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Bone Vol. 18, No. 5
May 1996:443–450

Ovariectomy-Induced High Turnover in Cortical Bone Is Dependent on Pituitary Hormone in Rats

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The aim of this study is to examine the interrelationship of pituitary and ovarian hormone deficiency on the regulation of bone growth and bone formation rate. 48 female rats, at 3 months of age, were divided into age-matched intact control, hypophysectomized (HX), ovariectomized (OV), and HX + OV groups. Ten rats were killed at 3 months of age as baseline controls, and the rest of the animals were killed 5 weeks after surgery. Serum levels of osteocalcin and dynamic histomorphometry on the periosteal surface of the tibial shaft and fifth lumbar vertebrae were measured to evaluate systemic and local bone turnover. Tibial and fourth lumbar vertebral bone area, bone mineral content, and bone density were measured by dual-energy X-ray absorptiometry (DXA). Our results confirmed that OV increased and HX suppressed systemic and periosteal bone formation parameters in both bone sites, OV increased and HX suppressed the gain in bone size and bone mass. When OV rats were HX, the serum levels of osteocalcin and periosteal bone formation parameters of the tibial shaft and the fifth lumbar vertebrae were, however, depressed and did not differ from that of the HX alone. DXA results show that the effect of OV on bone size and bone mass is also abolished by HX. In conclusion, we have demonstrated that OV increases tibial and lumbar vertebral bone formation and bone growth and this effect is pituitary hormone dependent. (*Bone 18:443–450; 1996*)

Key Words: Bone formation; Hypophysectomy; Bone density; Osteoporosis; Estrogen deficiency.

Introduction

Postmenopausal osteoporosis is related to the loss of ovarian hormones following menopause. The exact mechanism by which ovarian hormone deficiency results in bone loss continues to be elusive. Ovarian hormone deficiency results in a high bone turnover with resorption exceeding formation, resulting in osteopenia in women.[10,26] Ovariectomy (OV) in the rat also results in an increase in bone turnover rate and significant loss of cancellous bone.[14,34] In cortical bone in the rat, a high bone turnover rate after OV results in an increase in periosteal bone formation and in the circumference of cortical bone.[28,29]

Although some direct actions of estrogen on bone and bone cells in culture have been described,[5,8] and estrogen receptors, albeit low in number, have convincingly been demonstrated in bone cells of humans and animals including rats,[15,30] it is not totally clear how estrogens exert their action on the skeleton. Part of this effect may be indirect, i.e., through intermediate hormones or cytokines.[12,27]

Pituitary hormones play an important role in regulating the activity of various target endocrine glands, including the ovary. Hypophysectomy (HX) in the female rat results in ovarian atrophy and estrogen deficiency.[23] Although HX also results in an estrogen deficiency and cancellous bone loss,[11,23,38] the mechanism of alteration of osteogenesis differs from ovarian hormone deficiency. Hypophysectomy of the rat results in suppression of longitudinal growth-dependent bone gain and a decrease in tissue-based cancellous bone turnover with lower bone formation relative to bone resorption. There is no significant effect on the surface-based bone turnover indicating that the bone turnover rate is not changed by HX, but the decrease in total bone turnover activity is due to the decrease in bone volume.[38] In cortical bone, HX results in a decrease in the periosteal bone formation activity and, thereby, a cessation of the cortical bone growth in radius without a significant change in the cortical bone mass.[3] Martinez et al.[17] observed that mineralization and collagen maturation per volume of cortical bone were greater in the HX than in the intact rats.

A number of studies attempted to compare the site-specific effect on skeleton. Cancellous alteration in association with aging, physical activity or OV develops more rapidly in long bones than in vertebra.[16,25,31,33,36] However, comparisons of cortical bone alteration between long bone and vertebra are few.[22,35]

The aims of the present study are to investigate the interrelationship of pituitary and ovarian hormone deficiency on cortical bone turnover rate using histomorphometry and also to investigate bone mass using dual X-ray absorptiometry and bone dry weight in both tibia and lumbar vertebra. We intend to determine whether OV-induced high bone turnover in the two sites is pituitary hormone dependent. Dynamic histomorphometry on the periosteal surface of the tibial shaft and fifth lumbar vertebra was compared in response to OV and/or HX.

Materials and Methods

Animal Preparation

48 female Sprague-Dawley rats with an average body weight of 255 g were purchased from the Taconic Farms (Germantown, NY). Hypophysectomy, OV, or HX + OV (HO) were done at Taconic Farms when the rats were 3 months of age. Upon arrival, 3 days postoperatively, until the end of the experiment, the HX

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8756-3282/96/$15.00
PII S8756-3282(96)00045-2

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Table 1. Effect of ovariectomy and hypophysectomy on serum levels of calcium, phosphate, IGF-I, osteocalcin, estradiol, and progesterone

