

ACUTE EFFECT OF ALCOHOL ON ANDROGENS IN PREMENOPAUSAL WOMEN†
TAISTO SARKOLA, TATSUSHIGE FUKUNAGA1, HEIKKI MÄKISALO2 and C. J. PETER ERIKSSON*

National Public Health Institute, Department of Mental Health and Alcohol Research, P.O. Box 719, FIN-00101 Helsinki, Finland, 1Department of Forensic Medicine and Sciences, Mie University School of Medicine, Tsu, Japan and 2Department of Surgery, Helsinki University Central Hospital, Helsinki, Finland

(Received 1 April 1999; in revised form 21 June 1999; accepted 13 July 1999)

Abstract — The aim of the present study was to investigate the effect of alcohol on androgen levels among premenopausal women. Thirty-seven women in the mid-cycle phase of the menstrual cycle, 47 of whom used oral contraceptives (OC+), were included in the study. The range for reported alcohol consumption was 0–4 drinks/day. The total testosterone levels were significantly higher after alcohol intake (0.5 g/kg) than after placebo at 45 min and 90 min from the start of drinking among both OC– and OC+ subjects. This effect was also seen in the free testosterone fraction. The effect on testosterone was more prominent among OC+ subjects. Androstenedione levels were significantly lowered and the testosterone:androstenedione ratio significantly elevated by alcohol among both OC– and OC+ subjects. No effect of alcohol on dehydroepiandrosterone or dihydrotestosterone levels was observed. A positive correlation was observed between the change in testosterone levels and the change in androstenedione levels during placebo conditions. The correlation was significantly reduced during alcohol conditions among OC+ subjects, indicating an increased androstenedione to testosterone conversion. No significant dose (0.34, 0.68 and 1.02 g/kg) or time (45, 90 and 150 min) effects on total testosterone were observed in a substudy involving 10 OC+ subjects. The present results suggest that the testosterone effect is related to the zero-order mechanism of ethanol oxidation. The observed testosterone and androstenedione effects are suggested to be the result of an increased androstenedione to testosterone conversion in the liver caused by the alcohol-mediated elevation in the [NADH]:[NAD+] ratio. The present findings may be relevant in the development of hyperandrogenism and loss of female sexual characteristics associated with heavy alcohol consumption.

INTRODUCTION

Heavy alcohol consumption is associated with abnormalities of the menstrual cycle, sterility, miscarriages, and loss of female sexual characteristics, all of which are affected by the hormonal balance in women (Van Thiel and Lester, 1979). Thus, it seems reasonable to postulate that these adverse effects could at least in part originate from alcohol-mediated changes in hormone levels.

It is well known that acute alcohol intake leads to decreased levels of testosterone in normal healthy men (Ylikahri et al., 1974). Investigations on the hormonal effects of alcohol in women are complicated by the menstrual cycle and the use of hormonal preparations. Most studies have focused on a particular time in the menstrual cycle and on women not using hormonal preparations, usually with fewer than ten subjects. Probably as a consequence, these studies (McNamee et al., 1979; Välimäki et al., 1983; Becker et al., 1988) have not reported any significant effect of alcohol, although a tendency to higher testosterone concentrations was displayed in one of these studies (Välimäki et al., 1983).

We have shown in an earlier report that alcohol ingestion causes an acute elevation of the total testosterone levels in premenopausal women (Eriksson et al., 1994). This effect was found to be more prominent among women using oral contraceptives, but was also seen to a lesser degree during the mid-cycle phase among non-users as well. In line with our findings is a recent observation of testosterone elevations in four women using oral contraceptives 14 h after a large (2.0 g/kg) dose of alcohol (Karila et al., 1996).

In the present study, we focused on the mid-cycle phase. The aim of the study was to confirm our earlier observation and to find out whether the effect of alcohol on testosterone in premenopausal healthy women is dose-dependent. In addition, we wanted to focus on the possible mechanism by measuring androstenedione and dehydroepiandrosterone (DHEA), the principal precursors of testosterone in women. Furthermore, we wanted to find out how the observed acute effect is reflected in free testosterone and dihydrotestosterone levels.

