Hormonally mediated inheritance of acquired characteristics in Mongolian gerbils

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THE intrauterine position relative to members of the same or opposite sex that a rodent fetus occupies affects both its morphology and behaviour when adult[1–14]. Female fetuses that mature between males are androgenized by testosterone crossing fetal membranes[15,16], and their phenotypes as adults differ significantly from those of sisters that received less intrauterine exposure to exogenous testosterone[17–20]. We report here that adult female Mongolian gerbils that gestated between male fetuses produce litters containing a significantly greater proportion of sons than the litters produced by those that gestated between female fetuses. Consequently, daughters delivered by dams that gestated between male fetuses are more likely to have gestated between male fetuses and be androgenized *in utero* than are daughters of dams that gestated between female fetuses. Female gerbils thus tend to inherit the phenotype (either androgenized or not androgenized) of their respective mothers.

In Mongolian gerbils (*Meriones unguiculatus*), as in other rodents, the intrauterine position that a female occupies relative to the sex of its neighbours has a profound impact on its development. Female gerbil fetuses that gestate between two male fetuses (2M females) are exposed to higher levels of testosterone than those that mature between two female fetuses (2F females)[21]. The level of exposure to androgen *in utero* affects both the course of development and the reproductive life history of a female gerbil. For example, androgenized, 2M female gerbils achieve puberty at a significantly greater age than their 2F sisters[22] and, when adult, these late-maturing females have only half the lifetime fecundity of their early-maturing sisters[23].

Twenty-five 2M and 25 2F female gerbils were delivered by caesarian section on the last day of their normal gestation[24]. Each subject female and its littermates were then foster reared by a dam that had produced a litter vaginally on the same day[24].

We mated each of our 50 subject females with a sexually proven male when she was 67 days old. On the day of each vaginal delivery an experienced observer who was unaware of the intrauterine position that a dam had occupied as a fetus, examined the anogenital distance of each pup to determine its gender[25]. We found a significantly greater proportion of males in litters born to 2M females (57.1 ± 3.5%) than in litters born to 2F females (43.7 ± 4.8%; Student's *t*-test, $t = 2.73$, d.f. 48, $P < 0.01$). In addition, 2M females from litters that contained a majority of females ($N = 5$) produced a significantly greater percentage of sons throughout their reproductive lifetimes (53.9%) than 2F females from litters that contained a majority of males ($N = 4$; 44.7%; Mann–Whitney *U* test, $U = 4$, $P < 0.05$, one-tailed). Thus intrauterine position, rather than the sex ratio of litters at birth, predicted the proportion of males in litters. This is important because although the sex ratio of a litter might be influenced by the genotype of its dam, the positions of individual fetuses within uterine horns are random[25] and are unaffected by maternal genotype. The finding that a female's intrauterine position (rather than the sex ratio of her natal litter) predicts the sex bias of her lifetime reproductive effort is, therefore, not consistent with the hypothesis that differences in the genotype of 2M and 2F females are transmitted to their respective daughters and cause concordance in the sex bias of litters produced by mothers and daughters.

The probability that a fetus will develop between two fetuses of the same or opposite sex is affected by four variables: (1) the sex ratio; (2) size of the litter of which it is a member; and the distribution either (3) within or (4) between uterine horns of the male and female fetuses in a litter.

TABLE 1 Proportion of daughters born to 2M and 2F dams expected to gestate in 2M and 2F intrauterine positions

		Daughters	
		2M	2F
Mothers	2M	0.090	0.052
	2F	0.070	0.116

In previous studies, we determined the number of male and female fetuses carried in the left and right uterine horns of 253 caesarian-delivered gerbil dams on their last day of pregnancy[25], and the sex ratios of 265 vaginally delivered litters born in our colony[26]. The 253 caesarian-delivered dams gestated equal numbers of pups in each uterine horn, but carried a significantly greater proportion of male pups in their right uterine horns and female pups in their left uterine horns[25]. We observed no deviation from chance in the distribution of male and female pups within each uterine horn. The mean and distribution of the sex ratios of caesarian and vaginally delivered gerbil litters were not significantly different[26].

Using these data and the present observations of the sex ratios of our sample of 50 vaginally delivered litters, we computed the expected production of 2M and 2F daughters by both 2M and 2F dams (Table 1). We found the expected probability that the daughter of a 2M mother would be a 2M female was 1.73 times greater than the expected probability that she would be a 2F female. Conversely, the expected probability that the daughter of a 2F mother would be a 2M female was only 0.60 of the expected probability that she would be a 2F female.

The effect of intrauterine position on the sex ratios of litters produced by female gerbils shows that there is a form of hormonally mediated transmission of acquired characteristics. This produces concordance between Mongolian gerbil dams and their daughters in those phenotypic characteristics that are affected by level of exposure to testosterone early in life. □

Received 17 February; accepted 21 May 1993.

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ACKNOWLEDGEMENTS. We thank M. Bryden for technical assistance and D. Chiszar for his comments on earlier drafts. This research was funded by grants from the Natural Sciences and Engineering Research Council of Canada to M. M. C. and B. G. G.