INTRODUCTION

Growth retardation is one of the well-known features of severe vitamin D deficiency in infants and young animals. It is generally assumed that skeletal growth retardation is due to sub-optimal concentrations of calcium and phosphorus in the extra-cellular fluids. The soft tissue growth retardation seen in severe vitamin D deficiency is attributed to anorexia induced by hypocalcemia. However, based upon their investigations in the rat, Steenbock and Herting (1955) proposed that vitamin D may have widespread effects on organic metabolism, of which growth is one manifestation. Recently nuclear receptor sites for 1,25 dihydroxy vitamin D$_3$ [1,25(OH)$_2$D$_3$] have been reported in such diverse tissues as intestine, bone, skeletal muscle, cardiac muscle, mammary tissue, skin, testis, ovary, pancreas and parathyroid gland (Haddad and Birge, 1975; Stumpf et al., 1979; Reichel et al., 1989). Even in the fetus, placenta, yolk sac, kidneys, bones and skin have nuclear receptor sites for 1,25 (OH)$_2$D$_3$ (Haussler, 1986). These observations suggest that vitamin D$_3$ may have a more diverse physiological role than hitherto believed to be. Moreover it has been observed that 1,25(OH)$_2$D$_3$ promotes calcium binding protein synthesis in not only intestinal mucosa (a known target organ) but also in many of the tissues named above (Mayer et al., 1984; Clemens et al., 1985). Based on these reports, Haussler et al. (1985) have proposed that vitamin D may have a fundamental role in the regulation of cellular growth and differentiation.
It is generally accepted that daily administration of 100 IU of vitamin D is sufficient to prevent rickets in infants. However clinical observations suggest that optimum growth may not occur when vitamin D intake of the infant is 100 IU per day. Stearns et al. (1936) compared the length of infants on vitamin D supplements varying from 60-130 to 1800 IU per day. Optimum growth was shown by infants receiving 340-600 IU of vitamin D per day. Both the lower and higher doses decreased growth significantly. These findings were subsequently confirmed by many workers (Jeans and Stearns, 1938; Slyker et al., 1937; Greer et al., 1981).

Severe vitamin D deficiency in pregnant women is known since long to produce congenital rickets (Maxwell et al., 1939; Liu et al., 1940; Snapper, 1956). However the possible role of vitamin D in reproduction including intrauterine growth of the fetus has attracted attention only recently. In chicks, vitamin D seems to be essential for proper egg hatchability (Henry and Norman, 1978) and for normal embryo development (Sunde et al., 1978).

Halloran and De Luca (1980a) have reported decreased fertility, decreased litter size and greater incidence of neonatal deaths in vitamin D deficient female rats. Administration of toxic dose of vitamin D (20,000 IU per day) was also found to impede fertilization if given before mating or produce degeneration and resorption of the implanted blastocyst if given in early pregnancy (Nebel and Ornstein, 1966). Toxic doses
of vitamin D in pregnant rats also produced growth retardation in the fetus (Ornoy et al., 1968) as well as structural alteration in the placenta (Nebel and Ornoy, 1971).

All these experimental studies have been performed either on vitamin D deficient animals where the results are clouded by the concurrent maternal malnutrition because of anorexia or in pregnant rats on toxic doses of vitamin D. Effect of administration of vitamin D in moderately high but non-toxic doses in pregnancy has not been studied. The apparent benefits of such a therapy on intrauterine and neonatal growth have been demonstrated in a few clinical studies by the author (Marya et al., 1981a; Marya et al., 1988) and others (Brooke et al., 1980; Maxwell et al., 1981). Studied by the author were conducted in Hindu women of Maryana, who in non-pregnant state, do not show any evidence of overt or occult vitamin D deficiency (Marya et al., 1981b). Administration of 6 lac units of vitamin D, in 7th and 8th months of pregnancy led to birth of infants with significantly greater birth weight (Marya et al., 1981a) and increase in certain other anthropometric measurements like length, head circumference and skinfold thickness (Marya et al., 1988). Administration of 1200 IU of vitamin D₃ per day, throughout the third trimester also improved the fetal birth weight but to a lesser extent (Marya et al., 1981a). Brooke et al. (1980) administered 1000 IU of vitamin D₃ per day to Asian immigrants in the U.K. during the third trimester of pregnancy and observed a significant decrease in the incidence of low birth weight babies. There was no significant difference between the mean birth weight in the supplemented and non-supplemented groups but a follow up study revealed significantly
greater weight and height of babies from the supplemented group at the age of 9 months and 12 months even though neither the mothers nor the babies received any vitamin D supplements postnatally (Brooke et al., 1981). The clinical studies suggest that administration of moderately high doses of vitamin D during pregnancy not only improves the intrauterine growth of the fetus but continues to confer the beneficial effect on the growth of the baby during the first year of life also. However community nutritional studies are somewhat handicapped in that even when the subjects are taken from the same socio-economic strata of the society, the environmental and nutritional conditions cannot be rigidly controlled. These difficulties assume greater importance in the studies on vitamin D where subtle differences in the solar exposure, cutaneous pigmentation and manner of dress may produce important effects on the cutaneous production of vitamin D. Hence confirmation of the results obtained in human subjects by experimental studies in the rat was considered imperative. This study was designed to elucidate the effects of vitamin D supplementation during pregnancy on the skeletal and soft tissue growth in the rat pups.