Chapter 5

Discussion

The results of this study indicated that DMPA caused an increase in milk secretion only in the lactating mother with suckled pups. This came from evidence that mammary gland alveoli in DMPA treated lactating rats were more distended with secretion than the control and correlated well with the acidophil cell population. Although, the prolactin cells could not be differentiated from GH-producing cells by the PAS-Orange-G method used in this study, but the mean body weight of the litters whose mother administered DMPA and the control rats at the same age were not differ nearly all periods of lactation. In addition, fluctuation of GH secretion in adult animals were very unlikely (Kipnis, Hertelendy and Machlin, 1969). Therefore, it was resonable to assume that the significant increment of acidophil cell population in their mother treated with DMPA should be due to the increase in prolactin-producing cells rather than the GH-producing cells. Regarding to the role of contraceptive steroids on stimulation of adrenohypophyseal pituitary prolactin cell population, it has been observed that treatment with estrogen or estrogen combined with progesterone in ovariectomized rats markedly stimulated prolactin

cells activity (Climenti and Vigiliis, 1967; Sar and Meites, 1968; Mc Leod, Abad and Edison, 1969; Amenomori Chen and Meites, 1970; Chen and Meites, 1970). The suggested mechanism of the response to the combination of estrogenic and progestational steroid is said to be via the depletion of PIF in the hypothalamus (Sar and Meites, 1968).

The precise mechanism of action of DMPA on milk secretion is not known. As the suggested the major influences of steroid hormone on milk secretion (Sar and Meites, 1968, Meite and Climens, 1972; Horrobin, 1973; Tindal, 1974), it is felt that DMPA cause an increase in milk secretion by either inhibiting PIF of the hypothalamus or by directly releasing prolactin. Either mechanism would be reflected in raising the level of prolactin after administration of DMPA. In view of the role of other hormones in the process of milk secretion both at the pituitary and the target organ level estimations, estimations of prolactin, estradiol and LH remains further studies.

The results from the study of the effect of DMPA administered to lactating mother on sexual characteristics of female litters indicated the significant delay the age of vaginal canalization and the age of the first exhibition of the regularity of the estrous cycle. These showed the possible evidence that DMPA was transmitted

to their litters through the ingested milk. In addition, by using radioactivity, it had been reported the occurence of synthetic steroid, lynestrenol, norethynodrel, ethynodrel diacetate in the milk when administered to the lactating women (Pincus, Bialy, Layne, Paniagua and Williums, 1966; Laumas, Malkani, Bhatnagar and Laumas, 1967; Molen, Hart and Wijmenga, 1969). This delay may probably be a direct effect of DMPA on the sexual maturation process but not on the body weight because there were no apparent evidences of body weight change between DMPA and control animals. It had been suggested that the onset of puberty was controlled through the hypothalamus (Benoit and Assenmacher, 1955; Donovan and Harris, 1955; Donovan and Werff, 1959; Tanner, 1967; Christian, 1968), and may somehow influenced the availability of biogenic monoamines since it had been repeatedly demonstrated a number of biogenic monoamines affected the hypothalamic regulation of FSH-RF, LH-RF and PIF secretion (Lippman, Leonardi, Ball and Coppola 1967; Kamberi, Mical and Porter, 1970; Kamberi, 1973; Kordon, 1973). With regard to the central effect of these monoamines on hypothalamic regulation of the onset of puberty, serotonin and melatonin injected to neonatal female rats significantly delay the age of vaginal canalization and prolong diestrous phase of the cycle (Vaughan and Vaughan, 1969; Vaughab, Vaughan and O'Steen, 1969; Chulakasem, 1974). Moreover, rats injected

daily with DMPA at dose 1.5 mg/100 gm. from the second post-natal day to maturity showed irreversible suppression of ovulation and corpora lutea formation (Logothelopoulos, Sharma and Kraicer, 1961). Furthermore, DMPA when administered daily subcutaneously at high dose, 2.5 or 5 mg. from the 15thto the 20thday of pregnancy to the mother in rats induced musculinization (female pseudo-hermaphrodites) of the rat fetus (Revez, Chappel and Gaudry, 1960; Falconi, Gardi, Bruni and Ercoli, 1961). Although results of a single contraceptive dose injection of DMPA into the mother on day 3 of lactation observed in this study did not show serious effect of litter's gonadal function as other workers who used much higher dose of DMPA, but the results of the delay-onset of puberty and sexual maturity were very impressing since these effects were very similar to the effect of melatonin and serotonin injection found by Vaughan and Vaughan (1969), Vaughab, Vaughan and O'Steen (1969) and Chulakasem (1974). Furthermore, the role of pineal gland or melatonin on delaying the onset of sexual maturity were well established in most mammalian species (Setnikar, Murmann and Magistretti 1960; Parlow, 1961; Motta, Fraschini and Martini, 1967; Fraschini, Coller and Martini, 1971). Whether DMPA has any influences on availability of brain alkylamines or other pineal hormones on the hypothalamic differentiation controlling the onset of adult gonadal function are remained

to determine. Finally, although no apparent effect of DMPA on male litters but the follow up study was limited to 60 days of age only. Whether DMPA has any influences on male gonadal function await further studies.