SUBJECTS AND METHODS

Experimental subjects

Substudy A. Ninety-two non-pregnant healthy Caucasian female volunteers were recruited by advertising in a local newspaper and on a poster board in the University of Helsinki. The study was conducted in accordance with the guidelines proposed in the Declaration of Helsinki and approved by a local ethical committee. A questionnaire was sent to all subjects and participation was confirmed by obtaining a signed informed consent together with the filled-in questionnaire. The reported usual alcohol consumption was calculated by multiplying the reported number of drinks during a typical drinking occasion with the reported number of occasions per week. One standard drink was defined as containing 12 g of ethanol. The range for reported alcohol consumption among all participants was 0 to 4 drinks/day.

Five subjects were excluded on grounds of using a hormonal intrauterine device, using an oral contraceptive containing only the progestin component (minipill), or not reporting the menstrual cycle phase. In the final analysis, users of oral contraceptives (OC+, n = 47) all reported using preparations containing both synthetic ethinyl oestradiol (mean 29 μg, range 20–40 μg) and a progestin (75 μg gestodene, n = 16;
150 μg desogestrel, n = 15; 50–150 μg levonorgestrel, n = 10; 2 mg cyproterone acetate, n = 6) for several months before entering the study. OC+ subjects age was 26 ± 4 years (mean ± SD, range 19–38), body mass index (BMI) was 21.2 ± 2.1 kg/m² (mean ± SD, range 16.8–26.4), the median of the reported alcohol consumption was 7 drinks/week (range 0–30), and that of the menstrual cycle phase was 18 ± 3 days (mean ± SD, range 7–26). The non-user group (OC–, n = 40) did not use any form of hormonal medication. The mean age of the OC– subjects was 30 ± 7 years (range 19–46), their BMI was 21.5 ± 2.2 kg/m² (range 17.0–27.4), the median of their reported alcohol consumption was 6 drinks/week (range 0–26), and their menstrual cycle phase was 15 ± 4 days (range 8–21). All subjects had a history of regular menses and none used any medication other than oral contraceptives. None of them had a record of hirsutism or other diseases.

All subjects participated randomly in one placebo and one alcohol drinking event with the intervening time being 28 days. Participation in the sessions was scheduled as close as possible to the mid-cycle phase with reference to the phase reported in the questionnaire. Among subjects not using oral contraceptives mid-cycle ovarian activity was confirmed with oestradiol levels >70 pmol/l. All drinking events took place on Mondays (three times), Tuesdays (nine times), and Wednesdays (twice) starting at 18:00. All the subjects were told not to drink any alcohol on the previous evening. No instructions were given regarding meals and snacks. Alcohol (dose 0.5 g/kg, equal to about 2 to 3 standard drinks) was given diluted in lingonberry juice (10% w/v). The placebo drink contained an equal volume of lingonberry juice only. Blood samples were drawn from the median cubital vein before and at 45 and 90 min after the start of drinking. The participants remained seated throughout the experiment. Drinking time was 30 min. No ethanol was detected before the start of drinking and levels increased to 5.8 ± 2.9 mM (27 ± 13 mg/dl) at 45 min and to 7.1 ± 3.0 mM (33 ± 14 mg/dl) at 90 min from the start of drinking.

