Metabolism
Clinical and Experimental

VOL 45, NO 3 MARCH 1996

# Urinary Excretion of Testosterone and Estradiol in Chinese Men and Relationships With Serum Lipoprotein Concentrations

Linda S.M. Ooi, Nirmal S. Panesar, and John R.L. Masarei

**Urinary excretion of total and free testosterone and estradiol was measured in 46 healthy Chinese men, along with serum concentrations of total testosterone and estradiol and the calculated free (unbound) concentrations. Associations with serum concentrations of total, low-density lipoprotein (LDL), high-density lipoprotein-2 ($HDL_2$), and $HDL_3$ cholesterol, apolipoproteins (apos) A-I and B, and lipoprotein(a) [Lp(a)] were studied. Serum total and free testosterone concentrations were positively correlated with HDL and $HDL_2$ cholesterol and apo A-I. Serum total and free estradiol levels showed borderline-significant negative associations with total and LDL cholesterol levels. Among urinary variables, total estradiol excretion was negatively associated with apo B levels and showed borderline-significant associations with total and LDL cholesterol. Adjustment for potential confounders, including age, body mass index (BMI), and waist to hip ratio (WHR), strengthened the associations between urinary total estradiol and serum total cholesterol, LDL cholesterol, and apo B. Urinary free estradiol showed a significant correlation with $HDL_3$ cholesterol. Urinary excretion of total testosterone was significantly negatively associated with serum cholesterol and LDL cholesterol levels only after controlling for confounding variables. There were no significant associations between hormone variables and Lp(a) values. This study suggests that variation in sex hormone production accounts for some of the variation in serum lipid levels.**


ASSOCIATIONS between endogenous sex hormone and lipid concentrations are unclear. Studies have been inconsistent, and attempts to clarify the situation by measuring free (unbound) hormone levels have not been particularly helpful. Studies have suggested, for example, that there is a positive association between serum total testosterone and high-density lipoprotein (HDL) cholesterol levels in men.[1-2] Others have found a negative association[3] or no association.[4] Salivary testosterone levels, believed to be a good index of serum free testosterone levels, were reported to be positively associated with HDL cholesterol in men,[2] whereas others have reported a negative association[3] or no association[4] with free testosterone levels. Administration of androgens decreases HDL cholesterol levels,[5] although this may not be true for aromatizable androgens[6] or those without a 17α-alkyl group.[7] Furthermore, decreasing endogenous testosterone levels by administration of a long-acting gonadotropin-releasing hormone analog leads to an increase in HDL cholesterol concentrations.[8] In hypogonadal men, administration of androgens appears to increase levels of HDL cholesterol.[9] Serum estradiol concentrations have been reported to show both positive[4] and negative[3] associations with HDL cholesterol levels. It is therefore not clear what effects physiological levels of sex hormones have on serum lipid (particularly HDL cholesterol) levels within the sexes. This study was an attempt to obtain an answer in men.

To introduce a new approach to this problem, urinary excretion of testosterone and estradiol has been measured. Serum sex hormone concentrations show appreciable variation both episodically and diurnally. This variation might obscure associations. Because it is likely that 24-hour urinary excretion of sex hormones is independent of short-term fluctuations in plasma hormone levels, this was measured along with serum levels. In a further attempt to account for analytical and biological variation, which might also obscure associations, determinations were made on two occasions approximately 3 weeks apart and assays (except for sex hormone–binding globulin (SHBG) and gamma-glutamyl transferase (GGT) were performed in duplicate.

Testosterone and estradiol in the blood are largely bound

*From the Department of Chemical Pathology, The Chinese University of Hong Kong, Hong Kong.*
*Submitted May 26, 1994; accepted August 11, 1995.*
*Address reprint requests to Nirmal S. Panesar, PhD, Department of Chemical Pathology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N.T., Hong Kong.*

