Changes in the Level of Plasma Cortisol, Progesterone and Total Testosterone in Developing Hairless Dogs

Shohkichi IWAMURA, Nobuo KOIZUMI, Yutaka MATSUBARA, Kazuhito HONJO, Katsuhiro FUKUTA, and Yoshikazu HIROTA

National Institute of Animal Health, 3-1-1 Kannondai, Tsukuba, Ibaraki 305, Japan

(Received 6 May 1992/Accepted 21 August 1992)

ABSTRACT. Changes in the levels of plasma cortisol, progesterone and total testosterone were examined in developing hairless and haired dogs. Cortisol levels in the hairless dogs seemed to be higher than those in haired dogs within the age of 4–5 weeks. No apparent changes were seen in the level of plasma progesterone between the groups of hairless females and haired females. Total testosterone levels in hairless males showed to be significantly lower than those in haired males at the age of 13–21 weeks.—KEY WORDS: cortisol, hairless dog, sex steroid.

J. Vet. Med. Sci. 54(6): 1217–1218, 1992

Corticosteroids and sex hormones including progesterone and testosterone have a potent effect on immune functions [6]. There is little information concerning the kinetics of plasma cortisol and sex hormones in hairless descendants derived from Mexican hairless dogs. In developing hairless dogs, histologically degenerative alterations in the thymus including atrophy, lymphocyte depletion, the replacement of parenchyma with adipose tissue and dysplasia of epithelial tissue have been reported [2–5]. The purpose of this study is to examine the changes of plasma cortisol, progesterone and total testosterone levels in developing hairless dogs.

Hairless (5 males and 5 females) and haired (4 males and 3 females) dogs born from 3 hairless and 1 haired female descendants derived from Mexican hairless dogs were used in this experiment. All of these animals have been maintained at the National Institute of Animal Health, Tsukuba, Japan. They are kept in conventional animal rooms with commercial diet (DS; Oriental Yeast Ltd., Tokyo) and water *ad libitium*. No abnormalities have been found by routine clinical tests including physical, virological, bacteriological and parasitological examinations as reported previously [5]. Blood samples were taken at 9–10 a.m. from the jugular vein of littermates of hairless and haired dogs at different ages ranging from 1 to 30 weeks at a 2- or 3-weeks interval. Plasma was separated by centrifugation at 4°C and stored at −20°C until used. Cortisol levels in unextracted plasma samples were measured by ^{125}I radioimmunoassay using a commercial kit (Eiken Immunochemical Lab., Tokyo). Separation of bound steroid from free one was performed by polyethylene glycol, as reported by Fujii and Okuda [1]. Progesterone levels were evaluated by the method of Nakamura *et al.* [7]. In brief, antiserum (0.1 m*l*) against P-3-CMO-BSA (Teikoku Hormone Mfg. Co., Ltd., Tokyo) was mixed with ether extracted plasma (0.1 m*l*) and ^{3}H-progesterone (0.1 m*l*), and incubated at 4°C overnight. Free steroid from bound one was separated by dextran-coated charcoal. Then, radioactivities of bound steroid were counted by a scintillation counter (Beckman Instruments, Inc., California). Total testosterone levels in unextracted plasma samples were measured by ^{125}I radioimmunoassay using a commercial kit (Nippon DPC Corp., Tokyo), as reported by Tanaka *et al.* [9]. The lower limit of sensitivity was 0.5 *ng*/m*l* for cortisol, 0.1 *ng*/m*l* for progesterone and 0.1 *ng*/m*l* for total testosterone, respectively. The intra- and interassay coefficients of variation were 7.2 and 11.7% for cortisol, 12.3 and 14.7% for progesterone, and 8.7 and 12.9% for total testosterone, respectively. Student's *t* test was employed to examine the difference between the two groups of hairless and haired dogs.

The changes in the levels of plasma cortisol, progesterone and total testosterone are shown in Figs. 1, 2 and 3, respectively. Plasma levels of cortisol in the morning (9–10 a.m.) reflected that there were no sexual differences of the female and the male in the two of haired and hairless dogs. Combined data of plasma cortisol in hairless dogs were significantly higher than those in haired dogs at 1 week of age ($p<0.05$) (Fig. 1). Cortisol levels in hairless dogs seemed to be higher than those in haired dogs until 4–5 weeks old. Progesterone levels were at approximately 0.5 *ng*/m*l* in both of hairless and haired females (Fig. 2). No apparent changes were seen in the level of plasma progesterone between the groups of hairless and haired dogs. Haired male dogs showed a gradual increase in plasma total testosterone levels from 11–12 weeks old, whereas hairless male dogs did not show any increase even at 18–21 weeks old (Fig. 3). Total testosterone levels in hairless males over 11–12 weeks old seemed to be lower than those in haired males. At 13–15 and 18–21 weeks old a significant difference between the groups of hairless males and haired males was shown ($p<0.01$).