Group	N	Calcium (mg/dL)	Phosphate (mg/dL)	IGF-I (ng/mL)	Osteocalcin (ng/mL)	Estradiol (pg/mL)	Progesterone (ng/mL)
Basal	10	11.3 ± 1.40	9.24 ± 1.38	1187 ± 253	29.7 ± 3.98	18.4 ± 5.6	6.97 ± 4.61
CON	9	10.5 ± 0.34[a]	9.12 ± 0.52	1236 ± 252	19.7 ± 2.31[a]	18.0 ± 4.8	8.32 ± 4.87
OV	10	10.7 ± 0.42[c]	9.60 ± 0.58[c]	1241 ± 246[c]	28.7 ± 3.75[b,c]	5.52 ± 0.66[a,b]	0.27 ± 8.0[a,b]
HX	11	9.75 ± 0.38[a,b]	6.89 ± 1.04[a,b]	77.0 ± 11.1[a,b]	11.5 ± 1.75[a,b]	12.4 ± 3.60[a,b,c]	1.45 ± 0.64[a,b,c]
HO	8	9.39 ± 0.34[a,b]	7.20 ± 1.33[a,b]	75.9 ± 14.4[a,b]	13.0 ± 2.71[a,b]	7.41 ± 1.57[a,b]	0.13 ± 0.04[a,b]
Two-factor ANOVA							
HX		0.0001	0.0001	0.0001	0.0001	0.02	0.0028
OV		NS	0.04	NS	0.0001	0.0012	0.001
Interaction		0.02	NS	NS	0.0003	NS	0.03

Values are mean ± SD. CON: control; OV: ovariectomy; HX: hypophysectomy; HO: HX + OV. CON, OV, HX, and HO groups are included for the two-factor ANOVA.
[a] Significantly different from the basal group, [b]significantly different from the CON group, and [c]significantly different from the HO group by multiple comparison with ANOVA ($p < 0.05$).

and HO rats were supplemented daily with hydrocortisone in the form of sodium succinate (100 μg/100 g) and thyroxine at 2 μg/100 g, subcutaneously. The purpose of physiological replacement doses of hydrocortisone and thyroxin are to maintain O_2 consumption and basic metabolism.[38] They were also given 3% sucrose water ad libitum and allowed free access to a standard pelleted chow diet (Rodent Laboratory chow 5001, Ralston Purina). All animals were housed singly in cages (25 × 20 × 18 cm^3) under local vivarium conditions (temperature 23.8°C and 12 h on/off light cycle) during the experimental period. Ten rats were killed at the age of 3 months as baseline controls. The rest of the rats were killed after 5 weeks of surgery. Animals were maintained according to the *NIH Guide for the Care and Use of Laboratory Animals,* and animal protocols were approved by the Laboratory Animal Care Committee of the Winthrop-University Hospital. The body weight of the rats was monitored weekly and their serum level of insulin-like growth factor-I (IGF-I) was measured at time of killing to assess the completeness of HX. Serum levels of estradiol and progesterone were measured to assess the completeness of OV.

Preparation of Specimens

All rats were labeled with 15 mg/kg of demeclocycline intraperitoneally (Sigma Chemical Co., St. Louis, MO) and 8 mg/kg of calcein subcutaneously (Sigma) at 10 days and 3 days, respectively, before killing. Rats were killed under CO_2 anesthesia and blood specimens were collected from the choroidal aorta and jugular vein for serum chemistries. The right tibia and fifth lumbar (L-5) vertebrae were removed and processed for methylmethacrylate embedding without decalcification.[3]

Histomorphometric Analysis

Cortical bone histomorphometric parameters of the tibial shaft and L-5 vertebrae were measured with a digitizing morphometry system and the nomenclature standard[19] as described previously.[3] Briefly, the total tissue area, cortical area, marrow area, periosteal single- and double-labeled perimeter, interlabeled width, and endocortical eroded perimeter were measured. These parameters were then used to calculate percent cortical area, percent marrow area, percent labeled surface, mineral apposition rate, and bone formation rate on the periosteum and percent eroded surface on the endosteum. The region measured in the L-5 cortical bone is in the central part skipping 0.4 mm from both proximal and distal sides of the growth plate.[35]

Tibial and L-4 Vertebral Dry Weight and Densitometry

The left tibia and L-4 vertebra were dissected free of soft tissue and extracted with ethanol and chloroform to remove water and

Table 2. Tibial dry weight, DXA bone area, bone mineral content (BMC), bone density (BMD), and static histomorphometry of tibial shafts of rats

			Dual X-ray absorptiometry (DXA)					Static histomorphometry	
Group	N	Tibial dry weight (mg)	Tibial area (cm^2)	Tibial BMC (mg)	Tibial BMD (mg/cm^2)	Metaphyseal BMD (mg/cm^2)	Diaphyseal BMD (mg/cm^2)	Cortical area (%)	Marrow area (%)
Basal	10	391 ± 24.4	1.29 ± 0.069	291 ± 21.7	225 ± 8.7	258 ± 22.6	218 ± 8.2	81.6 ± 2.71	18.3 ± 2.73
CON	9	464 ± 35.1[a]	1.40 ± 0.078[a]	362 ± 30.3[a]	258 ± 13.7[a]	310 ± 22.8[a]	238 ± 8.8[a]	83.8 ± 2.24	16.2 ± 2.16
OV	10	502 ± 45.1[a,b,c]	1.63 ± 0.033[a,b,c]	379 ± 33.2[a,c]	232 ± 8.5[b]	242 ± 19.2[b]	230 ± 8.3[a,b,c]	84.3 ± 2.38[a]	15.7 ± 2.39[a]
HX	11	386 ± 18.3[b]	1.25 ± 0.060[b]	295 ± 13.1[b]	236 ± 10.1[a,b]	258 ± 16.9[b]	227 ± 7.8[a,b]	82.4 ± 2.65	17.6 ± 2.64
HO	8	390 ± 32.6[b]	1.28 ± 0.085[b]	294 ± 25.4[b]	230 ± 8.7[b]	255 ± 14.2[b]	222 ± 8.5[b]	83.3 ± 2.44	16.7 ± 2.81
Two factor ANOVA									
HX		0.0001	0.001	0.0001	0.0007	0.002	0.002	NS	NS
OV		0.045	0.0002	NS	0.0001	0.0001	0.027	NS	NS
Interaction		NS	0.002	NS	0.007	0.0001	NS	NS	NS