*0026-0495/96/4503-0001$03.00/0*

to SHBG. Variation in the concentration of SHBG will affect plasma concentrations of testosterone and estradiol without necessarily affecting concentrations of free (unbound) hormones, which are presumably biologically active. For this reason, attempts have been made to measure the concentration of free hormone directly or by calculation, or to derive an index of the concentration of free hormone by correcting the total concentration for the SHBG concentration. In some contexts, for example, when evaluating patients with the polycystic ovarian syndrome, derivation of a "free testosterone index" might be more diagnostically specific than the testosterone concentration. Failure to show definite relationships between sex hormone concentrations and lipid levels may be due to the effect of this binding to SHBG. It may be true also that calculation or measurement of the free hormone level or calculation of a free hormone index do not adequately reflect the influence of sex hormones on lipid metabolism. In this study, both total and free hormone levels were measured. Most serum testosterone in men is secreted by the gonads. Urinary free testosterone in men originates mainly from gonadal secretion rather than from peripheral transformation. Urinary conjugated testosterone in men is not uniquely a metabolite of testosterone; a substantial amount of adrenal androgens (mainly androstenedione) are transformed, metabolized, and excreted in urine as testosterone glucuronide. However, measurement of urinary total testosterone level is an index of testosterone production.[10] It has also been shown in animal studies that urinary free steroids are reliable indices of the secretory activity of the gonads after human chorionic gonadotropin administration. The testis secretes estrogenic hormones, but under normal conditions this accounts only for a small fraction of that present in the blood.[11] The major part of blood estradiol and estrone in normal men is derived from testosterone and androstenedione, respectively.[11] Estrogens are preferentially conjugated with glucuronic acid and sulfate and, together with other conjugates, are excreted in the urine.[12]

A number of other factors are believed to be important sources of variation in serum lipid levels. Among these are obesity, usually measured as the BMI, and regional adiposity, conveniently measured as the WHR. Triglyceride levels are associated positively with BMI and negatively with HDL cholesterol levels, and some investigators have reported significant relationships (negative) between WHR and HDL cholesterol levels.[13] GGT activity was also measured as a screening procedure for substantial alcohol consumption, which is known to increase HDL cholesterol and triglyceride concentrations in serum.

## SUBJECTS AND METHODS

Forty-six healthy Chinese men aged 19 to 53 years were studied. They were laboratory and academic staff who responded to an advertisement and stated that they were healthy. No subject was taking any antifungus/antiandrogen medication or engaging in any vigorous physical activity at the time of examination. Fasting blood samples were drawn in the morning between 8:30 and 10:00 AM, and 24-hour urine collections were made over a period to include the blood sampling time. Blood was collected by venipuncture without anticoagulant and allowed to clot over a period of 60 minutes. Serum was separated at 1,500 × *g* for 5 minutes at 4°C. Serum was placed in aliquots into screw-top plastic vials, snap-frozen in liquid nitrogen, and stored at −70°C. Urine was collected into plastic bottles without preservative. At the end of the collection, samples were dispensed in 8-mL volumes into glass tubes, frozen, and stored at −70°C. To reduce the effect of biological variation, these samplings were made on two occasions approximately 3 weeks apart. To reduce the contribution of analytical variation, assays for all variables except SHBG and GGT were performed in duplicate.

Adiposity was expressed as BMI (weight in kilograms divided by height in meters squared) and regional fat distribution as the WHR.[14] A history was recorded of the usual weekly consumption (number of standard drinks) of alcohol and the usual daily consumption of cigarettes.

Biochemical measurements were made as follows. Serum total cholesterol and triglyceride levels were measured enzymatically on a Cobas Bio analyzer (Roche Diagnostics, MontClair, NJ) with reagents from Roche Diagnostic System (Basel, Switzerland). The intrabatch coefficient of variation (CV) for cholesterol was 1.5% and for triglyceride 1.9%. Interbatch CVs were 6% and 4%, respectively. HDL cholesterol and its major subfractions, $HDL_2$ and $HDL_3$ cholesterol, were estimated by measuring cholesterol level in the supernatant after dual precipitation with $MgCl_2$/dextran sulfate.[15] Reagents were the same as above, except that the assay was calibrated with low-level cholesterol standards (0.54, 1.08, and 2.17 mmol/L) prepared from commercial standards by dilution with 40 g/L bovine serum albumin solution. The intrabatch CV for $HDL_3$ cholesterol was 1.6%, and the interbatch CV was 8.4%. Very–low-density and low-density lipoprotein (LDL) cholesterol levels were calculated from the Friedewald formula.[16] Apolipoprotein (apo) A-I and apo B levels were measured immunonephelometrically using the Beckman Array analyzer (Beckman Instruments, Brea, CA) using reagents also from Beckman. The assays were calibrated with the Beckman calibrator (lot M105114), and internal quality control was performed with control serum from Beckman (lot M109227). The within-run CV was 5% and between-run CV 8%. Lipoprotein(a) [Lp(a)] level was measured immunoturbidimetrically by the SPQ system (Incstar, Stillwater, MN) on a Cobas Bio analyzer. The limit of detection was 55 mg/L, and within- and between-batch CVs were 3% and 9%, respectively. Serum albumin concentration was measured by a bromcresol purple dye–binding procedure on a Dimension AR analyzer (Dupont Medical Products, Wilmington, DE). Creatinine level was measured by an end-point Jaffe reaction procedure on the Dimension AR analyzer. Creatinine excretions were measured as an index of completeness of urine collection.