Substudy B. Ten non-pregnant healthy Caucasian female student volunteers were recruited. All the subjects, aged 20–32 (mean 24) years and weight 52–63 (mean 58) kg, reported using oral contraceptives containing both synthetic oestradiol and a progestin (brands similar to those used in substudy A) for several months before entering the study. All the subjects had a history of regular menses and none used any medication other than oral contraceptives. None of them had a record of hirsutism or other diseases. The menstrual cycle phase was not documented. All the subjects were light drinkers with no record of heavy drinking or any kind of alcohol problem. Each subject participated randomly in four drinking events, one of which was with a placebo (lingonberry juice) and the other three with different amounts of alcohol (0.34, 0.68 and 1.02 g/kg diluted in lingonberry juice 10% w/v), starting at 18:00. The intervals between each session were longer than 1 week. The conditions were the same as in substudy A, except that venous blood samples were taken before, and at 40, 90 and 150 min from start of, drinking. No ethanol was detected before the start of drinking and levels increased to 5.2 ± 0.6 mM (24 ± 3 mg/dl, at 90 min) with the dose of 0.34 g/kg, to 13.2 ± 1.0 mM (61 ± 5 mg/dl, at 150 min) with the dose of 0.68 g/kg, and to 25.6 ± 0.6 mM (117 ± 3 mg/dl, at 150 min) with the dose of 1.02 g/kg.

Analytical procedures

Blood samples were collected into tubes containing 22.5 mg of sodium fluoride and 22.5 mg of potassium oxalate as anticoagulants for a volume of 10 ml of blood. Plasma samples were prepared within 4 h and stored at −20°C until determinations. Ethanol levels were determined in plasma by headspace gas chromatography (Perkin-Elmer F40). Testosterone levels [within-assay variability 6.6% and between-assay variability 7.0% at the level of 0.96 nmol/l (n = 10), detection limit 0.1 nmol/l], free testosterone levels [within-assay variability 4.3% and between-assay variability 5.5% at the level of 4.6 pmol/l (n = 10), detection limit 0.5 pmol/l] and androstenedione levels [within-assay variability 10.4% and between-assay variability 4.3% at the level of 5.3 nmol/l (n = 10), detection limit 0.14 nmol/l] were determined by standard radioimmunoassay reagent sets (Orion Diagnostica, Finland, for testosterone; Diagnostic Products Corporation, Los Angeles, CA, USA for free testosterone and androstenedione).

Dehydroepiandrosterone levels [DHEA; within-assay variability 5.9% and between-assay variability 8.3% at the level of 7.6 nmol/l (n = 38), detection limit 2 nmol/l] were determined by a method based on extraction into petroleum ether followed by a radioimmunoassay (RIA) using tritiated DHEA as the labelled antigen (DHEA[1,2,6,7-3H(N)], NET-814, 250 μCi/250 μl ethanol, NEN® Research Products) and Anti-DHEA (cat no. 07-129016 ICN) as the antibody. Sample and standard extracts were dissolved in buffer and incubated at 2–8°C overnight, and dextran-coated charcoal [0.32% Norit A (active charcoal) and 0.032% Dextran T70 in 0.045 mol/l phosphate-buffered saline (PBS) with 0.1% gelatine, pH 7.0] was used to separate the bound and free steroids.

Dihydrotestosterone levels [within-assay variability 9.1% and between-assay variability 17.8% at the level of 2.5 nmol/l (n = 10), detection limit 0.2 nmol/l] were determined as described by Apter et al. (1976). Briefly, the method is based on extraction into ethylether-ethylacetate (7:3 v/v) twice followed by chromatographic separation on a Lipidex-5000 column (hydroxylalkoxypropyl Sephadex, petroleum-chloroform 98:2 as eluant) and a RIA using tritiated dihydrotestosterone [5α-dihydro(1,2,4,5,6,7-3H)testosterone, Amersham TRK 443] as the labelled antigen and antisera raised in rabbits (forimmunization procedures see Jänne et al., 1974). Samples taken 45 min and 90 min after the start of drinking were pooled in equal volumes for dihydrotestosterone determinations.

