120 mg/mouse. Uterine ODC activity and polyamine concentrations were measured by methods previously described (Prakash, Schechter, Grove & Koch-Weser, 1978). Tissues were examined histologically after fixation in Bouin's solution and staining of serial sections with Haematoxylin-Eosin.

Uterine ODC activity was low (0.5–3.1 nmol g^{-1} h^{-1} total CO_2) in non-pregnant mice and during the first 5 days of gestation. It increased sharply between days 6 and 7 to reach a peak of 26.8 ± 4.6 (mean $\pm$ s.e. mean; $n = 8$) nmol g^{-1} h^{-1} total CO_2 on day 8, and declined significantly by days 9 and 10. Qualitatively similar changes were observed in the uterine putrescine and spermidine concentrations, but spermine levels remained unchanged. On day 8 of gestation, the levels of ODC activity and putrescine concentrations in individual uteri correlated significantly with the number of implantation sites. Treatment with α-DFMO from day 5 to day 9 of gestation abolished the increases in uterine ODC activity and putrescine and spermidine concentrations. Spermine concentrations were significantly elevated compared to untreated mice. Uteri from treated animals showed no signs of pregnancy when examined on day 18 of gestation. Histological examination of uteri from treated mice from the sixth gestational day onwards revealed decidualization and implantation to be normal but subsequent embryogenic development to be greatly retarded. As early as day 9, signs of resorption were evident. Decidual swellings in uteri from 16 day pregnant mice contained no embryos. Deciduomata became smaller and increasingly detached from the uterine endometrium, culminating in their total resorption/explusion between days 16 and 18.

These results provide direct proof of a fundamental role for ODC in a normal mammalian physiological process, namely, the early stage of murine embryogenesis.

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Decreased nephrotoxic effect of mercuric chloride on the regenerating kidneys

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Pretreatment with Hg^{2+} (Yoshikawa, 1970) or Cd^{2+} (Magos, Webb & Butler, 1974) decreased the sensitivity of the kidneys of rats to a following dose of sublimate. As both Hg^{2+} and Cd^{2+} are known to induce metallothionein, the protective effect could be explained by the induction of thionein and the competition of thionein for Hg^{2+} with vital binding sites. However, it was shown that Cd pretreatment increased both the amount of thionein and non-thionein bound mercury in the kidneys (Webb & Magos, 1976) and therefore, thionein synthesis alone cannot explain the protection.

Renotoxic agents which do not induce thionein offered a way to separate the effects of regeneration and thionein synthesis on this protective effect. Thus, the effects of pretreatment with sodium chromate (20 mg/kg, s.c.), uranyl acetate (4 mg/kg, s.c.), p-aminophenol (100 mg/kg, s.c.) and sodium maleate (500 mg/kg, s.c.) were studied on $HgCl_2$ nephrotoxicity.

Mercuric chloride (1.5 mg/kg, i.p.) was given 7 days after the administration of a renotoxic dose of one of the four compounds. The urinary excretion of alkaline phosphatase, glutamic oxalacetic transaminase and lactic dehydrogenase and renal histology were used to evaluate the damage. The results of these experiments suggested that the regenerating kidneys, irrespective whether the pretreatment was with a thionein inducer or other renotoxic agents, mitigated the nephrotoxicity of $HgCl_2$.

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Tributyl S,S,S-phosphotrithiolate (DEF), a potential tool in thermoregulation research

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A number of organophosphorous compounds depress core temperature transiently in rats, although not mice (Meeter & Wolthius, 1968), but the effect is complicated by excitatory effects. DEF (tributyl S,S,S-phosphotrithiolate) is an organophosphorous defoliant used in the preparation of cotton for harvesting, and in rats and mice it can be used to produce a pronounced and prolonged fall in core temperature at ambient temperatures below 30°C. Thus at 20°C the rectal temperature of ten female rats (250 g) given DEF 200 mg (637 μM)/kg, fell from 37.7 ± 0.14°C (mean ± s.e.) before i.p. injection to 32.9 ± 0.6°C at 2.5 h and 27.8 ± 0.9°C at 24 hours. Rectal temperature recovered slowly over the next 2 to 3 days. Mice showed more rapid falls to 23–25°C at 5–6 hours. The falls in temperature were dose-related over the range 20–200 mg/kg, the latter producing the maximal effect and being the approximate threshold for acute cholinergic organophosphorous symptoms.

Following DEF injection, exposure to 35°C ambient did not increase rectal temperature above that of solvent injected rats, all showing skin vasodilation and hypoactivity. At 30–32°C DEF produced few external symptoms other than a reduction in spontaneous movement. Reaction to external stimuli was normal, and the EEG activated readily from a state suggesting mild sedation. The tail vascular responses (as indicated by surface temperature) to heating and cooling of the body were normal, and restrained rats provided with additional heat in this way were able to maintain normal body temperatures by regulating tail blood flow.

Oxygen consumption measured by the method of Stock (1975) showed DEF to produce little reduction in Vo_2 at 30°C ambient (from 1.35 ± 0.18 to 1.18 ± 0.05 l kg^{-1} h^{-1}), but a large reduction at 15°C ambient (from 2.46 ± 0.06 to 1.01 ± 0.11 l kg^{-1} h^{-1}), effectively blocking the response to lowered environmental temperature. Oxygen consumption was measured in groups of 5 rats during the last 90 min of exposure to 15 or 30°C 4.05 h after injecting DEF (200 mg/kg), and mean rectal temperatures were 36.1 ± 0.3°C at 30°C and 27.8 ± 0.7°C at 15°C.

DEF pretreatment did not reduce the response to noradrenaline (1.5 mg/kg) given i.p. at 30°C 6 h later, the increases in oxygen consumption for 5 DEF and 5 solvent treated rats being 1.35 ± 0.18 and 1.13 ± 0.09 litre/kg above baseline respectively.

The ability of DEF treated animals to regulate core temperature at elevated ambient temperatures, the persistance of vascular tone and thermal reflexes, the normal thermogenic response to noradrenaline, and the lack of such a response to cold stress, suggests a blocking action at the CNS or adrenal level, and we are currently investigating these possibilities.

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