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REVIEW

THE EFFECTS OF MODERATE ALCOHOL CONSUMPTION ON FEMALE HORMONE LEVELS AND REPRODUCTIVE FUNCTION

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Abstract — Studies that have investigated the effect of moderate alcohol consumption on the level of oestrogens and progesterone in both pre- and post-menopausal women are reviewed. It is concluded that several lines of evidence point to an alcohol-induced rise in natural or synthetic oestrogen levels in women. Proposed mechanisms include an increased rate of aromatization of testosterone or a decreased rate of oxidation of oestradiol to oestrone. Moderate alcohol consumption has also been linked to decreased progesterone levels in pre-menopausal women. The relevance of these findings to female health, fertility and the timing of the menopause is considered.

INTRODUCTION

It is clear that recent studies which have investigated the biochemical consequences of moderate alcohol consumption in humans have, in part, been responsible for the revision of the safe drinking limits within the UK (Department of Health, 1995). What is now also beginning to emerge is the realization that health promotion advice to women may be seriously inadequate; the health consequences of moderate alcohol consumption for a woman may vary with the life stage.

The pharmacokinetic response of premenstrual women to moderate alcohol intake has been reviewed (Gill, 1997). The present work considers evidence for an effect of moderate alcohol consumption on: (1) the levels of the female hormones oestrogen and progesterone; (2) the timing of the onset of the menopause; (3) fecundity.

IS MODERATE ALCOHOL INTAKE ASSOCIATED WITH CHANGES IN THE LEVELS OF FEMALE REPRODUCTIVE HORMONES?

Oestrogens

In this section, three subsets of literature evidence will be reviewed: studies investigating the effect of alcohol on pre-menopausal women, on post-menopausal women, and finally on levels of ingested synthetic oestrogen.

Pre-menopausal studies. Research findings cited are summarized in Table 1.

Studies by Mendelson and co-workers (Mendelson *et al*., 1987, 1988, 1989) have reported increased levels of plasma oestradiol associated with acute alcohol intake in pre-menopausal women. In their 1988 study, alcohol levels of 70–75 mg/dl produced a significant increase (55–66% above pre-drinking levels) in the level of plasma oestradiol. This group of researchers have also reported increases in plasma oestrogens in response to concurrent luteinizing hormone-releasing hormone (LHRH) and ethanol administration, and to administration of the opioid antagonist naloxone with alcohol. Naloxone is thought to act within the hypothalamus promoting the release of luteinizing hormone (LH), follicle stimulating hormone (FSH) and prolactin from the pituitary. Mendelson has made two important proposals: first, that the effect of alcohol on reproductive hormone levels may be most evident in situations where gonadotropin levels are high, namely the early stages of pregnancy and during the peri-ovulatory surge of LH, around the midpoint of the menstrual cycle; second, that the alcohol-induced rise in oestrogen levels is a consequence of the metabolic breakdown of alcohol in the liver. Enzymatic degradation of alcohol is accompanied by a change in the proportions of the two forms of the coenzyme nicotinamide-adenine dinucleotide (NAD). The accumulation of the reduced form, NADH, means that the breakdown of oestradiol to oestrone is less favoured and so oestradiol accumulates.

A major study also involving pre-menopausal women was conducted by Reichmann *et al*. (1993). Six consecutive menstrual cycles were investigated in 34 women assigned randomly to two groups. A cross-over design was adopted in this controlled diet study. The women drank 30 g of ethanol per day (in the evening) for three consecutive cycles and no alcohol for the other three. All food and alcohol were provided by the study. Plasma hormone levels were determined from pooled samples obtained between 6 and 8 a.m. after an overnight fast on days 5–7 (follicular), 12–15 (peri-ovulatory) and 21–23 (luteal). On the third and sixth cycles, 24-h urine samples were also analysed, as was self-reported usual alcohol consumption. Alcohol consumption was associated with a rise in the levels of plasma dehydroepiandrosterone sulphate during the follicular phase; plasma oestrone, oestradiol and urinary oestradiol in the peri-ovulatory phase and urinary oestrone, oestradiol and oestriol in the luteal phase. For the peri-ovulatory phase, evidence for a rise in the absolute amount of bioavailable oestradiol was presented.