Values are mean ± SD. CON: control; OV: ovariectomy; HX: hypophysectomy; HO: HX + OV. CON, OV, HX, and HO groups are included for the two-factor ANOVA.
[a] Versus basal group, [b]versus CON group, and [c]versus HO group by multiple comparison with ANOVA ($p < 0.05$).

Table 3. Fourth lumbar-(L-4) vertebral dry weight, DXA bone area, bone mineral content (BMC), bone mineral density (BMD), and the static histomorphometry of L-4 vertebrae of the rats

			Dual X-ray absorptiometry (DXA)			Static histomorphometry	
Group	N	L-4 dry weight (mg)	Bone area (cm^2)	BMC (mg)	BMD (mg/cm^2)	Cortical area (%)	Marrow area (%)
Basal	10	165.7 ± 10.2	0.447 ± 0.025	114 ± 9.1	256 ± 9.1	19.8 ± 3.37	80.2 ± 3.37
CON	9	201 ± 21.6[a]	0.506 ± 0.031[a]	139 ± 15.6[a]	275 ± 14.5[a]	21.2 ± 3.17	78.8 ± 3.17
OV	10	208 ± 30.0[a,c]	0.555 ± 0.062[a,b,c]	135 ± 19.0[a,c]	243 ± 13.0[a,b]	20.6 ± 4.03	79.4 ± 4.03
HX	11	162 ± 11.83[b]	0.434 ± 0.023[b]	109 ± 7.1[b]	251 ± 10.0[b]	20.7 ± 3.25	79.3 ± 3.25
HO	8	164 ± 19.6[b]	0.441 ± .046[b]	109 ± 15.5[b]	247 ± 10.9[b]	19.2 ± 4.64	80.8 ± 4.64
Two factor ANOVA							
HX		0.0001	0.0001	0.0003	0.02	NS	NS
OV		NS	0.048	NS	0.0001	NS	NS
Interaction		NS	NS	NS	0.001	NS	NS

Values are mean ± SD. CON: control; OV: ovariectomy; HX: hypophysectomy; HO: HX + OV. CON, OV, HX, and HO groups are included for the two-factor ANOVA.
[a] Versus the basal group, [b]versus CON group, and [c]versus HO group by multiple comparison with ANOVA ($p < 0.05$).

fat for dry weight analysis.[36] After the tibial and L-4 lumbar vertebral dry weight were measured, their bone area, mineral content (BMC), and bone mineral density (BMD) were determined utilizing a Hologic QDR-1000W dual-energy X-ray absorptiometer (DXA).[36] The tibial metaphysis in 7 mm lengths from 3 to 10 mm distal to the growth plate and tibial diaphysis in 10 mm lengths between the junction of the tibia and fibula were measured for BMC and BMD. The coefficient of variance (CV = 100 × SD/mean) for the repeated measurements from 10 rats was 2.9% for the BMC and 1.1% for the BMD in all regions measured.

Chemical Analysis

Serum calcium was measured by atomic absorption spectrophotometry (Perkin-Elmer 560). Inorganic phosphate was measured by the method of Fiske and Subbarow.[6] Serum levels of IGF-I were measured with a commercial RIA kit after acid-ethanol precipitation (Nichols Institute, San Juan Capistrano, CA).[37] Serum osteocalcin was measured by radioimmunoassay using goat anti-rat osteocalcin and donkey anti-goat IgG as antibodies (Biomedical Technologies, Stoughton, MA) based on the method of Gundberg et al.[9] Serum estradiol and progesterone were measured with commercial kits from Diagnostic Products Corp. (Los Angeles, CA).

Statistical Analysis

All data are presented mean and standard deviation (SD) in Tables 1, 2, and 3 or as the mean and standard error (SE) in Figures 4 and 5. The multiple comparisons between groups were done by Fisher's Protected Least Significant Difference Test. Serum data were converted to logarithm when two-factor analysis of variance (ANOVA) was used to examine the individual effect and interaction between treatments.[24] Statistical analyses including correlation coefficients were done using the StatView II program on a Macintosh computer. A significance level of $p < 0.05$ was used for all comparisons.

