Mammary Transfer of ^{203}Hg from Mothers to Brains of Nursing Rats[1] (37102)

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The major routes of excretion of mercury by animals thus far studied are the kidney and gastrointestinal tract. However, lungs and mammary glands have also been known to excrete mercury (1). The mammary gland has been reported to contain radioactivity when mice were intravenously injected with $^{203}HgCl_2$ (2). Women (3, 4), guinea pigs[2] and rats (5–7) have also been reported to secrete milk containing mercury. To our knowledge, studies to determine the quantitative transfer of mercury from lactating mothers to the nursing animals have not been reported although Trenholm *et al.* found from indirect evidences, insignificant concentration of mercury in guinea pigs' milk.[2] Thus, our objectives were to determine quantitatively the transfer of ^{203}Hg from mother to nursing pup and to determine the distribution of the ^{203}Hg in various parts of maternal and pup brain.

Methods. Four litters of 8 pups each of Sprague–Dawley rats at 16 days of age were allowed to suckle their own mothers. Each mother during the 16th day of lactation received a single oral dose of 30 μCi of ^{203}Hg as CH_3HgCl dissolved in 1 ml of corn oil. The specific activity of this compound was 2.25 mCi/mg Hg. When the pups were 17, 18, 19, and 21 days of age, 2 from each litter were killed. Mothers were killed at the same time as their last 2 progeny. All were killed by over-etherization and bled by an incision in the heart. The brains were obtained and dissected into cerebrum, cerebellum, pons plus midbrain, medulla, hypothalamus and pituitary. Brain parts were weighed except for the pituitary from the pups. Radioactivities in brain parts were determined by means of a scintillation detector-counter using ^{203}Hg standards and corrected for physical decay and background activities. The brain parts were each counted to an accuracy of $\pm 2\%$ according to the statistical procedure of Loevinger and Berman (8).

Results and Discussion. No clinical symptoms were expected or found in the pups and mothers since the dose was only less than 1% of the dose required to produce neurological symptoms in adult rats (9). Five days after force-feeding the $CH_3{}^{203}HgCl$ to the mother rats, their brains contained 0.218% of the dose. The percentages of the dose in brain parts reflected the size of the part, thus cerebrum contained the highest and pituitary the lowest (Fig. 1). The concentration (% of dose/g tissue) appeared to be highest in the pituitary but it also had a greater variability than other brain tissues. This was due to the inaccuracy inherent in weighing pituitaries. The other brain parts ranged from an average of 0.117–0.167% of dose/g tissue (Fig. 2). Since the concentrations of labeled mercury in the brain parts excluding the pituitary differed only by 0.05 percentage units between the two extreme values, it is tempting to postulate that mercury is evenly distributed in brain tissues. The deposition of the radioactive mercury in the brain or individual brain parts is comparable to that found for rats force-fed the same mercury compound during gestation (10). It is also of interest to note that mer-

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[2] H. L. Trenholm, C. J. Paul, J. Baer and F. Iverson, Tox. and Appl. Pharmacol. **19**, 409 (1971).

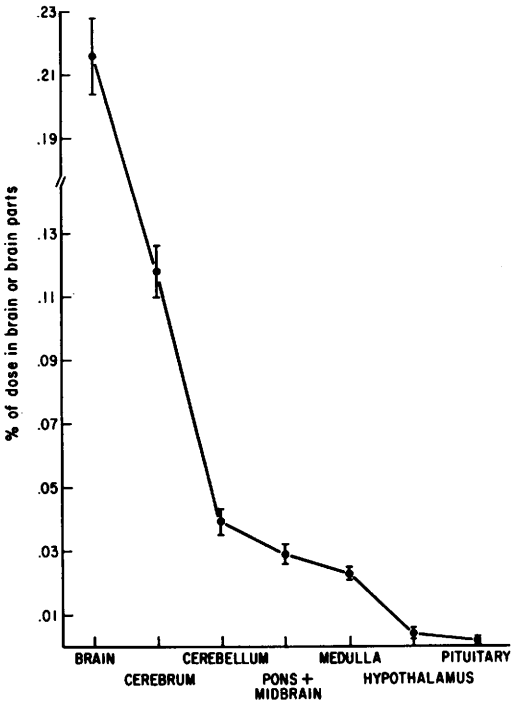

FIG. 1. Average ± SE percent of dose in brain or brain part of lactating rats 5 days after force-feeding $CH_3{}^{203}HgCl$.

cury has been found in brains of cats (12), dogs (13), monkeys (14), mice (15), and rabbits (14) when these animals were treated with mercurial compounds.