A related study failed to replicate these findings. Dorgan *et al*. (1994) performed a cross-sectional study with 107 women. Data and blood specimens were collected during one cycle and alcohol was not administered, but intake was assessed by diary and questionnaires. No association between alcohol ingestion and plasma oestrogens in any of the three cycle phases monitored was found. The pattern of drinking

Table 1. Studies investigating the effect of moderate alcohol consumption on pre-menopausal women

Reference	Subjects: no., mean age and other details	Phase of cycle	Alcohol intake	Analysis performed	Main conclusions
Mendelson *et al*. (1988)	12 (26.2 years, range 21–32) (6 placebo)	Follicular	0.695 g/kg (~5 UK units) in 19 min	Plasma oestradiol Plasma ethanol	Plasma oestradiol levels increased significantly (18 pg/ml, $P < 0.01$) after alcohol intake
Reichman *et al*. (1993)	34 (30.4 years; range 21–40) Cross-over design Diet controlled	Follicular (F) (days 5–7) Peri-ovulatory (PO) (12–15) Mid-luteal (L) (21–23)	30 g (3.75 UK units) per day for 3 of 6 cycles studied. Consumed in the evening	Pooled plasma (fasting) and 24 h urine samples collected during each third and sixth menstrual cycle. Analysed for hormone levels	*F phase* Rise in plasma dehydroepiandrosterone sulphate (7%, $P = 0.05$) *PO phase* Rise in plasma oestrone (21.2%, $P = 0.01$) Rise in plasma oestradiol (27.5%, $P = 0.01$) Rise in urinary oestradiol (31.9%, $P = 0.009$) *L phase* Rise in urinary oestrone (15.2%, $P = 0.05$) Rise in urinary oestradiol (21.6%, $P = 0.02$) Rise in urinary oestriol (29.1%, $P = 0.03$) Evidence of rise in absolute amounts of bioavailable oestradiol in PO phase
Dorgan *et al*. (1994)	107 (29.6 ± 5.1 years) Cross-sectional study	Follicular (F) days 5–7 Midcycle (M) days 12–15 Luteal (L) days 21–23	Assessed by food records and drinking pattern questionnaire. 15% abstainers 32% light drinkers (<0.75 UK units/day) 43% moderate (<3.5 units/day) 10% heavy (>3.5 units/day)	Plasma hormone levels. Data and blood collected for one menstrual cycle. Plasma (fasting) pooled to produce one sample for each of 3 cycle phases examined	No association between plasma oestrogens at any of 3 cycle phases studied. Significant positive association between alcohol and average plasma androstenedione
Muti *et al*. (1998)	60	Luteal Two samples 1 year apart	Assessed by questionnaire	Plasma (fasting) hormone levels	Significant association between alcohol intake and average oestradiol level. Women with intakes of around 12 UK units per week characterized by higher plasma oestradiol levels
Sarkola *et al*. (1999)	*Group A* 31 OC users (24 years, range 20–31) 30 OC non-users (24 years, range 19–33)	All phases	One placebo and one drinking event 28 days apart (3.75 UK units drunk in 30 min at 6 p.m.)	Plasma ethanol. Plasma hormones	Among OC users oestradiol levels increased and progesterone levels decreased
	Group B 47 OC users (26 years, range 19–38) 40 OC non-users (30 years, range 19–46)	Mid-cycle phase	One placebo and one drinking event 28 days apart (3.75 UK units drunk in 30 min at 6 p.m.)		Among OC non-users no significant effect was seen on oestrogens at mid-cycle
	Group C 10 OC users (24 years, range 20–32)	Phase not recorded	One placebo and 3 drinking events at least 1 week apart (2.5, 5.0 or 7.5 UK units)		Progesterone levels decreased ($P = 0.004$) (Groups A and B combined)

OC, oral contraceptive.

was not considered in this study in which the median weekly alcohol intake was ~51 g. Urinary hormonal levels were not investigated. In the previous study the alcohol dose was 30 g per day, hormone measurements were made using blood sampled the morning immediately after alcohol intake, and individual differences in hormone levels were noted.

More recent evidence supporting the proposal that alcohol intake is indeed associated with elevated oestrogen levels is provided by the report of Muti *et al*. (1998). They measured oestradiol levels in women twice (at an interval of 12 months) and attempted to control for the natural variability in the serum levels of this hormone. Alcohol intake in the sixty study participants was estimated by questionnaire. Those women with consistently high serum oestradiol levels were also typified by high weekly alcohol intake (almost 93 g), whereas women whose intake was approximately one-third of this displayed low serum oestradiol levels.

Oestradiol and oestrone levels in two groups of women (oral contraceptive users and non-users) were investigated by Sarkola *et al*. (1999). Blood was removed 40–150 min after alcohol intake (~2.5–7.5 UK units consumed in 30 min at 6 p.m.). Food intake was not controlled. In oral contraceptive users, an assumed alcohol-induced rise in oestradiol, but not oestrone, levels was evident. In the non-users the evidence was less convincing. In agreement with the proposal of Mendelson *et al*. (1988), these authors suggest that a change in the redox state of liver cells induced by alcohol metabolism is responsible for increased enzymatic conversion of oestrone to oestradiol. Furthermore, they cited the work of Tseng and Gurpide (1979), which reported that the enzyme responsible, 17β-hydroxysteroid dehydrogenase type 2 enzyme, is induced by the synthetic progestins contained within some oral contraceptives.