In order to check for possible changes of hormone levels in vitro caused by alcohol as well as for possible interactions of alcohol with hormone assays, ethanol was added to fresh blood from 10 OC– and six OC+ 18–24 year old healthy female subjects to a final concentration of 10 mM. No significant effects on androstenedione and total testosterone were observed. A negligible reduction of the DHEA levels, confined to higher hormone levels, could be observed (16.8 ± 2.9 and 15.6 ± 2.8 nmol/l, P = 0.017, n = 16), which was perhaps due to the procedure of extraction with petroleum ether. The possible in vitro effect of alcohol was not determined for dihydrotestosterone.

Data analysis

Results are expressed as means ± SEM unless otherwise specified. The magnitude of the effect of alcohol on hormone levels was defined as the change in concentration (%)
observed during the placebo session subtracted from the change in concentration observed during the alcohol ingestion session. Statistical significance was tested using two-factor analyses of variance for repeated measures (drug and time as within-group factors) and matched paired t-test. Absolute hormone values were used in the analyses of variance. For correlations, Spearman’s rank-order correlation was used. Difference between the two $r$-values was tested by transforming $r$ to $r'$ (Fisher’s transformation) as described (Howell, 1992). Data were analysed using SPSS (version 6.1) and GraphPad Prism (version 2.0) statistical software.

RESULTS

Among both OC– and OC+ subjects, in substudy A, total testosterone levels were significantly elevated during the alcohol sessions compared with the placebo sessions ($F = 7.9$, $P = 0.008$ for OC– and $F = 40$, $P < 0.001$ for OC+). An elevation relative to placebo was observed in 75% of the OC– subjects and in 95% of the OC+ subjects. The magnitude of the effect of alcohol among OC– subjects was $+13\%$ ($95\%$ CI $= −2, +27$) at 45 min and $+19\%$ ($95\%$ CI $= 1, 38$) at 90 min (Fig. 1). The effect of alcohol among OC+ subjects was $+123\%$ ($95\%$ CI $= 91, 154$) at 45 min and $+152\%$ ($95\%$ CI $= 117, 187$) at 90 min (Fig. 2). Before intake of alcohol or placebo, total testosterone levels were clearly lower among OC+ subjects than OC– subjects ($P < 0.001$).

The effect of alcohol on free testosterone levels (i.e., the absolute change in hormone concentration during placebo subtracted from the change during alcohol) was observed to correlate with the effect on total testosterone levels among OC– ($r = 0.47$, $P = 0.004$) and among OC+ ($r = 0.69$, $P < 0.0001$) subjects. An elevation relative to placebo was observed in 50% of the OC– subjects and in 79% of the OC+ subjects. In the OC– group the overall effect of alcohol on free testosterone levels did not reach statistical significance ($F = 1.5$, $P = 0.22$; Fig. 1). The magnitude of the effect was $+8\%$ ($95\%$ CI $= −1, 18$) at 45 min and $+1\%$ ($95\%$ CI $= −12, 13$) at 90 min. However, when analysing the effect among OC– subjects as a function of cycle phase, we found that during menstrual cycle days 9–14 the effect of alcohol on free testosterone was $+14\%$ ($95\%$ CI $= 2, 27$, $P = 0.03$, $n = 20$) at 45 min and $+13\%$ ($95\%$ CI $= −3, +28$, $P = 0.09$, $n = 20$) at 90 min. In the OC+ group, alcohol elevated free testosterone levels ($F = 9.3$, $P = 0.004$; Fig. 2) and the magnitude of the effect was $+54\%$ ($95\%$ CI $= 24, 83$) at 45 min and $+44\%$ ($95\%$ CI $= 17, 71$) at 90 min. Before intake of alcohol or placebo, free testosterone levels were clearly lower among OC+ subjects than OC– subjects ($P < 0.001$).

The unbound fraction of testosterone expressed in percentages as the ratio of free to total testosterone was seen to decline during alcohol compared with placebo sessions among both OC– and OC+ subjects (drug by time interaction; $F = 3.2$, $P = 0.049$ for OC– and $F = 4.3$, $P = 0.018$ for OC+; Fig. 3). The overall ratio of free to total testosterone was clearly lower among OC+ subjects than OC– subjects ($P < 0.001$).

