration of mercuric chloride resulted in an increased ^{75}Se retention in the maternal organism ($P < 0.01$), and in a simultaneous decrease in the ^{75}Se content in sucklings fed by these rats ($P < 0.01$). No similar effect of zinc chloride administration was observed.

TEXT-FIG. 5. The effect of mercuric chloride on the retention of ^{75}Se in lactating rats and on the passage of ^{75}Se into the sucklings. [^{75}Se]selenite ($250 \mu\text{Ci/kg}$ b.wt corresponding to $1.3 \mu\text{mol/kg}$ b.wt) given to lactating rats on the 8th day after delivery. C: controls, ^{75}Se only ($n = 6$). Hg: mercuric chloride $5 \mu\text{mol/kg}$ b.wt ($n = 11$). Zn: zinc chloride $5 \mu\text{mol/kg}$ b.wt ($n = 6$). Situation 24 hr after the ^{75}Se administration.

DISCUSSION

In spite of the fact that the passage of selenium compounds across the placenta and through the mammary gland has been studied previously by a number of authors (see e.g. Westfall, Stohlman & Smith, 1938; McConnell, 1948; Hadjimarkos, Bonhorst & Mattice, 1959; Cousins & Cairney, 1961; Burton *et al.*, 1962; Jones & Godwin, 1962, 1963; McConnell & Roth, 1964; Wright & Bell, 1964; Rosenfeld & Beath, 1964; Jacobsson, Oksanen & Hansson, 1965; Jacobsson & Oksanen, 1966; Hansson & Jacobsson, 1966) the exact nature of the processes connected with the transmission of selenium into foetuses and into milk does not yet seem to be fully elucidated. The experiments reported here confirmed that significant amounts of ^{75}Se can be detected in the foetuses and in the milk and sucklings of pregnant or lactating rats given [^{75}Se]selenite. Mercuric chloride or mercuric acetate administration had analogous effects on the transfer of ^{75}Se from the maternal organism into the foetuses and into the milk and sucklings which were not shared by zinc chloride. It seems, therefore, that the effect observed can be attributed to mercuric cations, though it is not possible to exclude the fact that salts of some other metals such as cadmium or thallium could act in a similar way. The mathematical analysis of the data given in Text-figs. 2 and 3 suggests that, under the condi-

tions of the experiment, mercury was not able to effect a complete block to the transfer of ^{75}Se into the foetuses. Thus, the passage of a certain proportion of ^{75}Se —given to the mother in the form of selenite—did not seem to be influenced by the administration of a mercuric salt, even in the highest of those doses which were used.

Two possibilities seem to deserve particular consideration in discussing the mechanisms by which mercury could affect the transmission of ^{75}Se from the maternal organism into the offspring: (a) mercury might act directly on the placenta and on the lactating mammary gland effecting a direct or indirect change in the local conditions which, in turn, may affect the passage of ^{75}Se through these organs; (b) the decreased passage of ^{75}Se into the offspring could result from a change in the chemical form of ^{75}Se in the blood of mercury-treated mothers, so that it could not pass as easily across the barrier represented by the placenta or mammary gland as under normal conditions.

Even if (a) cannot be excluded in full and could, perhaps, play some additional rôle, there would seem to be several points in favour of (b).

Mercuric compounds have been shown to have a similar effect on the transmission of selenium through such different organs as the placenta and the mammary gland and affected a decrease not only in the passage of ^{75}Se into the offspring but also in the excretion of ^{75}Se from the maternal organism in general. This was in good agreement with the effect of mercuric chloride on the excretion of ^{75}Se by non-pregnant and non-lactating rats described earlier (Pařízek *et al.*, 1967, 1969b; Levander & Argrett, 1969).

No serious damage was detected in the placentae (Pařízek, 1964) or lactating mammary glands (Pařízek *et al.*, 1969d) of rats injected even with the higher doses of mercuric chloride. This was in accordance with the fact that no foetal death was observed as a result of the administration of mercuric chloride to pregnant rats nor was there any significant difference between the body weight of foetuses and sucklings from mothers treated with mercuric salts and those from control animals.

The second possibility also seems to be supported by the results of previous experiments (Pařízek *et al.*, 1969a, d) when the administration of selenite to pregnant or lactating rats given a tracer dose of ^{203}Hg increased the retention of mercury in the whole maternal organism and the ^{203}Hg level in the maternal blood, but decreased the passage of ^{203}Hg from the mother to the foetuses and to the milk and sucklings. As reported elsewhere (Pařízek, Beneš, Ošťádalová, Babický, Beneš & Lener, 1969c) a highly increased amount of ^{203}Hg was found in the macromolecular fractions of the blood plasma of rats given selenite and mercuric salts. It has been suggested (Pařízek *et al.*, 1969c, d) that a reaction between selenite or some of its metabolites (perhaps bound to proteins) and mercury could explain the pronounced effect of selenium compounds on the toxicity of mercury (Pařízek & Ošťádalová, 1967) and also the altered metabolism of mercury and of selenium in animals receiving simultaneous injections of compounds of both of these elements. The same mechanism could well explain the increased retention of selenium and mercury in the maternal organism and the changed organ distribution of these elements, as well as their decreased passage into foetuses and into milk and sucklings.

The increased level of ^{75}Se in the blood of mothers treated with mercuric compounds was reflected in the maternal organs, while the foetal blood and organs showed the reverse trend. This seems to be of importance for the interpretation of the results on the ^{75}Se content in whole non-dissected uteri and in the placentae, where both maternal and foetal components were present in the samples analysed. Preliminary experiments revealed that in the mothers given mercuric chloride and $[\text{}^{75}\text{Se}]$ selenite, the radioactivity detected in the placentae could be markedly reduced by perfusing the maternal part of the placentae with saline. This and the comparison of ^{75}Se concentrations found in the placentae and in the maternal blood (Table 1) seem to suggest that a substantial proportion of ^{75}Se found in the placentae of mercury-treated rats could be present in bound form in the maternal blood retained in this organ. This does not exclude the possibility that mercuric salts could directly alter the binding of selenium in the placenta (and in other maternal organs) by a similar mechanism to that which appears to affect the level of ^{75}Se in the blood.

The fact that mercuric compounds seemed to be able to decrease the transmission of selenium to the offspring during the whole period of their nutritional dependence on the maternal organism could have some practical implications from the aspect of the provision of an adequate selenium supply for the developing organism. In the experiments reported here, only the acute effects of a single parenteral administration of inorganic salts of mercury were studied and ^{75}Se was given as sodium selenite. Further experiments should show whether the passage of organic compounds of selenium into the offspring could be affected by administration of mercuric compounds in a similar way and also whether a long-term exposure of pregnant or lactating mothers to very small amounts of inorganic or organic mercuric compounds, given in food or in water, could also decrease the selenium content in the offspring, particularly in animals with a longer period of gestation. It should also be possible to learn how far, in this way, the symptoms of selenium deficiency could be evoked in the newborn and suckling young of mothers exposed to small amounts of salts of certain metals (or, on the other hand, how far salts of these metals given during pregnancy and lactation could prevent the known teratogenic effects of toxic amounts of selenium compounds).

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