Post-menopausal studies. Table 2 summarizes the main findings of studies described in the following section.

With respect to post-menopausal women, Katsouyanni *et al*. (1991), Hankinson *et al*. (1995) and Nagata *et al*. (1997) have all reported a positive association between alcohol and oestrogen levels. All three groups monitored drinking behaviour retrospectively. Katsouyanni *et al*. (1991) analysed urinary hormone levels while the two other groups investigated plasma levels. Hankinson *et al*. (1995) reported that oestrone sulphate levels rose by 30% in women drinking at least 30 g (almost 4 UK units) of alcohol per day while Katsouyanni *et al*. (1991) noted that the levels of urinary oestradiol and oestrone in post-menopausal women increased by 16% and 20% respectively in response to a daily intake of one drink.

Gavaler and co-workers have also investigated a possible relationship between alcohol intake and oestrogen levels (Gavaler *et al*., 1991, 1993; Gavaler and Love, 1992; Gavaler and Van Thiel, 1992). They have made the following proposals; firstly that the relationship may not be observed unless drinking behaviour is monitored prospectively and secondly that a correlation is evident between oestradiol levels and the number of weekly drinks consumed (0.2–8.2 drinks per week). Another observation was that moderate drinkers were distinguished from abstainers by lower testosterone levels and

Table 2. Studies investigating the effect of moderate alcohol consumption on post-menopausal women not using hormone replacement therapy

Reference	Subjects, no. and age (years)	Alcohol intake and how monitored	Main conclusions
Katsouyanni *et al*. (1991)	88 (55–65) Greece	'Moderate'. Assessed by food frequency questionnaire	Positive association between alcohol intake and urinary oestrone (20% increase $P < 0.05$) and oestradiol (16% increase $P < 0.05$). A 15% increase in urinary oestriol was not significant
Gavaler *et al*. (1991)	62 (64) Danish 35 (58) Portuguese 20 (57) Spanish	82.8 ± 9.6 g/week 148.8 ± 31.2 g/week 64.8 ± 15.6 g/week Self-report	In Danish and Portuguese populations, oestradiol levels significantly increased in alcohol users, compared to abstainers. Oestradiol levels significantly correlated with total weekly drinks consumed
Gavaler *et al*. (1993)	128 (57.7 ± 0.4) USA	Among users mean intake 4.8 ± 0.6 US drinks per week (range 0.1–28). Self-report questionnaire and 3 day food record (21% abstainers)	Alcohol abstainers characterized by lower oestradiol levels than moderate alcohol users (27.5 ± 3.3; 44.3 ± 3.0 pg/ml). Oestradiol to testosterone ratio elevated (abstainers 44.5 ± 5.8; users 73.6 ± 4.4)
Hankinson *et al*. (1995)	217 (61.5 ± 5.0) USA	Mean intake (8.0 ± 12.8 g/day). Semiquantitative food frequency questionnaire covering previous year	After controlling for age, height, smoking status, body mass index, alcohol consumption was positively correlated with levels of serum oestrone sulphate ($P = 0.02$, $r = 0.17$). No associations between serum oestrone and oestradiol with alcohol
Ginsberg *et al*. (1996)	12 (54.5 ± 4.0) USA	0.7 g/kg (~5 UK units) or placebo consumed in 15 min (09.00) after overnight fast. 24 h later regime repeated with either alcohol or placebo	No significant effect of alcohol on serum oestradiol or oestrone levels
Nagata *et al*. (1997)	61 (60.5 ± 6.3) Japanese	7.1 ± 13.8 g/day. Self-administered questionnaire covering previous year	After controlling for age, height, smoking status, body mass index, alcohol consumption associated significantly with oestradiol (P for trend = 0.001). Statistically significant association between alcohol and dehydroepiandrosterone sulphate (P for trend = 0.01) (age and history of hysterectomy controlled)

higher oestradiol to testosterone ratios. This, it is suggested, reflects an increased rate of aromatization of testosterone stimulated by ethanol [an effect of alcohol reported elsewhere, e.g. Gordon *et al*. (1976)]. The alcohol-induced increase in oestradiol levels was only evident up to a consumption level of one drink per day. Higher levels of intake were not associated with further increases in oestradiol.