Results

Serum Levels of Calcium, Phosphate, IGF-I, Osteocalcin, Estradiol, and Progesterone

Table 1 shows that no significant difference in the serum levels of calcium, phosphate, and IGF-I were found between the OV and basal or age-matched control rats. Hypophysectomy with and without OV resulted in a significant decrease in these variables in comparison with either the basal or age-matched controls. While the OV rats had a significant increase in serum levels of osteocalcin as compared to the age-matched control rats, the HX rats with and without OV had a significant decrease in the serum level of osteocalcin. The serum levels of estradiol and proges-

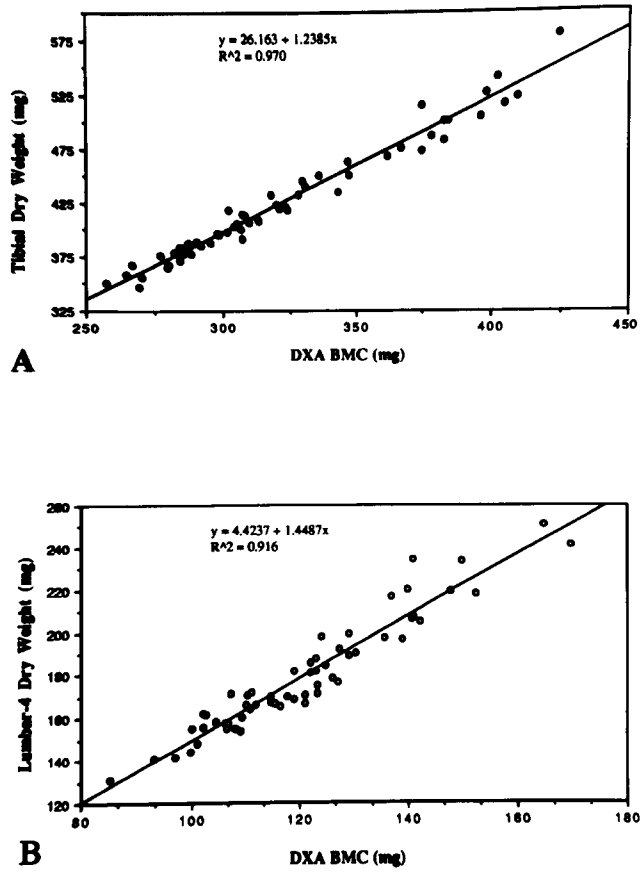

Figure 1. The correlation coefficient of tibial dry weight versus tibial bone mineral content (A) and of L-4 vertebral dry weight versus L-4 bone mineral content (B).

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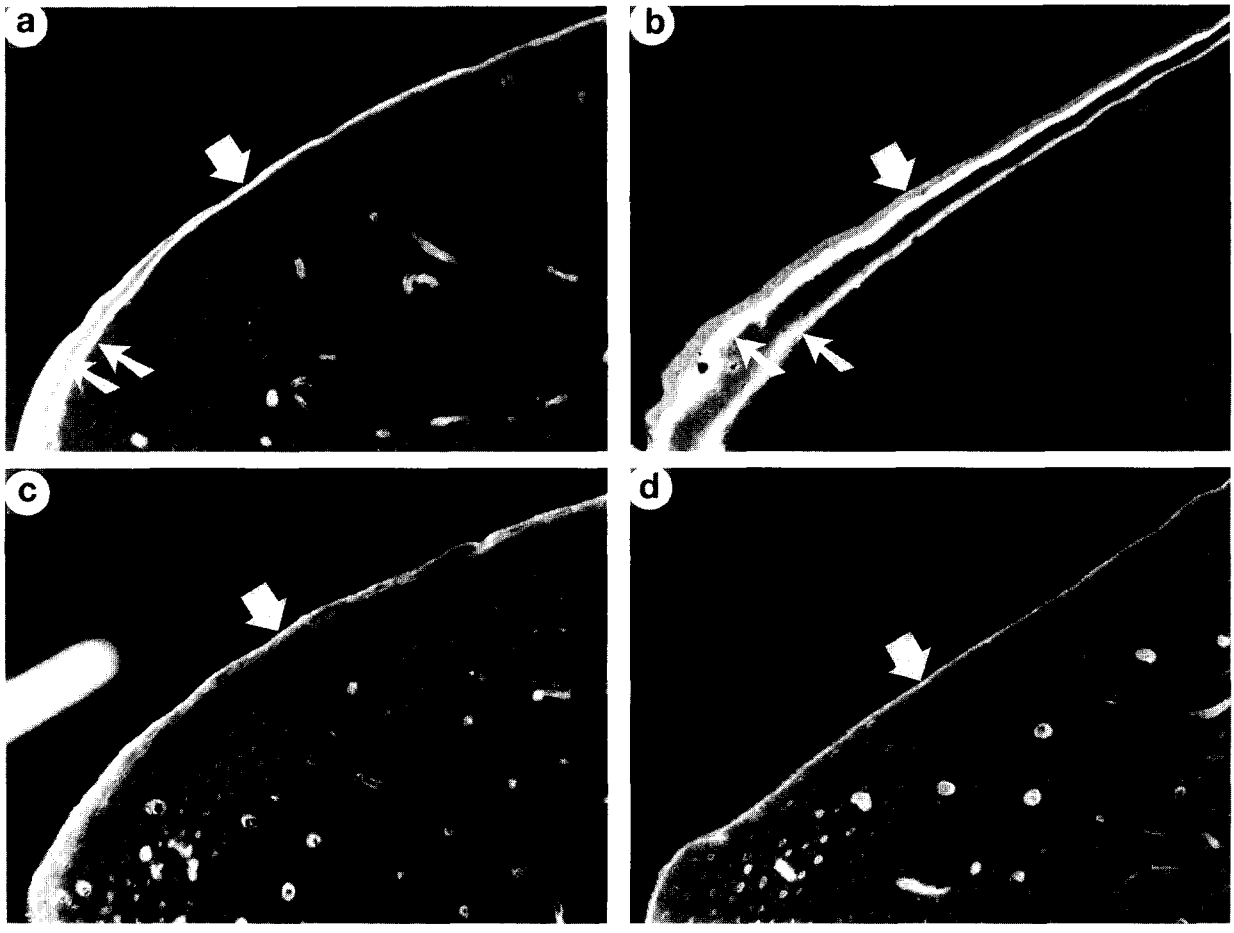