Present study showed that 1) the level of plasma cortisol was higher in hairless dogs than in haired dogs, when they were younger than 1 month old; 2) no apparent change was seen in the kinetics of plasma progesterone between hairless females and haired females; 3) plasma total testosterone levels in hairless male dogs over 11 weeks old were lower than those in haired male dogs. Histological studies in hairless dogs more than 2 months old demonstrated that the thymus was atrophied and the population of lymphocytes was too sparse to demarcate the cortex and the medulla [2]. Hairless dogs also show a decrease in the relative proportion of T lymphocyte population in their peripheral bloods at 1 month old when tested in flow cytometry (unpublished data). Furthermore, the hairless dogs showed the reduced immune responses, when evaluated by IgG antibody responses against sheep red blood cells and *Brucella abortus* and by a delayed type

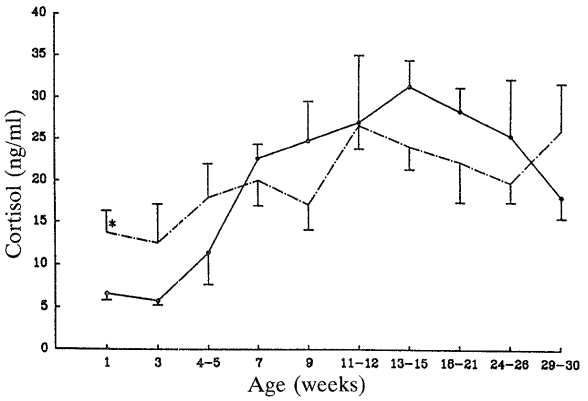

Fig. 1. Changes in the mean and standard error of the mean (S.E.M.) plasma cortisol levels in developing hairless (-·-) and haired (—) descendants derived from 4 littermates. *$p<0.05$, when compared to haired dogs.

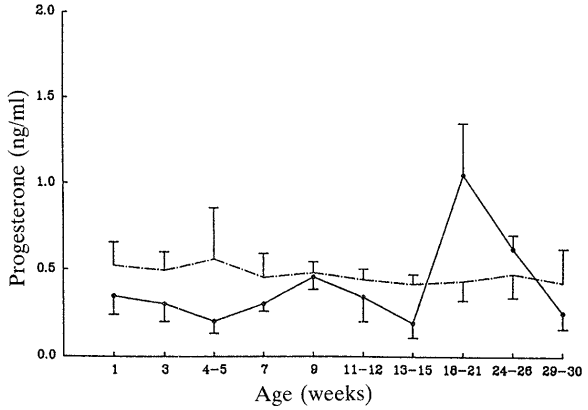

Fig. 2. Changes in the mean±S.E.M. plasma progesterone levels in developing hairless female (-·-) and haired female (—) descendants derived from 4 littermates.

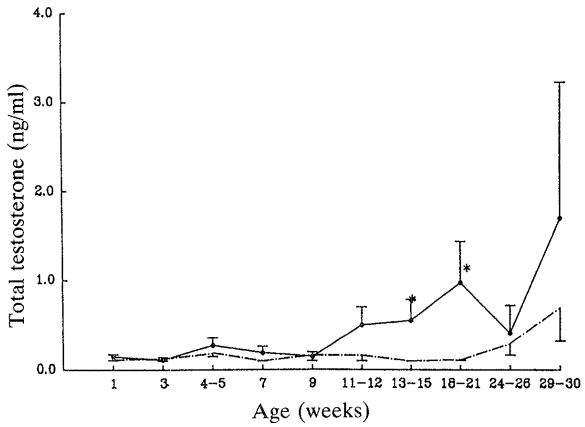

Fig. 3. Changes in the mean±S.E.M. plasma total testosterone levels in developing hairless male (-·-) and haired male (—) descendants derived from 4 littermates. *$p<0.01$, when compared to hairless.

skin reaction against human γ globulin [4]. The level of plasma cortisol in hairless dogs was higher than that in haired dogs at less than 1 month old. These reduced immunocompetence in developing hairless dogs may be associated with the kinetics in the cortisol levels within 1 month after birth.

Sex hormones, progesterone and total testosterone, as well as corticosteroids were well known to have immunosuppressive effects. Any of the increase of progesterone and the sign of puberty were not observed in hairless females and haired females before the age of 30 weeks. On the other hand, plasma total testosterone levels in hairless male dogs over 11 weeks old seemed lower than those in haired male dogs. Pierpaoli and Besedovky [8] demonstrated that nude mice showed diminished testosterone, progesterone and estradiol levels as compared to normal littermates of the same age and sex, suggesting that the thymus might have an essential role to establish hypothalamus-pituitary-gonadal axis. Thymic atrophy might be attributable to delay in an increase of total testosterone levels in hairless male dogs. Further detailed studies are needed to define the relationship between reproductive functions and degenerative alterations of lymphoid organs in developing hairless dogs.

ACKNOWLEDGEMENTS. This work was entrusted to the Laboratory of Immune Cytology, National Institute of Animal Health, Ministry of Agriculture, Forestry and Fisheries by the Science and Technology Agency, using the Special Coordination Fund for Promoting Science and Technology. We want to express our gratitude to Dr. Onodera, Faculty of Agriculture, The University of Tokyo, for his constructive criticism during the final preparation of this manuscript.

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