Attempts to substantiate this claim for an alcohol-induced rise in plasma oestrogen levels by the investigation of post-menopausal women in three European cities (Gavaler *et al*., 1991) were only partially successful. Oestradiol levels correlated with total weekly drinks in Copenhagen and Lisbon, but not in Madrid.

One study (Ginsburg *et al*., 1996) differed from those cited above in that it administered a known amount of alcohol (0.7 g/kg) to post-menopausal women. No significant change in plasma oestradiol levels was observed.

Studies in this field have been elegantly reviewed by Purohit (1998) who concluded that the question of whether an alcohol-induced rise in plasma oestrogen levels occurs in post-menopausal women not using hormone replacement therapy remains as yet unanswered. He suggested that the disparate results to date may be explained in part by: the type of beverage being critical (wine being more effective than spirits or beer); oestrogen rises being more evident in women when alcohol intake has been moderate (in terms of daily intake) but also chronic (regular and long term); and by investigators failing to analyse plasma oestrogen levels with the urgency that a 2 h half-life demands. (Any alcohol-induced rise in oestrogen levels may have subsided in some studies before blood sampling had occurred.)

Administered synthetic oestrogen. Three studies by Ginsburg *et al*. (1995*a*,*b*, 1996) provide evidence for an effect of alcohol on synthetic oestrogen administered to post-menopausal women either as a patch or orally. Alcohol (blood level 117 mg/dl) was associated with a rise in baseline concentrations of oestradiol from 179 to 219 pg/ml 35 min after alcohol intake. Levels were also significantly greater than those of control subjects. Evidence is also presented that alcohol may be associated with decreased oestradiol clearance rates after removal of a patch. This occurred in the absence of significant changes in oestrone levels. Finally the effect of alcohol on oestradiol levels in women receiving oral hormone replacement was also investigated (Ginsburg *et al*., 1996). Using a randomized cross-over study design, the authors found that alcohol (0.7 g/kg) prompted a threefold increase in the levels of circulating oestradiol. Levels of oestradiol remained above baseline values for 5 h, and were significantly correlated with blood alcohol levels.

Progesterone. No change in baseline progesterone levels has been reported in pre-menopausal women administered LHRH and alcohol at both the follicular and mid-luteal phases of the cycle (Mendelson *et al*., 1989), or in women receiving naloxone and alcohol during the mid-luteal phase of the cycle (Mendelson *et al*., 1987). However, Teoh *et al*. (1988) reported that alcohol suppressed progesterone levels during the early follicular phase of the cycle following naltrexone administration. They suggested that the breakdown of alcohol would be accompanied by the conversion of NAD^+ to NADH. This, in turn, would affect adversely the rate of conversion of pregnenolone to progesterone, which requires NAD^+. However, it should be noted that there was no significant difference in plasma progesterone levels between the placebo- and alcohol-receiving groups after naltrexone administration. The significant fall in progesterone levels was noted within the group receiving naltrexone and alcohol.

A further study by this same group (Teoh *et al*., 1990) administered human chorionic gonadotropin (hCG) to 10 women during the luteal phase of the menstrual cycle in an attempt to mimic the hormonal status of pregnancy. Alcohol (~46 g) was administered after an overnight fast over a 15-min period. A control group received a placebo solution. Only in the control group did hCG promote a significant increase in plasma progesterone levels. hCG is a hormone secreted after blastocyst implantation by the developing chorion. It acts to prolong the life of the corpus luteum, which in turn continues unabated to produce large amounts of oestrogen and progesterone so essential to the maintenance of the early stages of pregnancy. It was suggested by Teoh *et al*. (1990) that, by decreasing progesterone production, alcohol may compromise the survival of the blastocyst.

Sarkola *et al*. (1999) monitored progesterone levels in response to acute alcohol intake (0.34 to 1.02 g/kg) in a group of women comprising both oral contraceptive users and non-users. A significant fall in progesterone plasma levels in both groups was reported.

From studies *in vitro* using human placental cells exposed to alcohol concentrations of 20–40 mM, Ahluwalia *et al*. (1992) reported that alcohol caused a significant decrease in progesterone synthesis. Studies with low density lipoprotein implicated a detrimental role for ethanol, not at the enzymatic level, but at the point of entry of cholesterol into cell organelles prior to progesterone synthesis. It should be noted that 20 and 40 mM alcohol concentrations are equivalent to blood levels of 100 and 200 mg/dl respectively.