Figure 2. Fluorochrome label of demeclocycline and calcein (indicated by small arrow) on the periosteal surface (large arrow) of the tibial shaft: in control (a); ovariectomized (OV) (b); hypophysectomized (HX) (c); and HX + OV (HO) (d) rats. No label observed on the surface of HX and HO rats. Original magnification ×80.

terone were significantly lower in the OV, HX, and HO rats than in either the basal or age-matched control rats, but the levels of these variables were significantly lower in the OV and HO than in the HX groups.

Effects on Tibial and L-4 Vertebral Dry Weight, DXA Bone Area, BMC and BMD, and Static Histomorphometry of Cortical Bone

Although both the age-matched controls and OV rats had an increase with age in the tibial dry weight, DXA tibial area, and BMC as compared to the baseline control rats at 5 weeks, those increases (except tibial BMC) were significantly higher in the OV rats than in the age-matched control rats ($p < 0.05$) (**Table 2**). Conversely, the HX rats with and without OV did not show an increase in these variables and their levels did not differ from baseline controls. The effects of HX on tibial dry weight, DXA tibial area, and tibial BMC were found to be statistically significant by ANOVA. There was no significant difference in the percent cortical area and marrow area of the tibial shaft among the four experimental groups.

While the age-matched control rats had a significant increase with age in the BMD of the tibia, including metaphysis and diaphysis, OV or HX resulted in a significant suppression of gain in these variables ($p < 0.05$ by ANOVA). Significant differences were not found between HX and HO rats in any of the variables (Table 2).

The results from the L-4 vertebral dry weight determination, DXA bone area, BMC and BMD, and percent cortical and marrow area of the L-5 vertebrae from static histomorphometry were similar to the alteration of the tibia (**Table 3**). An exception is that the BMD of the L-4 vertebra was significantly lower in the OV than in the baseline control rats, whereas the BMD of the tibial diaphysis was higher and the metaphysis was lower than the baseline control rats (but this was not statistically significant).

The BMC in both tibiae and L-4 vertebrae were highly correlated with their respective bone dry weights (**Figure 1**). The correlation coefficient (r^2 value) of tibial dry weight versus the DXA BMC was 0.97 ($p < 0.0001$) and of L-4 vertebral dry weight versus the DXA BMC was 0.916 ($p < 0.0001$).

Effect on Histomorphometry of Tibial Shaft and L-5 Vertebrae

Ovariectomy resulted in a significant increase in the periosteal-labeled surface, mineral apposition rate, and bone formation date rate of the tibial shaft and L-5 vertebrae (**Figures 2 and 3**) as compared with the age-matched control rats ($p < 0.05$) (**Figures 4 and 5**). Hypophysectomy with and without OV resulted in a