An acute effect on androstenedione levels was observed among both OC– (drug by time interaction; $F = 8.3$, $P < 0.001$) and OC+ subjects (drug by time interaction;
The ratio of total testosterone to androstenedione was found to be elevated during alcohol relative to placebo sessions among both OC– subjects ($F = 30.1$, $P < 0.001$; $0.17 \pm 0.01$ vs $0.18 \pm 0.01$ before intake; $0.17 \pm 0.01$ vs $0.23 \pm 0.01$, $P < 0.001$, at 45 min; $0.16 \pm 0.01$ vs $0.25 \pm 0.01$, $P < 0.001$, at 90 min) and OC+ subjects ($F = 45.3$, $P < 0.001$; $0.18 \pm 0.02$ vs $0.17 \pm 0.02$ before intake; $0.16 \pm 0.01$ vs $0.44 \pm 0.03$, $P < 0.001$, at 45 min; $0.16 \pm 0.01$ vs $0.55 \pm 0.05$ at 90 min).

Among both OC– and OC+ subjects, DHEA levels were not statistically significantly different during the alcohol sessions compared with the placebo sessions (Fig. 5, top) and no drug by time interaction was observed. The magnitude of the effect of alcohol among OC– subjects was $+2\%$ ($95\%$ CI $= -8$, $+13$) at 45 min and $-13\%$ ($95\%$ CI $= -29$, $+4$) at 90 min, whereas that of alcohol among OC+ subjects was $+3\%$ ($95\%$ CI $= -6$, $+13$) at 45 min and $-5\%$ ($95\%$ CI $= -13$, $+4$) at 90 min. DHEA levels were clearly lower among OC+ subjects than OC– subjects ($P < 0.001$) (Fig. 5).

Fig. 3. Acute effect of alcohol on the ratio of plasma free to total testosterone.

The fraction of free to total testosterone expressed as percentage before (0 min), and at 45 and 90 min from the start of drinking placebo or alcohol was calculated. OC– subjects ($n = 39$) and OC+ subjects ($n = 47$). *$P < 0.05$ and ***$P < 0.001$ compared with placebo.

Fig. 4. Acute effect of alcohol on plasma androstenedione.

Androstenedione levels among women using (OC+) and women not using (OC–) oral contraceptives were measured before (0 min), and at 45 and 90 min from the start of drinking placebo or alcohol ($n = 39$ and $n = 47$, respectively). *$P = 0.038$ for OC– and $P = 0.012$ for OC+; **$P = 0.009$ and ***$P < 0.001$ compared with placebo.

Fig. 5. Acute effect of alcohol on plasma dehydroepiandrosterone (DHEA) and dihydrotestosterone.

DHEA levels among women using (OC+) and women not using (OC–) oral contraceptives were measured before (0 min), and at 45 and 90 min from the start of drinking placebo or alcohol. Dihydrotestosterone levels among OC– and OC+ subjects were also measured before (0 min), and at the pooled timepoint 45–90 min from the start of drinking placebo or alcohol. $n = 39$ for OC– and $n = 47$ for OC+. No statistically significant differences between alcohol and placebo sessions were observed.
Among both OC− and OC+ subjects, dihydrotestosterone levels (also shown in Fig. 5, bottom) were not statistically significantly different during the alcohol sessions compared with the placebo sessions, and no drug by time interaction was found. In the determination, the subjects’ samples from 45 and 90 min were pooled in equal volumes. The magnitude of the effect of alcohol at the pooled timepoint (45–90 min) was −11% (95% CI = −32, +9) among OC− subjects and −2% (95% CI = −16, +12) among OC+ subjects (Fig. 5). Dihydrotestosterone levels were significantly lower among OC+ than OC− subjects before intake (P = 0.0035).