THE TIMING OF THE ONSET OF THE MENOPAUSE

Recent research has suggested that the timing of the onset of the menopause may be influenced by smoking (Thorell and Svardsudd, 1993), dietary factors (Nagata *et al*., 1998) and in particular alcohol (Torgerson *et al*., 1994, 1997). Specifically, the latter authors concluded that the onset of the menopause is delayed by moderate alcohol consumption. This conclusion was based on the result of a cross-sectioned survey of 1227 women who, 2 years previously, had all been pre-menopausal. Significant univariate associations were reported between menopausal status and age of maternal menopause and between menopause status and alcohol consumption. Alcohol consumption was significantly correlated with oestradiol levels and was found to be independently associated with menopausal status.

EVIDENCE FOR AN EFFECT ON FERTILITY

Grodstein *et al*. (1994) investigated the cause of infertility in just over 3800 women. Retrospective data relating to alcohol consumption before the onset of infertility were collected. Moderate alcohol intake (100 g, 12.5 UK units per week) was reported to be associated with a significant, but small, increased risk of ovulatory infertility and an increased risk of

endometriosis. Olsen *et al*. (1997) linked high, but not moderate, alcohol consumption to decreased fecundity.

Jensen *et al*. (1998) investigated prospectively alcohol intake in 430 Danish couples attempting to conceive for the first time. A maximum of six menstrual cycles were studied. Records of vaginal bleeding and sexual intercourse were kept daily. Alcohol consumption was monitored retrospectively for 1 week every month. It was concluded that the chances of successful conception decreased with increasing alcohol intake. The fecundity odds ratio (odds of conception among exposed couples divided by the odds amongst those not exposed) fell from 0.61 (10–50 g of alcohol per week) to 0.34 (100 g of alcohol).

Another prospective study (Hakim *et al*., 1998) reached a similar conclusion.

Investigation of 124 women attempting to conceive and who had ovulated (as evidenced by urinary hormone analysis) revealed that the number of conceptions (expressed as a percentage of the number of menstrual cycles) was 24.5% for nonsmokers and abstainers, 21.6% for abstainers who smoked, 14.3% for women drinking 1–12 g of alcohol per week, 10.5% (13–90 g alcohol per week) and 10.9% for >91 g alcohol per week. Incidents of sexual intercourse were recorded and thus a measure of menstrual cycles where conception was likely was obtained. It is important to note that women with anovular cycles were excluded from analysis and neither Hakim *et al*. (1998) nor the previous study authors (Jensen *et al*., 1998) investigated the pattern of drinking across the days of the cycle. Indeed Jensen *et al*. (1998) investigated drinking behaviour only in the week corresponding to days 14–21 of the cycle. Hakim *et al*. (1998) monitored consumption in the previous month.

Several studies have failed to show a negative effect of moderate alcohol consumption on fecundity (Florack *et al*., 1994; Zaadstra *et al*., 1994; Curtis *et al*., 1997; Parazzini *et al*., 1999). In this last study the mean recall period for alcohol drinking was 10 years. Zaadstra *et al*. (1994) investigated women attending an artificial donor insemination clinic and alcohol drinking was only assessed for the 1 week immediately before admission. Parazzini *et al*. (1999) reported that alcohol consumption up to a level of three 'glasses' per week had no effect on fertility in 1769 Italian women, but neither Parazzini *et al*. (1999) nor Florack *et al*. (1994) obtained drinking data prospectively.

If indeed there is an association between alcohol intake and reduced fecundity, then it is possible to suggest, albeit speculatively, a link between literature reports of a decreased incidence of ovulation in young women (Friedman and Meares, 1979; Metcalf and Mackenzie, 1980) and the level of binge drinking reported within this same age group (24% within female university students according to Webb *et al*., 1996).

GENERAL DISCUSSION

Consideration of the implications of the findings discussed above must be preceded by three important caveats. Firstly it must be stressed that it is often difficult to compare directly the alcohol dose administered in the various studies. The amount of alcohol in a standard 'drink' varies between countries (e.g. 8 g in the UK and 12 g in the US). Fortunately, some investigators routinely quote alcohol intake in grams, but others still persist with the more elastic measure of 'drinks'. The second point is that the protocol employed in some experimental studies may have compromised the relevance of the findings to the situation of the normal, socially drinking woman. For example, women have been asked to consume several units of alcohol, in a set time period, after an overnight fast; a situation far removed from usual drinking behaviour and one which may have quite different ramifications for the reproductive system. Finally, it must be emphasized that a too simplistic approach to the interpretation of study findings and therefore their physiological relevance must be avoided. It is not possible to overstate the complexity of the hormonal interplay that exists between the hypothalamus, pituitary and gonads. Indeed, considerable intra- and inter-individual variations in hormone levels exist in the normal population. Furthermore, the simple change in the level of a hormone does not necessarily imply that a physiological change must ensue. Changes in a particular fraction of a hormone, or in its ratio to another hormone, may be far more biologically significant.