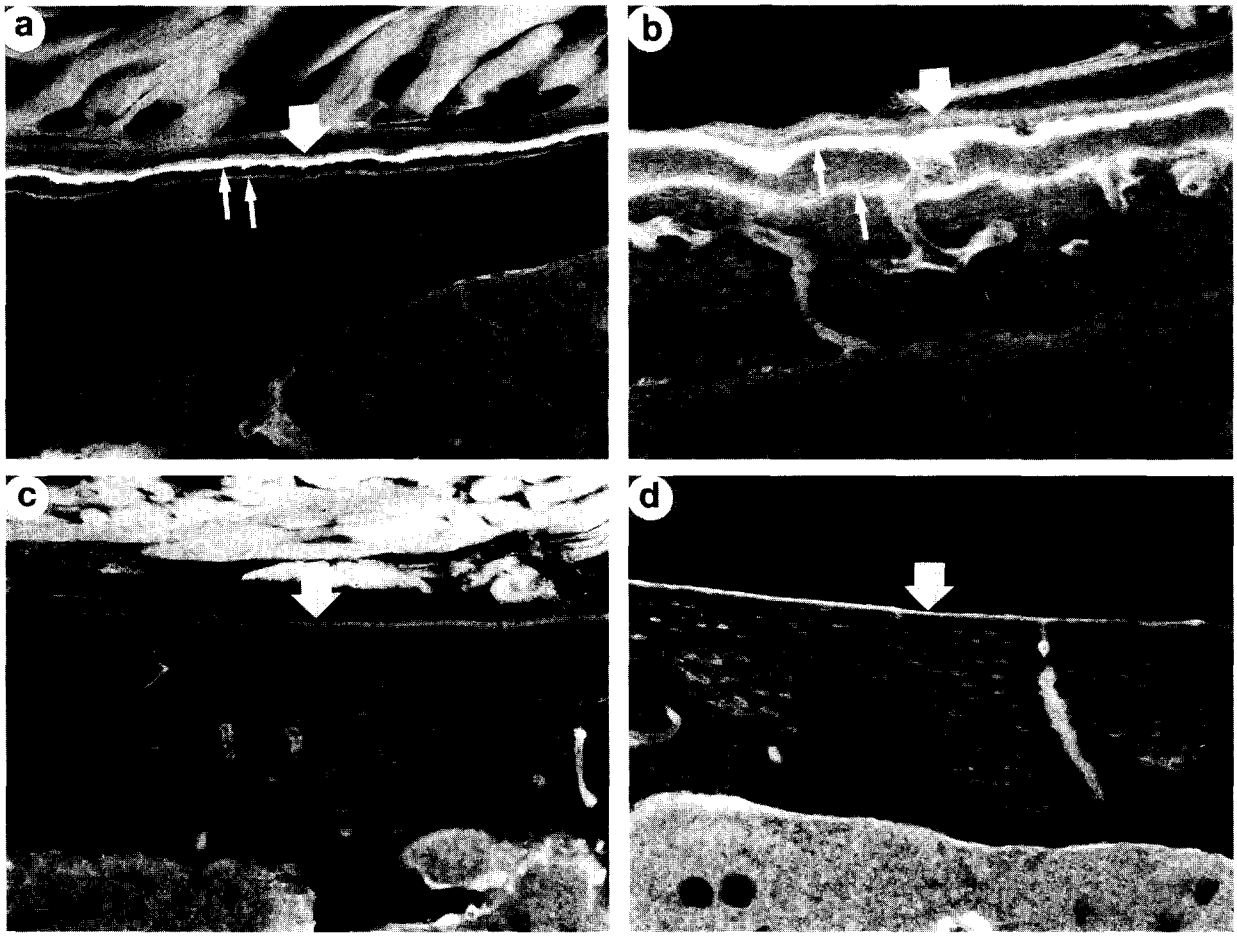

Figure 3. Fluorochrome label of demeclocycline and calcein (small arrow) on the periosteal surface (large arrow) of L-5 vertebra in: control (a); ovariectomized (OV) (b); hypophysectomized (HX) (c); and HX + OV (HO) (d) rats. No label observed on the surface of HX and HO rats. Original magnification ×80.

significant decrease in these variables. No significant difference was found in these bone formation parameters between the HX and HO rats. A greater eroded surface area of the tibial endosteum was observed in the OV, HX, and HO rats relative to the age-matched control rats.

Discussion

Our present study confirms that OV increases and HX suppresses periosteal bone formation of the tibia.[3,28,29] This increase in bone formation rate by OV and the suppression by HX are also observed in the periosteal surface of lumbar vertebrae. When the OV rat was HX, we observed that the bone formation rate in the periosteal surface was suppressed and did not differ from that of the HX group. These findings, along with the change in serum markers of osteocalcin indicate that the effect on the dynamic histomorphometry of cortical bone and the systemic bone turnover in the HO rat is due primarily to pituitary hormone deficiency.

Morphologically, OV results in an increase in cortical periosteal expansion (bone area by DXA) and the bone mass (BMC by DXA and bone dry weight) in the tibia and the L-4 vertebra. Since the marrow area of cortical bone is also enlarged and cancellous bone is decreased,[14,28,29,34] the BMD of the tibia and the L-4 vertebra are lower in the OV rat than in the age-matched control rat. Conversely, HX suppresses radial and longitudinal growth-associated bone gain in cortical and cancellous bones.[3,38] Thus, the BMD of the tibia and L-4 vertebra remained at baseline levels. When the OV rat was HX, the bone area and bone mineral content did not increase as observed in the HX group, suggesting that the effects of ovariectomy on bone growth and remodeling depend on the pituitary.

