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Letter to the Editor: Vitamin D in Pregnancy and the Infantile Hypercalcemic Syndrome

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G. M. Chan *et al.* (2) reported that huge doses of vitamin D given to pregnant rabbits "contributed to the development of supravalvular aortic lesions in the fetus which might lead to the infantile hypercalcemic syndrome." Others have made similar suggestions in the past (9). However, the doses of vitamin D employed in these experiments were enormous, and far in excess of the usual amounts taken by pregnant women. Chan *et al.* found aortic lesions in 8 of 31 rabbit fetuses whose mothers had received doses which can be calculated to be equivalent to 2,500–25,000 units/kg/day throughout pregnancy, but no such lesions in 13 fetuses where the dose was 250 units/kg/day. Friedman and Roberts (6) also used huge doses (25,000 units/kg/day) in their rabbit experiments, as did Gillman and Gilbert (7) in their studies on rats (80,000–400,000 units/kg/day).

Although it has been suggested that vitamin D toxicity or sensitivity during gestation is responsible for the severe form of the infantile hypercalcemic syndrome (see ref. 2), evidence to support this contention is far from conclusive (I refer here to the full-blown Williams syndrome (10) which includes cardiac lesions, nephrocalcinosis, a peculiar facies and mental retardation; it is apparent that the mild form of infantile hypercalcemic syndrome is related to generous intakes of vitamin D). The vast majority of such infants have not been exposed to large amounts of the vitamin during fetal life (5, 9). The only attempt to assess the question of vitamin sensitivity was reported by us several years ago (4). This involved the inadvertent administration of 10,000 units of vitamin D daily (equivalent to 150 units/kg) early in pregnancy to a mother who had already given birth to a child with the syndrome. The mother gave no evidence of hypersensitivity to the vitamin, and the infant born of this pregnancy showed no evidence of the syndrome, and remains in good health at age 8 yr. One cannot help wondering whether the animal experiments are germane to the human syndrome, because the doses employed are equivalent to about 1,000,000 units of the vitamin per day for the pregnant woman.

The cause of this syndrome remains unknown. Some years ago we (3) and others (1) reported that these infants were unable to deal efficiently with administered calcium loads. Lindquist (8) suggested that it represented a disorder of calcium homeostasis, and we (4) speculated that there was an abnormality in thyrocalcitonin production or release. Unfortunately, we were not in a position to test this hypothesis.

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