A variety of study designs have reported an alcohol-induced rise in oestrogen levels. Mendelson *et al*. (1987) attributed this to a side-effect of alcohol metabolism on the oxidation of oestradiol, whereas Gavaler *et al*. (1993) attributed it to increased aromatization of testosterone to oestradiol. It is possible that both mechanisms may be operating.

In considering the implications of an alcohol-induced rise in plasma oestrogen level, two questions merit discussion. Does the rise in oestrogen have implications for women's reproductive health and also their general health? With respect to the first question, Mendelson *et al*. (1989) suggested that increased oestradiol levels reduce FSH secretion to levels which in turn, by suppressing folliculogenesis, lead to anovulation. The most obvious consequences of this scenario would be infertility. Studies cited earlier do indeed provide some evidence for a link between moderate alcohol consumption and decreased fecundity. However, it must be noted that one of these investigations (Hakim *et al*., 1998) excluded women showing evidence of anovulatory cycles. However, failure to ovulate is only one of several reasons for infertility. Alcohol may also affect implantation or early development of the blastocyst. A detrimental effect of alcohol on progesterone levels could, if proven, be relevant here.

If Mendelson *et al*. (1989) are correct and ovulation is indeed prevented by moderate alcohol intake, then even for women not wanting to become pregnant there are still harmful effects to consider; the cardioprotective hormone characteristic of the second (luteal) phase of the menstrual cycle will not be produced. The implications of the long-term loss of these hormones in young women are considerable.

In terms of general health, both negative (for example cancer risk) and positive (for example, protection against osteoporosis and cardiovascular disease) repercussions of raised oestrogen levels merit discussion. In addition, Eriksson *et al*. (1996) have reported an oestrogen-related rise in acetaldehyde levels in blood in women after alcohol intake (acetaldehyde has well-described toxic effects), while Tang *et al*. (1996) have reported that oestrogens may both delay the onset of Alzheimer's disease and decrease the risk of its development.

Further studies are required to investigate the proposal by Torgerson *et al*. (1994, 1997) that chronic moderate alcohol

intake is responsible for a delayed onset of the menopause, as this finding is in sharp contrast to the evidence from studies which have investigated alcohol-misusing women (Gavaler, 1985). In the latter case, alcohol is associated with an early menopause. The menopause signals the end of the period of life associated with high levels of the cardioprotective reproductive hormones. Therefore a relatively simple way of delaying this occurrence would seem, at first sight, to have obvious health benefits for women and merit investigation. Cessation of menstrual cycles is attributed to the limited supply of ovarian follicles present at birth, a small number being lost at each cycle. Thus the timing of the menopause is preprogrammed. Does chronic moderate alcohol use prolong reproductive life by decreasing the number of follicles in the cohort destined for maturation each cycle? Alternatively, does alcohol, via increased oestrogen levels, ensure that menstrual cycles continue but that they are all anovular? In the latter case, any benefits for women's health of a delayed menopause would be reduced.

Presently, research provides more questions than answers. For older women, the potential health benefits of chronic moderate alcohol consumption have received some attention, but the consequences for those on hormone replacement therapy merit further clarification. For younger women, it seems certain that binge drinking (although still remaining within weekly guidelines) is likely to have quite different health repercussions than regular moderate consumption. In the specific case of reproductive health, binge drinking may be most detrimental at certain times, namely puberty, the cyclical selection of follicles for maturation, ovulation and the implantation and subsequent survival of the blastocyst. It is clear, however, that, if women at all life stages are to receive meaningful and beneficial health messages, further investigations are urgently required.

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REFERENCES

Ahluwalia, B., Smith, D., Adeyiga, O., Akbasak, B. and Rajguru, S. (1992) Ethanol decreases progesterone synthesis in human placental cells: mechanism of ethanol effect. *Alcohol* **9**, 395–401.

Curtis, K. M., Savitz, D. A. and Arbuckle, T. E. (1997) Effects of cigarette smoking, caffeine consumption and alcohol intake on fecundability. *American Journal of Epidemiology* **146**, 32–41.

Department of Health (1995) *Sensible Drinking*. Report of an interdepartmental working group. Department of Health, London.

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

Eriksson, C. J., Fukunaga, T., Sarkola, T., Lindholm, H. and Ahola, L. (1996) Estrogen-related acetaldehyde elevation in women during alcohol intoxication. *Alcoholism: Clinical and Experimental Research* **20**, 1192–1195.

Florack, E. I. M., Zielhuis, G. A. and Rolland, R. (1994) Cigarette smoking, alcohol consumption and caffeine intake and fecundability. *Preventive Medicine* **23**, 175–180.