The change in total testosterone levels (the average of changes seen at 45 and 90 min) during placebo sessions correlated with the change in androstenedione (r = 0.49, P = 0.003 for OC− and r = 0.62, P = 0.001 for OC+) and DHEA (r = 0.31, P = 0.07 for OC− and r = 0.27, P = 0.09 for OC+) levels. Among OC− subjects, these correlations were similar during the alcohol sessions (r = 0.51, P = 0.002 for androstenedione and r = 0.29, P = 0.08 for DHEA), whereas among OC+ subjects the correlations disappeared (r = −0.03, P = 0.85 for androstenedione and r = −0.007, P = 0.96 for DHEA). This reduction in the correlation coefficient among OC+ subjects was statistically significant for androstenedione (z = 3.19, P = 0.005) and a tendency was observed for DHEA (z = 1.22, P = 0.13).

In substudy B, total testosterone levels (Fig. 6) were significantly higher during all the alcohol events than in the placebo session (F = 5.34, P = 0.011, all doses P < 0.001). No significant dose or time effects were observed. The present dose–response results have previously been presented in preliminary form (Eriksson et al., 1994).

**DISCUSSION**

The present results confirm our earlier finding (Eriksson et al., 1994) that alcohol intake is associated with an acute elevation in total testosterone levels among premenopausal women. The effect is more prominent among women using oral contraceptives, but occurs during the mid-cycle phase among non-users as well. The effect on total testosterone is reflected in the free testosterone fraction. The failure of earlier reports (McNamee et al., 1979; Vilmiä et al., 1983; Becker et al., 1988) to detect the testosterone effect can probably be explained by lack of statistical power and the fact that they included exclusively OC− subjects in the luteal or early follicular phase.

Testosterone levels can be affected either by changes in its synthesis in the adrenals or gonads, through changed peripheral conversion from androstenedione and DHEA or through changed catabolism in the liver (Yen and Jaffe, 1991). Since alcohol intake had no effect on DHEA, a major part of which is of adrenal origin (Yen and Jaffe, 1991), it is unlikely that the testosterone elevation is caused by an acute increase in adrenal androgen synthesis. The finding that the testosterone effect was not alcohol dose-dependent suggests that it is related to the zero-order mechanism of ethanol elimination and mediated by the change in the redox state. It is well known that this effect is rather constant during different dose and time conditions of ethanol oxidation (Forsander, 1970). The facts that alcohol intake is associated with a decline in androstenedione levels, an elevation in testosterone levels, and an elevation in the testosterone to androstenedione ratio suggest an increase in the conversion of androstenedione to testosterone. The positive correlation between the change in testosterone levels and the change in androstenedione levels after intake of placebo can be explained by the similar circadian rhythm of these hormones (Yen and Jaffe, 1991). The fact that this positive correlation was significantly reduced during alcohol conditions among women using oral contraceptives, i.e. the group displaying the more pronounced testosterone effect, provides further evidence of an increased androstenedione to testosterone reaction superimposed on the circadian hormonal changes.

Ethanol oxidation has earlier been shown to be coupled to steroid reduction in the liver (Andersson et al., 1986). More specifically, ethanol oxidation was shown to cause an increased rate of the reduction catalysed by the liver NAD-dependent 17β-hydroxysteroid dehydrogenase type 2 enzyme (Andersson and Moghrabi, 1997) with a secondary change in the equilibrium between conjugated 17-hydroxy- and 17-ketosteroids. These findings on conjugated steroids in men are similar to our results on unconjugated testosterone/androstenedione and oestradiol/oestrone in premenopausal women (Sarkola et al., 1999). The finding that the effect in the present study was pronounced among women using oral contraceptives may be explained by the fact that the 17β-hydroxysteroid type 2 enzyme is induced by the synthetic progestins found in the contraceptive preparation (Tseng and Gurpide, 1979). Thus, the present results suggest that the testosterone effect is the result of an inhibited catabolism in the liver, i.e. a decreased overall oxidation of testosterone due to the increased reduction of androstenedione to testosterone, mediated by the alcohol-induced elevation in the [NADH]:[NAD+] ratio (Fig. 7).