Because of the need to detect the low levels of estradiol present in the serum of men and to measure urinary free testosterone and estradiol levels, optimized assays were developed in our laboratory. Antitestosterone antiserum raised in rabbit to testosterone-3-(*o*-carboxymethyl)oxime–bovine serum albumin conjugate was a gift from the Division of Steroid Endocrinology, Leeds University, England. Antiserum to 17β-estradiol was purchased from the Shanghai Institute of Endocrinology, Shanghai, China. [1,2,6,7-$^3$H]-Testosterone and [2,4,6,7,16,17-$^3$H]-estradiol were obtained from Amersham International, Amersham, England. Urine samples were centrifuged at 1,500 × *g* for 5 minutes before assay. Samples were extracted with diethyl ether. For assay of testosterone, serum samples were diluted 1:10 with 0.9% saline before extraction.

Dextran-coated charcoal containing activated charcoal (0.5% wt/vol; Sigma Chemical, St Louis, MO) and dextran (0.05% wt/vol; BDH Chemicals, Poole, England) was used to remove excess free steroids during the radioimmunoassay. The limit of detection for testosterone was 347 pmol/L and for estradiol 73 pmol/L. This was well below what was needed for the assay of these hormones in men. Within-run CVs were 8% and 5% for testosterone and estradiol, respectively, and between-run CVs were 8% and 10%, respectively. To measure urinary total testosterone and estradiol levels, the conjugates were hydrolyzed with acid. The "non-specific non-specificity" associated with this procedure was overcome by diluting the hydrolysates 1:25 with charcoal-stripped urine before extraction.[17] Serum concentrations of SHBG were measured by a two-site immunoradiometric assay (IRMA Count for SHBG; DPC, Llanberis, UK).

Calculations of free concentrations of testosterone and estradiol in serum were made as described by Södergärd et al.[18] The procedure uses the relevant dissociation constants and serum concentrations of SHBG and albumin.

### *Statistical Methods*

Associations between variables were assessed by calculating Pearson's correlation coefficients. Variables showing skewed distributions (triglyceride and each of the urinary hormone excretion variables) were transformed by taking the log values before statistical analysis. For calculations involving Lp(a), values were transformed by taking the reciprocals. Stepwise multiple regression was performed to study independent associations between hormones and lipids.

## RESULTS

Anthropometric and biochemical characteristics of the subjects are shown in Tables 1 and 2. It was thought that correcting hormone excretions by the ratio of daily excretion of hormone and creatinine might reduce the variation between the two collections, but this did not prove to be the case. Analysis of the data with the corrected variables did not provide results that differed meaningfully from the uncorrected data, so only results using uncorrected variables are shown.

### *Simple Associations Between Sex Hormones and Lipoprotein Variables*

Simple correlation coefficients between sex hormones and lipoproteins are shown in Table 3. A number of statistically significant associations were identified, most notably positive associations between serum total and free testosterone and HDL and $HDL_2$ cholesterol and apo A-I. There were also significant positive associations between serum total and free estradiol and $HDL_2$ cholesterol. There were borderline-significant negative associations between serum total and free estradiol and total and LDL cholesterol. Serum total and free testosterone and estradiol were all negatively associated with serum triglyceride concentrations. Among urine variables, total estradiol excretion showed a significant negative association with apo B and borderline-significant associations with total and LDL cholesterol levels. Urinary free estradiol showed a weak positive association with $HDL_3$ cholesterol. There were no significant associations between hormone variables and transformed (reciprocal) Lp(a) values. The same was true when the associations were tested using the nonparametric Spearman rank correlation (coefficients not shown).