The transfer of mercury from mothers' milk to the pup must have started in less than a day after force-feeding the compound since radioactivities in pups' brain were detected after allowing the pup one day of suckling (Fig. 3). In the pup, just as it was in the mothers, labeled mercury was deposited in proportion to size of the brain part. The deposition in the brain and brain parts increased with each succeeding day of nursing. Furthermore, the concentration of mercury (% of dose/g tissue) in the brain and brain parts more than quadrupled from 1 day to 5 days of nursing (Fig. 4). However, the rate of deposition during the 5-day nursing period varied since the acceleration in concentration was markedly greater from 17th to 18th than from 18th to 19th day of suckling (Fig. 4).

Despite the fact that mercury was fed to the mother and deposited in the pup after a circuitous journey, the concentration was higher in the brain and brain parts of the pups. Five days after nursing, the concentration in the pups' brain was 2.3 times that in the mothers' brain (Fig. 2 vs Fig. 4). However, a greater difference appeared in the medulla wherein the pup had 2.8 times the concentration found in the mother. The brain tissues of the pup must, therefore, have a greater affinity or a slower biological half life for mercury than that of the mothers' brain since the quantity of mercury available for deposition in the pups' brain is most likely much less than that available for the mother.

Additional evidences to support this theory that neonatal brain affinity for mercury plays an important role and that mammary transfer plays a minor role, came from other experiments done in our laboratory. In these experiments, feeding 1 mg mercury/day as CH_3HgCl for as long as 7 days to lactating mothers produced neurological symptoms resembling Minamata disease in mothers but not in their suckling pups. Pups from the mercury-treated mothers were smaller in size at weaning but this most likely resulted more

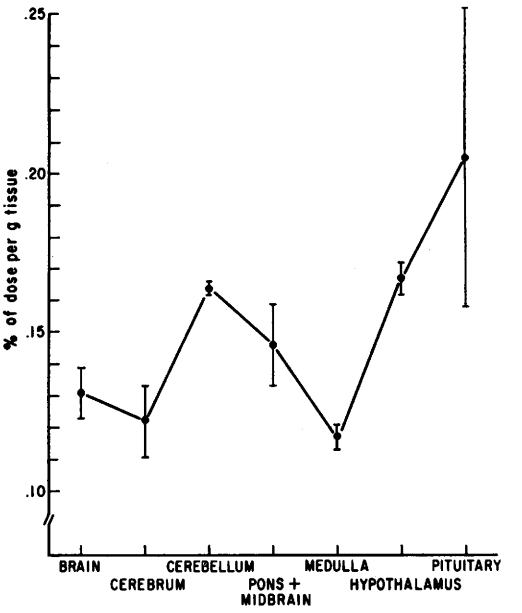

FIG. 2. Average ± SE percent of dose per gram brain or brain part of lactating rats 5 days after force-feeding $CH_3{}^{203}HgCl$.

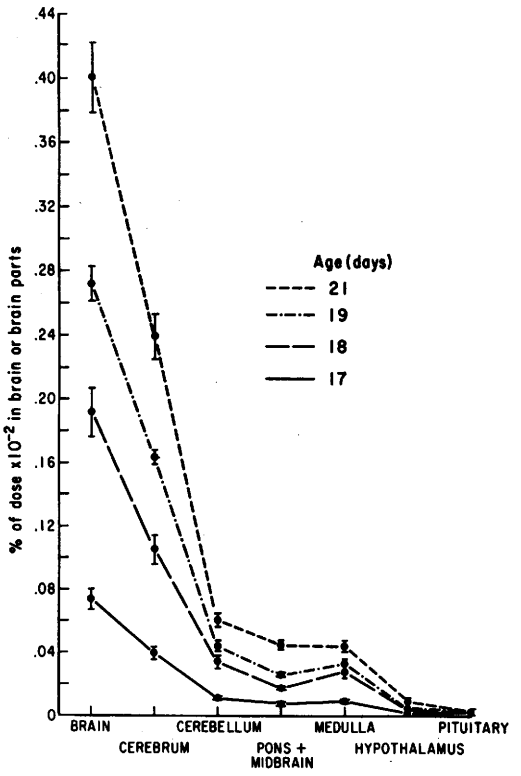

FIG. 3. Average ± SE percent of dose in brain or brain part of rat pups nursing from 1 to 5 days on lactating rats force-fed $CH_3{}^{203}HgCl$.