Friedman, J. and Meares, R. A. (1979) The menstrual cycle and habituation. *Psychosomatic Medicine* **41**, 369–381.

Gavaler, J. S. (1985) A review of alcohol effects on endocrine function in postmenopausal women: What we know, what we need to know, and what we do not yet know. *Journal of Studies on Alcohol* **46**, 495–516.

Gavaler, J. S. and Love, K. (1992) Detection of the relationship between moderate alcoholic beverage consumption and serum levels of estradiol in normal postmenopausal women: effect of alcohol consumption, quantitative methods and sample size adequacy. *Journal of Studies on Alcohol* **53**, 389–394.

Gavaler, J. S. and Van Thiel, D. H. (1992) The association between moderate alcoholic beverage consumption and serum estradiol and testosterone levels in normal postmenopausal women; relationship to the literature. *Alcoholism: Clinical and Experimental Research* **16**, 87–92.

Gavaler, J. S., Love, K., Van Thiel, D., Farholt, S., Gluud, C., Monteiro, E., Galvao-Teles, A., Ortego, T. C. and Cuervas-Mons, V. (1991) An international study of the relationship between alcohol consumption and postmenopausal estradiol levels. *Alcohol and Alcoholism* **26** (Suppl. 1), 220–227.

Gavaler, J. S., Deal, S. R., Van Thiel, D. H., Arria, A. and Allan, M. J. (1993) Alcohol and estrogen levels in postmenopausal women: the spectrum of effect. *Alcoholism: Clinical and Experimental Research* **17**, 786–790.

Gill, J. S. (1997) Women, alcohol and the menstrual cycle. *Alcohol and Alcoholism* **32**, 435–441.

Ginsburg, E. S., Walsh, B. W., Gao, X., Gleason, R. E., Feltmate, C. and Barbeiri, R. L. (1995*a*) The effect of acute ethanol ingestion on estrogen levels in postmenopausal women using transdermal estradiol. *Journal of the Society for Gynecologic Investigation* **2**, 26–29.

Ginsburg, E. S., Walsh, B. W., Shea, B. F., Gao, X., Gleason, R. E. and Barbeiri, R. L. (1995*b*) The effects of ethanol on the clearance of estradiol in postmenopausal women. *Fertility and Sterility* **63**, 1227–1230.

Ginsburg, E. S., Mello, N. K., Mendelson, J. H., Barbeiri, R. L., Teoh, S. K., Rothman, M., Gao, X. and Sholar, J. W. (1996) Effect of alcohol ingestion on estrogens in postmenopausal women. *Journal of the American Medical Association* **276**, 1747–1751.

Gordon, G. G., Altman, K. and Southern, A. L. (1976) Effect of alcohol (ethanol) administration on sex-hormone metabolism in normal men. *New England Journal of Medicine* **295**, 793–797.

Grodstein, F., Goldman, M. B. and Cramer, D. W. (1994) Infertility in women and moderate alcohol use. *American Journal of Public Health* **84**, 1429–1432.

Hakim, R. B., Gray, R. H. and Zacur, H. (1998) Alcohol and caffeine consumption and decreased fertility. *Fertility and Sterility* **70**, 632–637.

Hankinson, S. E., Willett, W. C., Manson, J. E., Hunter, D. J., Colditz, G. A., Stampfer, M. J., Longcope, C. and Speizer, F. E. (1995) Alcohol, height and adiposity in relation to estrogen and prolactin levels in postmenopausal women. *Journal of the National Cancer Institute* **87**, 1297–1302.

Jensen, T. K., Hjollund, N. H., Henriksen, T. B., Scheike, T., Kolstad, H., Giwercman, A., Ernst, E., Bonde, J. P., Skakkebaek, N. E. and Olsen, J. (1998) Does moderate alcohol consumption affect fertility? Follow-up study among couples planning first pregnancy. *British Medical Journal* **317**, 505–510.

Katsouyanni, K., Boyle, P. and Trichopoulous, D. (1991) Diet and urine estrogens among post-menopausal women. *Oncology* **48**, 490–494.

Mendelson, J. H., Mello, N. K., Cristofaro, P., Ellingboe, J., Skupny, A., Palmieri, S. L., Benedikt, R. and Schiff, I. (1987) Alcohol effects on naloxone-stimulated luteinizing hormone, prolactin and estradiol in women. *Journal of Studies on Alcohol* **48**, 287–294.

Mendelson, J. H., Lukas, S. E., Mello, N. K., Amass, L., Ellingboe, J. and Skupny, A. (1988) Acute alcohol effects on plasma estradiol levels in women. *Psychopharmacology* **94**, 464–467.