**Table 1. Subject Characteristics (N = 46)**

| Variable | Mean ± SEM | Range |
|---|---|---|
| Age (yr) | 33 ± 1 | 19-53 |
| BMI (kg/m²) | 22.6 ± 0.37 | 17.6-30.2 |
| WHR | 0.85 ± 0.009 | 0.72-1.00 |
| Serum albumin (g/L) | 47.4 ± 0.33 | 42.4-52.5 |
| GGT (U/L) | 18.1* | 2.5-60 |
| Urinary creatinine (mmol/L) | 13.65 ± 0.35 | 8.58-19.34 |

*GGT levels were markedly positively skewed.

**Table 2. Serum Lipid and Lipoprotein Values (N = 46)**

| Variable | Mean ± SEM | Range |
|---|---|---|
| Cholesterol (mmol/L) | 4.79 ± 0.15 | 2.8-7.0 |
| Triglyceride (mmol/L) | 1.3 ± 0.11 | 0.49-3.4 |
| LDL cholesterol (mmol/L) | 2.9 ± 0.14 | 1.23-4.95 |
| HDL cholesterol (mmol/L) | 1.29 ± 0.04 | 0.84-2.02 |
| $HDL_2$ cholesterol (mmol/L) | 0.38 ± 0.031 | 0.13-0.96 |
| $HDL_3$ cholesterol (mmol/L) | 0.92 ± 0.023 | 0.63-1.25 |
| Apo A-I (g/L) | 1.45 ± 0.029 | 1.06-1.84 |
| Apo B (g/L) | 1.36 ± 0.029 | 0.98-1.79 |
| Lp(a) (mg/L) | 168.2* | 55-868 |

*Lp(a) concentrations were markedly positively skewed.

### *Multivariate Associations Between Sex Hormones and Lipoprotein Variables*

These associations were reexamined for the effects of several potential confounders, ie, age, BMI, and WHR, by stepwise multiple regression analysis. Alcohol consumption was low in this sample, and although GGT showed correlations with the anthropometric variables BMI, WHR, and age, and all the lipoprotein-lipid fractions, it did not correlate with the latter after stepwise regression analysis.

After stepwise multiple regression against the independent variables (Table 4), borderline-significant associations between total cholesterol and serum total and free estradiol became nonsignificant. However, the negative borderline-significant association with urinary total estradiol became stronger, ie, urinary total estradiol accounts significantly for further variation in cholesterol level when BMI is in the equation. Similar results were obtained for LDL cholesterol and for apo B. Whereas total urinary testosterone excretion showed no significant simple associations with any of the lipid variables, on multivariate analysis it was associated negatively with LDL cholesterol and weakly with total cholesterol. For triglyceride, significant associations with serum total and free testosterone and estradiol remained, again with BMI accounting significantly for much of the variation. For HDL cholesterol, significant associations with serum total and free testosterone persisted, with no other variable significant in the equation. Associations with serum total and free estradiol remained nonsignificant. For $HDL_2$ cholesterol, associations with total and free

**Table 3. Pearson Correlation Coefficients and Probabilities for the Association Between Measured Hormone and Lipoprotein Variables**