from the poor lactation and performance of the mothers than from mercury in the milk. In support of this contention, calculations revealed that a litter of pups weighing a total of 300 g will require 3 mg of mercury in the milk to develop neurotoxicity; this value is thus equivalent to an excretion rate of nearly 43% of the amount given the mother.

Nevertheless, neurological lesions could be produced in rat pups whose only source of mercury came from mothers' milk (7). The affinity of developing pup brains for mercury probably played a major role in producing the neurological disorder. Calculations revealed that it will require feeding about 17 to 25 mg of CH_3HgCl to mothers in order to produce neurological effects in nursing rats. This is based on the assumption that the oral dose of mercury required to produce neurological symptoms in neonatal rats is 1.0 mg/100 g body weight or less than half the dose for adults and on the basis that approximately 1% of that fed the mother is transferred to the pup during a 21-day lactation. This calculated dose approximates that found by Deshimaru to be effective in producing neurological lesions in nursing rats (7). The dose found to be effective was 14–16 mg spread over an 18-day period. This level of mercury also produced neurological symptoms as well as lesions in the mother, and is equivalent to about 2 times LD_{50} if the mercury were fed as a single dose.

Summary. At the 16th day of lactation, rats were force-fed a tracer dose of ^{203}Hg as $CH_3{}^{203}HgCl$ and allowed to continue to nurse their pups. After 1, 2, 3, and 5 days of nursing, representative pups were killed and brains obtained. The mother was also killed at the end of the study and its brain and those from the pups were separated into brain parts and radioactivities determined. In the mother, the concentrations of ^{203}Hg ranged from 0.117 in the medulla to 0.167 in the hypothalamus and 0.205% of dose/g tissue

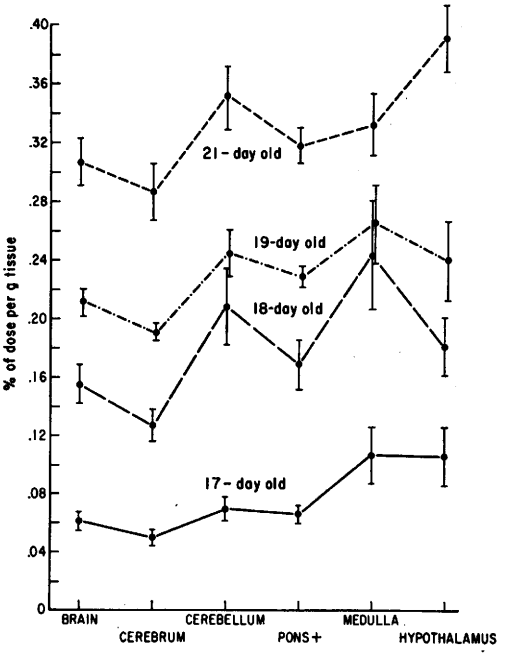

FIG. 4. Average ± SE percent of dose per gram brain or brain part of rat pups nursing from 1 to 5 days on lactating rats force-fed $CH_3{}^{203}HgCl$. Pons+ = pons plus midbrain.

in the pituitary. In the pups, the quantity of labeled mercury deposited in the brain or brain parts increased from 1 day to 5 days of suckling. The concentration (% of dose/g of brain or brain part) also increased with succeeding day of nursing so that at the end of 5 days the pup brain contained a higher concentration than their mothers' brain (0.307 vs 0.131). Correspondingly, pup brain parts contained greater concentrations of labeled mercury than their mothers' brain parts: Cerebrum, 0.287 vs 0.122; cerebellum, 0.353 vs 0.164; pons plus midbrain, 0.319 vs 0.146; medulla, 0.330 vs 0.117; and hypothalamus, 0.392 vs 0.167.

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