In the comparison of cortical bone formation between the tibia and L-5 vertebra, there is some difference in response to ovariectomy. An increase in the periosteal bone formation rate of the tibia by OV is attributed to the increase in both the labeled surface and mineral apposition rate, as observed by others.[28,29] However, the increase in bone formation rate in the periosteum of the L-5 vertebra by OV is attributed primarily to the increase in the mineral apposition rate without a significant alteration in the labeled perimeter. Ovariectomy increased endocortical eroded surface of the lumbar vertebra without a significant increase in that of the tibia, but HX suppressed the increase of eroded surface in lumbar vertebra, yet increased it in the tibia.[3] The increase in endocortical eroded surface by HX could be due to a decreased osteoclast surface and an interruption of ongoing resorption and formation, not permitting filling in of the resorption defect.[38] An increase in eroded surface by OV, however, is

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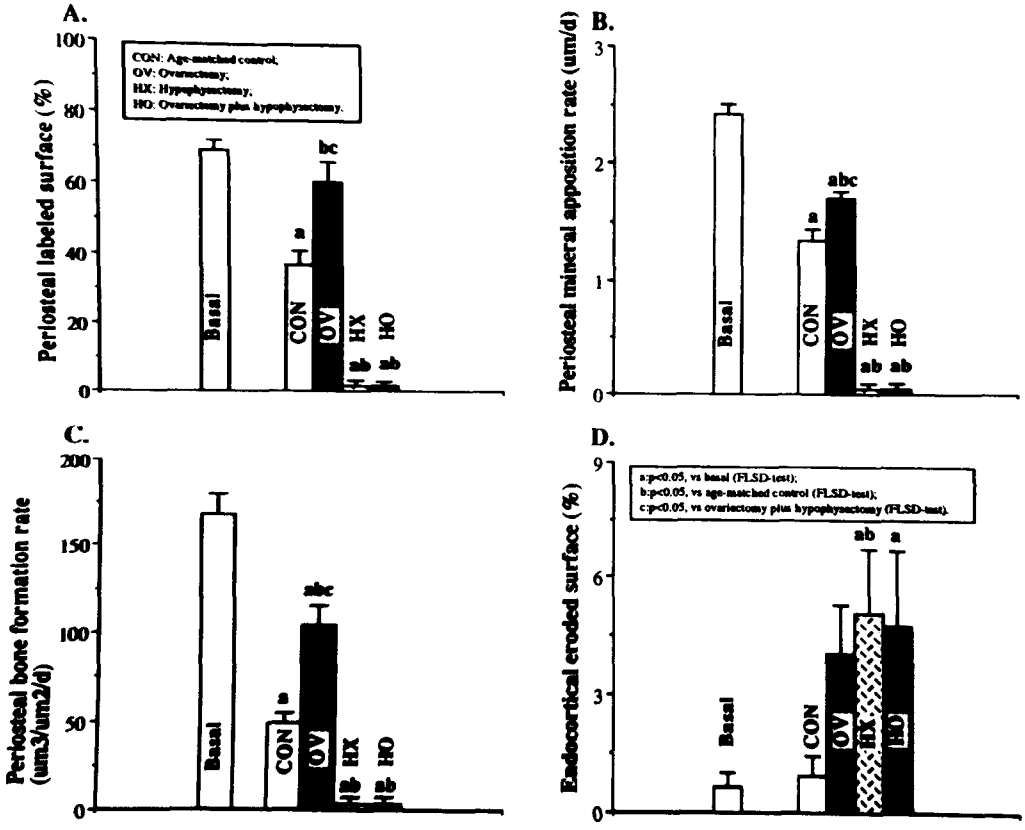

Figure 4. The periosteal-labeled surface, mineral apposition rate, bone formation rate, and endocortical eroded surface of the tibial shaft in basal, control (CON), ovariectomized (OV), hypophysectomized (HX), and HX + OV (HO) rats. (a) Versus basal, (b) versus CON, and (c) versus HO groups by multiple comparison with ANOVA ($p < 0.05$).

due to increased osteoclast surface and resorptive activity.[33,34] Recently, we observed that osteoclast surface decreased at 5 days after OV + HX (unpublished data) suggesting that the bone resorptive activity of the HO rat is decreased and the decrease is caused by HX.

The female HX rat lacks LH and FSH to stimulate the production of estrogen and progesterone, however, the atrophic ovary might still secrete insignificant amounts of the hormones.[23] This could explain why the serum levels of estrogen and progesterone were slightly but significantly higher in the HX rats than in the OV rats. Yet, these small differences in estrogen and progesterone levels do not have any effect on bone turnover. Although, both OV and HX result in estrogen deficiency, bone loss following HX is due to low bone turnover with less bone formation than bone resorption, which is different from the bone loss by OV, a high bone turnover rate with more resorption than bone formation. Obviously, bone loss following HX or HO is due to a lack of pituitary hormones rather than of estrogen deficiency. Consistent with this hypothesis, Bryant et al. observed that daily administration of ethynyl estradiol to the OV rat with HX could not prevent the bone loss caused by OV.[1] Thus, the beneficial effect of estrogen on preventing OV-induced bone loss is diminished by HX. Whether the beneficial effect of estrogen is pituitary hormone dependent needs further investigation.

It has been reported that hypophysectomy in the rat causes a rapid and substantial decrease in the estrogen receptor content of the target organs including the liver.[18] It is not known whether the estrogen receptor content of bone is decreased by pituitary hormone deficiency. Nevertheless, the decrease in bone formation by HX is not likely to be due to the decrease in the estrogen receptor alone, because the HX rats were supplemented with T_3 in the current study and supplementation with thyroid hormones alone increases the estrogen receptor concentration in the liver of female HX rats.[7]

Bone remodeling is regulated by systemic and local factors and by mechanical stimulation. The mechanism of the regulation is not fully understood. Numerous endocrine and autocrine factors have been recently shown to participate in modulating bone formation and bone resorption and many of them are directly or indirectly dependent on pituitary and/or ovarian hormones.[2,21] The high bone turnover induced by OV has been speculated to be related to a change in production and/or activity of cytokines.[12,27] The current finding that HX suppresses bone turnover rate and abolishes the high bone turnover induced by OV suggests that the factors modulating bone turnover are regulated by the pituitary gland.