| Variable | Cholesterol | Log Triglyceride | HDL | $HDL_2$ | $HDL_3$ | LDL | Apo A-I | Apo B |
|---|---|---|---|---|---|---|---|---|
| Serum | | | | | | | | |
| Total | | | | | | | | |
| *r* | −.082 | −.462 | .430 | .503 | .127 | −.078 | .314 | −.026 |
| *P* | .588 | .001 | .003 | .000 | .399 | .606 | .033 | .862 |
| Free T | | | | | | | | |
| *r* | −.070 | −.476 | .460 | .542 | .132 | −.066 | .331 | −.015 |
| *P* | .645 | .001 | .001 | .000 | .382 | .664 | .025 | .919 |
| Total $E_2$ | | | | | | | | |
| *r* | −.290 | −.409 | .240 | .298 | .048 | −.287 | .030 | −.276 |
| *P* | .050 | .005 | .108 | .044 | .751 | .053 | .843 | .063 |
| Free $E_2$ | | | | | | | | |
| *r* | −.288 | −.413 | .246 | .303 | .050 | −.285 | .035 | −.274 |
| *P* | .052 | .004 | .100 | .040 | .741 | .055 | .815 | .066 |
| SHBG | | | | | | | | |
| *r* | .083 | −.404 | .373 | .398 | .163 | .130 | .336 | .125 |
| *P* | .583 | .005 | .010 | .006 | .278 | .388 | .022 | .409 |
| Log urine | | | | | | | | |
| Total T | | | | | | | | |
| *r* | −.211 | .011 | −.082 | .043 | −.217 | −.234 | −.086 | −.208 |
| *P* | .158 | .943 | .588 | .773 | .147 | .118 | .570 | .164 |
| Free T | | | | | | | | |
| *r* | −.098 | −.170 | .093 | .100 | .038 | −.099 | .093 | −.076 |
| *P* | .518 | .260 | .540 | .507 | .798 | .512 | .537 | .615 |
| Total $E_2$ | | | | | | | | |
| *r* | −.280 | −.043 | −.052 | .038 | −.152 | −.283 | −.096 | −.348 |
| *P* | .060 | .779 | .732 | .800 | .311 | .056 | .524 | .018 |
| Free $E_2$ | | | | | | | | |
| *r* | .101 | −.027 | .035 | −.167 | .298 | .113 | .116 | .039 |
| *P* | .502 | .860 | .819 | .265 | .044 | .453 | .442 | .793 |

Abbreviations: T, testosterone; $E_2$, estradiol.

testosterone remained significant, again with BMI remaining significant in the equation. The weak associations with serum total and free estradiol were nonsignificant on stepwise regression, with the only remaining variable in the equation being BMI. The results were similar for apo A-I, although the values for $R^2$ with serum total and free testosterone were smaller.

## DISCUSSION

The notable findings of this study in healthy Chinese men are as follows: (1) statistically significant associations of serum total and calculated free testosterone levels with serum triglyceride levels (negative), and HDL cholesterol, $HDL_2$ cholesterol, and apo A-I levels (positive); and (2) significant negative associations of urinary total estradiol excretion with total cholesterol, LDL cholesterol, and apo B levels, and a significant but weaker negative association between urinary total testosterone excretion and cholesterol and LDL cholesterol levels only after controlling for confounding variables.

Women, in whom estrogen production is greater, have lower serum levels of total and LDL cholesterol than men. In this study, both free and total estradiol excretions were used as indices of estradiol production. There is some evidence from this study that among men, variation in estrogen production is associated with variation in plasma lipid levels. The associations between serum levels of total estradiol and lipids might have been explained by common associations with SHBG due to some metabolic connection, but this seems unlikely because calculated levels of the free hormone and urinary excretion of total estradiol were also associated with serum levels of lipids. Estrogens are known to increase LDL receptor activity in the liver of certain animals,[19] and the same may be true in man.[20] If LDL receptor numbers or activity were associated with the rate of estrogen production, this might account for the inverse associations shown here. Estrogens decrease the activity of hepatic lipoprotein lipase,[21] which is involved in the removal of HDL by the liver.[22] Men have higher activities of this enzyme and lower HDL levels than women.[21,23] It is possible that estrogen production affects HDL levels through such a mechanism. Negative associations between urinary total testosterone excretion and serum cholesterol and LDL cholesterol levels might be accounted for by the fact that serum cholesterol levels increase with age and testosterone levels decline. Although multivariate analysis was used to control for the effect of age, it may not have been completely effective. Serum total and free estradiol levels also declined with age in this population, but the greater strength of negative associations on multivariate analysis suggests that this was not the entire explanation for the associations seen with cholesterol, LDL cholesterol, and apo B levels.