Mendelson, J. H., Mello, N. K., Teoh, S. K. and Ellingboe, J. (1989) Alcohol effects on luteinizing hormone releasing hormone-stimulated anterior pituitary and gonadal hormones in women. *Journal of Pharmacology and Experimental Therapeutics* **250**, 902–909.

Metcalf, M. G. and MacKenzie, J. A. (1980) Incidence of ovulation in young women. *Journal of Biosocial Sciences* **12**, 345–352.

Muti, P., Trevisan, M., Micheli, A., Krogh, V., Bolelli, G., Sciaryno, R., Schunemann, H. J. and Berrino, F. (1998) Alcohol consumption and total oestradiol in premenopausal women. *Cancer Epidemiology, Biomarkers and Prevention* **7**, 189–193.

Nagata, C., Kabuto, M., Takatsuka, N. and Shimizu, H. (1997) Associations of alcohol, height and reproductive factors with serum hormone concentrations in postmenopausal Japanese women. *Breast Cancer Research and Treatment* **44**, 235–241.

Nagata, C., Takatsuka, N., Inaba, S., Kawakami, N. and Shimizu, H. (1998) Associations of diet and other lifestyle with the onset of menopause in Japanese women. *Maturitas* **29**, 105–113.

Olsen, J., Bolumar, F., Boldsen, J. and Bisanti, L. and the European Study Group of Infertility and Subfecundity (1997) Does moderate alcohol intake reduce fecundability? A European multicentre study on infertility and subfecundity. *Alcoholism: Clinical and Experimental Research* **21**, 206–212.

Parazzini, F., Chalenoud, L., DiCintio, E., LaVecchia, C., Benzi, G. and Fedele, L. (1999) Alcohol consumption is not related to fertility in Italian women. *British Medical Journal* **318**, 397.

Purohit, V. (1998) Moderate alcohol consumption and estrogen levels in postmenopausal women: a review. *Alcoholism: Clinical and Experimental Research* **22**, 994–997.

Reichman, M. E., Judd, J. T., Longcope, C., Schatzkin, A., Clevidence, B. A., Nair, P. P., Campbell, W. S. and Taylor, P. R. (1993) Effects of moderate alcohol consumption on plasma and urinary hormone concentrations in premenopausal women. *Journal of the National Cancer Institute* **85**, 722–727.

Sarkola, T., Mäkisalo, H., Fukunaga, T. and Eriksson, C. J. P. (1999) Acute effect of alcohol on estradiol, estrone, progesterone, prolactin, cortisol and luteinizing hormone in premenopausal women. *Alcoholism: Clinical and Experimental Research* **23**, 976–982.

Tang, M., Jacobs, D., Stern, Y., Marder, K., Schofiled, P., Garland, B., Andrews, H. and Mayeaux, R. (1996) Effect of oestrogen during menopause on risk and onset of Alzheimer's disease. *Lancet* **348**, 429–432.

Teoh, S. K., Mendelson, J. H., Mello, N. K. and Skupny, A. (1988) Alcohol effects on naltrexone-induced stimulation of pituitary, adrenal and gonadal hormones during the early follicular phase of the menstrual cycle. *Journal of Clinical Endocrinology and Metabolism* **66**, 1181–1186.

Teoh, S. K., Mendelson, J. H., Mello, N. K., Skupny, A. and Ellingboe, J. (1990) Alcohol effects on hCG-stimulated gonadal hormones in women. *Journal of Pharmacology and Experimental Therapeutics* **254**, 407–411.

Thorell, B. and Svardsudd, K. (1993) Myocardial infarction risk factors and well-being among 50-year-old women before and after the menopause. The population study '50-year-old people in Kungsor'. *Scandinavian Journal of Primary Health Care* **11**, 141–146.

Torgerson, D. J., Avenall, A., Russell, I. T. and Reid, D. M. (1994) Factors associated with the onset of menopause in women aged 45–49. *Maturitas* **19**, 83–92.

Torgerson, D. J., Thomas, R. E., Campbell, M. K. and Reid, D. M. (1997) Alcohol consumption and age of maternal menopause are associated with menopause onset. *Maturitas* **26**, 21–25.

Tseng, L. and Gurpide, E. (1979) Stimulation of various 17β- and 20α-hydroxysteroid dehydrogenase activities by progestins in human endometrium. *Endocrinology* **104**, 1745–1748.

Webb, E., Ashion, C. H., Kelly, P. and Kamili, F. (1996) Alcohol and drug use in UK university students. *Lancet* **348**, 922–925.

Zaadstra, B. M., Habbema, J. D. F., Looman, C. W. N., Karbaat, J. and Velde, E. R. (1994) Moderate drinking: no impact on female fecundity. *Fertility and Sterility* **62**, 948–954.