Pituitary hormone deficiency suppresses both bone formation and resorption.[3,38] When HX suppresses OV-induced high bone turnover rate in HO rats, the net bone volume of the cancellous bone is decreased.[4] Lack of growth hormone is likely to be a major cause of the suppression since the anabolic effect of growth hormone plays an important role in bone growth and bone turnover.[13,20] Recently, our laboratory observed that ovine growth hormone administration to the HO rat increases bone formation rate, but only partially restores cortical and cancellous bone mass.[39] However, Wright et al.[32] observed that recombinant human growth hormone (GH) treatment in GH-deficient dwarf rats restored bone volume to levels found in normal con-

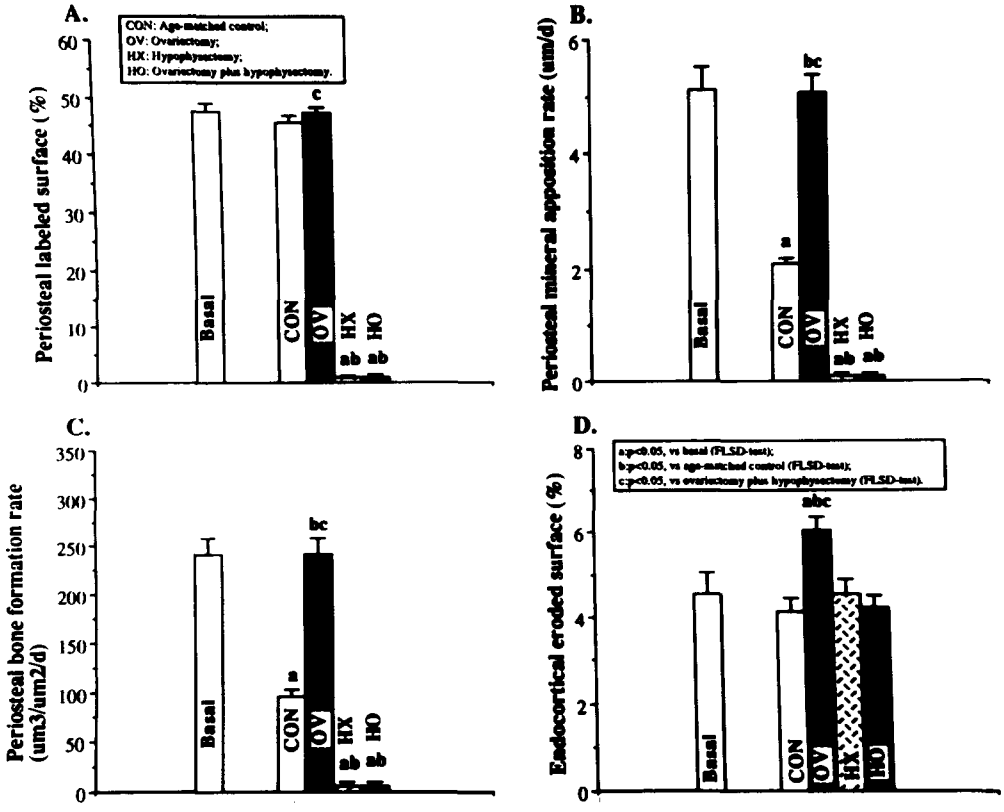

Figure 5. The periosteal-labeled surface, mineral apposition rate, bone formation rate, and endocortical eroded surface of the L-5 vertebra in basal, control (CON), ovariectomized (OV), hypophysectomized (HX), and HX + OV (HO) rats. (a) Versus basal, (b) versus CON, and (c) versus HO groups by multiple comparison with ANOVA ($p < 0.05$).

trol rats. This implies that other hormones besides growth hormone are involved in the regulatory process. Discovery of the hormones or factors responsible for high bone turnover induced by estrogen deficiency could be important in the prevention of postmenopausal osteoporosis. Hypophysectomized and ovariectomized rats could be used as an animal model to investigate the interrelationships among those factors in their regulation of bone turnover.

In summary, the present study shows that hypophysectomy plus ovariectomy results in a decrease in cortical bone gain of the tibial shaft and L-5 vertebrae without a bone loss in young rats at 5 weeks after surgery. The decrease in bone gain is due primarily to a suppression in modeling-dependent bone formation. A greater eroded surface of the tibial endosteum was found in the HX with and without OV rats relative to the age-matched control rats. Based on the alterations in cortical bone mass (bone dry weight and DXA) and bone turnover (serum marker and dynamic histomorphometry of cortical bone) after HX plus OV are the same as HX alone. Thus, we conclude that the ovariectomy-induced high turnover rate of cortical bone is dependent on the pituitary gland.

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Date Received: October 4, 1995
Date Revised: December 1, 1995
Date Accepted: January 15, 1996