Our results suggest that the acute effect exerted by alcohol on testosterone is rapidly compensated for by binding, as the ratio of free to total testosterone was observed to decline after alcohol intake in both study groups. Testosterone is bound to sexhormone binding globulin (SHBG) and albumin in the ratio of 2:1 and the rate of the binding is rapid: the dissociation coefficient (t½) for testosterone is only 20 s for SHBG and 4 s for albumin (Yen and Jaffe, 1991). The levels of SHBG and
the present results. Both possibilities may explain earlier positive associations between drinking and androgen levels (Dorgan et al., 1994; Cigolini et al., 1996) as well as findings of hyperandrogenicity (Pettersson et al., 1990; Välimäki et al., 1990) and loss of female sexual characteristics (Van Thiel and Lester, 1979) among women drinking heavy amounts of alcohol.

Acknowledgements — The authors wish to thank Dr David Sinclair for comments on the manuscript and Mrs Hilikka Salohalla, Mrs Tuula Mäkelä, and Mrs Pirikko Johansson for skilful technical assistance.

REFERENCES


Dorgan, J. F., Reichman, M. E., Judd, J. T., Brown, Ch., Longcope, Ch., Schatzkin, A., Campbell, W., Franz, Ch., Kahle, L. and Taylor, P. R. (1994) The relation of reported alcohol ingestion to plasma levels of estrogens and androgens in premenopausal women (Maryland, United States). Cancer Causes Control 5, 53–60.


Fig. 7. Coupling of ethanol and androgen metabolism in the liver.

ADH, alcohol dehydrogenase; ALDH, aldehyde dehydrogenase; NAD+, oxidized nicotinamide adenine dinucleotide; NADH, reduced nicotinamide adenine dinucleotide; 17β-HSD, 17β-hydroxysteroid dehydrogenase. The dashed arrow denotes a decreased reaction rate.

albumin were not measured in the present study, since acute changes in these proteins during alcohol intake are unlikely.

No acute effect of alcohol on dihydrotestosterone levels was observed during the present dose and time conditions. In view of the testosterone effect, one could expect an elevation in dihydrotestosterone as well. The lack of an elevation in dihydrotestosterone is, however, not surprising, in view of the fact that, in women, the main source of dihydrotestosterone in plasma is androstenedione, with <20% being derived from testosterone (Ito and Horton, 1971). The present dihydrotestosterone finding may thus be the net result of a decline and an elevation caused by androstenedione and testosterone respectively.

An important question is how long the elevating effect of alcohol on testosterone levels could be expected to last. In view of the present results, it seems reasonable to postulate that the acute effect could last at least throughout the period of ethanol elimination. This is supported by the finding (Karila et al., 1996) that the testosterone level was found to be elevated 14 h after intake of alcohol (2.0 g/kg) but not at 38 h (T. Karila, personal communication), compared to levels preceding the day of alcohol intake.

The present finding with consistently lower basal androgen levels in women using oral contraceptives has been reported earlier (Jung-Hoffman et al., 1988). The reduced basal testosterone and androstenedione level is probably caused by the inhibition of the ovarian function (Jung-Hoffman et al., 1988). The mechanism of the reduced basal DHEA level, which mostly originates from the adrenals (Yen and Jaffe, 1991), is to our knowledge unknown. The fact that the use of oral contraceptives is associated with an increase in SHBG (Jung-Hoffman et al., 1988) may well explain the finding of a reduced free to total testosterone ratio in this study group.

In conclusion, the present androgen effects of alcohol are suggested to be the result of a change in the steroid metabolism in the liver. Whether repeated doses of alcohol would have a cumulative effect on androgen levels or whether heavy alcohol consumption is merely associated with repeated testosterone elevations in women cannot be determined from