On univariate analysis, serum testosterone variables show significant positive associations with plasma HDL

**Table 4. Stepwise Multiple Regression of Serum Lipid/Lipoprotein Variables on One Hormone Variable and BMI, WHR, and Age (significant variables only)**

| Lipid Variable | Significant Variable | *t* | *P* | $R^2$ |
|---|---|---|---|---|
| S-cholesterol | Log U-total testosterone | −2.212 | .04 | .487 |
| | BMI | 3.29 | .002 | |
| | Log U-total estradiol | −2.329 | .025 | .502 |
| | BMI | 3.161 | .003 | |
| S-LDL cholesterol | Log U-total estradiol | −2.194 | .034 | .534 |
| | BMI | 2.35 | .023 | |
| | Log U-total testosterone | −2.236 | .031 | .478 |
| | BMI | 3.111 | <.001 | |
| Log triglyceride | S-total testosterone | −2.16 | .036 | .607 |
| | BMI | 3.25 | .002 | |
| | S-total estradiol | −2.38 | .022 | .618 |
| | BMI | 3.864 | <.001 | |
| | S-free testosterone | −2.224 | .031 | .610 |
| | BMI | 3.16 | .003 | |
| | S-free estradiol | −2.398 | .021 | .619 |
| | BMI | 3.847 | <.001 | |
| S-HDL cholesterol | S-total testosterone | 2.2 | .033 | .497 |
| | S-free testosterone | 2.217 | .019 | .514 |
| $S\text{-}HDL_2$ cholesterol | S-total testosterone | 2.597 | .013 | .624 |
| | BMI | −3.104 | .003 | |
| | S-free testosterone | 2.942 | .005 | .642 |
| | BMI | −2.955 | .005 | |
| $S\text{-}HDL_3$ cholesterol | Log U-free estradiol | 2.075 | .044 | .298 |
| Apo B | Log U-total estradiol | −2.644 | .011 | .428 |
| Apo A-I | S-total testosterone | −2.196 | .033 | .314 |
| Apo A-I | S-free testosterone | −2.326 | .025 | .331 |

Abbreviations: S, serum; U, urine.

cholesterol levels, but urinary testosterone variables do not. It might have been expected that they would, because serum free testosterone concentrations and urinary free testosterone excretion were significantly correlated ($p = .008$, $r = .388$). HDL cholesterol levels are strongly negatively associated with BMI, as are serum testosterone (free and total) levels (data not shown). This may produce an association between serum testosterone and HDL cholesterol levels, whereas because the urinary variables are not associated with BMI (data not shown), a significant association with these is not seen.

The absence of any associations between sex hormone variables and serum levels of Lp(a) is consistent with the strong genetic determination of serum concentrations of this lipoprotein.[24] Nevertheless, there have been suggestions that sex hormones contribute to variation in Lp(a) in men,[25] and to changes in Lp(a) postmenopausally[26] and with hormone replacement therapy[27] in women.

### *Conclusions*

This study of relationships between urinary excretion of sex hormones and serum lipoprotein concentrations suggests a role for estrogen production in contributing to variation in serum lipid and lipoprotein-lipid levels. A search for other explanations of the associations should be made and further studies performed to see whether similar results are obtained in other populations.

## REFERENCES


1. Friedman DS, O'Brien TR, Flanders WD, et al: Relation of serum testosterone levels to high density lipoprotein cholesterol and other characteristics in men. Arterioscler Thromb 11:307-315, 1991
2. Heller RF, Wheeler MJ, Micallef J, et al: Relationship of high density lipoprotein cholesterol with total and free testosterone and sex hormone binding globulin. Acta Endocrinol (Copenh) 104:253-256, 1983
3. Stefanick ML, Williams PT, Krauss RM, et al: Relationship of plasma estradiol, testosterone, and sex-hormone–binding globulin with lipoproteins, apolipoproteins, and high density lipoprotein subfractions in men. J Clin Endocrinol Metab 64:723-729, 1987
4. Kiel DP, Baron JA, Plymate SR, et al: Sex hormones and lipoproteins in men. Am J Med 87:35-39, 1989
5. Solyom A: Effects of androgens on serum lipids and lipoproteins. Lipids 7:135-141, 1972
6. Friedl KE, Hann CJ Jr, Jones RE, et al: High-density lipoprotein cholesterol is not decreased if an aromatizable androgen is administered. Metabolism 39:69-74, 1990
7. Glazer G, Suchman AL: Lack of demonstrated effect of nandrolone on serum lipids. Metabolism 43:204-210, 1994
8. Goldberg RB, Rabin D, Alexander AN, et al: Suppression of plasma testosterone leads to an increase in serum total and high density lipoprotein cholesterol and apoproteins A-I and B. J Clin Endocrinol Metab 60:203-207, 1985
9. Hromadová M, Hácik E, Malatinsky A, et al: Lipid metabolism in young males with hypotestosteronaemia and oligospermia prior to, during, and after treatment. Int Urol Nephrol 23:69-75, 1991
10. Camacho AM, Migeon CJ: Studies on the origin of testosterone in the urine of normal adult subjects and patients with various endocrine disorders. J Clin Invest 43:1083-1089, 1964
11. Bardin CW: Pituitary-testicular axis, in Yen SSC, Jaffe RB (eds): Reproductive Endocrinology (ed 2). Philadelphia, PA, Saunders, 1986, pp 177-199
12. Lipsett MB: Steroid hormones, in Yen SSC, Jaffe RB (eds): Reproductive Endocrinology (ed 2). Philadelphia, PA, Saunders, 1986, pp 140-153
13. Terry RB, Wood PD, Hasdell WL, et al: Regional adiposity patterns in relation to lipids, lipoprotein cholesterol, and lipoprotein subfraction mass in men. J Clin Endocrinol Metab 68:191-199, 1989
14. Wilmore JH, Behnke AR: An anthropometric estimation of body density and lean body weight in young men. J Appl Physiol 27:25-31, 1969
15. Warnik GR, Benderson J, Albers JJ: Dextran sulfate-$Mg^{2+}$ precipitation procedure for quantitation of high density-lipoprotein cholesterol. Clin Chem 28:1379-1388, 1982
16. Friedewald WT, Levy RI, Fredrickson DS: Estimation of the concentration of LDL cholesterol in plasma without the use of the preparative ultracentrifuge. Clin Chem 18:499-502, 1972
17. Chard T: An introduction to radioimmunoassay and related techniques, in Burdon RH, van Knippenberg PH (eds): Laboratory Techniques in Biochemistry and Molecular Biology, vol 6 (ed 4). Amsterdam, The Netherlands, Elsevier, 1990, pp 187-207
18. Södergärd R, Bäckström T, Shanbhag V, et al: Calculation of free and bound fractions of testosterone and estradiol-17β to

human plasma proteins at body temperature. J Steroid Biochem 16:801-810, 1982

19. Ma PTS, Yamamoto T, Goldstein JL, et al: Increased mRNA for low density lipoprotein receptor in livers of rabbits treated with 17 alpha ethinyl estradiol. Proc Natl Acad Sci USA 83:792-796, 1986

20. Eriksson M, Berglund L, Rudling M, et al: Effects of estrogen on low density lipoprotein metabolism in males. Short-term and long-term studies during hormonal treatment of prostatic cancer. J Clin Invest 84:802-810, 1989

21. Applebaum DM, Goldberg AP, Pykalisto OJ, et al: Effect of estrogen on post heparin lipolytic activity. J Clin Invest 59:601-608, 1977

22. Tikkanen MJ, Nikkila EA, Kuesi T, et al: High density lipoprotein-2 and hepatic lipase: Reciprocal changes produced byestrogen and norgestrol. J Clin Endocrinol Metab 54:1113-1117, 1982

23. Krauss RM, Levy RI, Fredrickson DJ: Selective measurement of two-lipase activities in post-heparin plasma from normal subjects and patients with hyperlipoproteinemia. J Clin Invest 54:1107-1124, 1974

24. Boerwinkle E, Leffert CC, Lin J, et al: Apolipoprotein (a) gene accounts for greater than 90% of the variation in plasma lipoprotein(a) concentrations. J Clin Invest 90:52-60, 1992

25. Henriksson P, Angelin B, Berglund L: Hormonal regulation of serum Lp(a) levels. Opposite effects after estrogen treatment and orchidectomy in males with prostatic carcinoma. J Clin Invest 89:1166-1171, 1992

26. Heinrick J, Sandkamp M, Kokott R, et al: Relationship of lipoprotein(a) to variables of coagulation and fibrinolysis in a healthy population. Clin Chem 37:1950-1954, 1991

27. van der Mooren MJ, Demacker PNM, Thomas CMG, et al: Beneficial effects on serum lipoproteins by 17β-oestradiol-dydrogensterone therapy in postmenopausal women: A prospective study. Eur J Obstet Gynecol Reprod Biol 47:153-160, 1992