Effect of chronic alcoholism on male fertility hormones and semen quality

K. R. Muthusami, M.Phil., and P. Chinnaswamy, Ph.D.

The Tamil Nadu Dr. M.G.R. Medical University, Chennai, India

Objective: To evaluate the effects of chronic alcoholism on the male fertility hormones and quality of semen.
Design: Non-probability purposive clinical study.
Setting: Addiction treatment center and an academic research environment.
Patient(s): Sixty-six alcoholics free from smoking and drug abuse who consumed a minimum of 180 mL of alcohol per day (brandy and whisky, both 40%–50% alcohol content) for a minimum of 5 days per week for ≥1 year were included. Thirty nonsmoking nonalcoholics were selected as controls.
Intervention(s): Before starting the addiction treatment for alcoholics, venous blood and semen samples were collected.
Main Outcome Measure(s): Complete blood counts, biochemical parameters, levels of the male fertility hormones FSH, LH, T, PRL, P, and E_2 in blood, and semen parameters.
Result(s): In alcoholics, FSH, LH, and E_2 levels were significantly increased, and T and P levels were significantly decreased. No significant change was noted in PRL levels. Semen volume, sperm count, motility, and number of morphologically normal sperm were significantly decreased.
Conclusion(s): Chronic alcohol consumption has a detrimental effect on male reproductive hormones and on semen quality. (Fertil Steril® 2005;84:919–24. ©2005 by American Society for Reproductive Medicine.)

Key Words: Alcohol, FSH, LH, testosterone, progesterone, estradiol, semen, sperm

Impotence, testicular atrophy, gynecomastia, and loss of sexual interest are often associated with alcoholism in men (1). Sexual disorders have been reported in men who are long-term alcohol users, with the prevalence ranging from 8% to 58% (2). Lemere and Smith (3) reported that 8% of 17,000 patients treated for alcoholism were impotent. The reported prevalence of lack of sexual desire ranged from 31% to 58% in long-term alcohol users (4–6). Fifty-four percent of hospitalized alcoholic men and 24% of healthy controls had erectile impotence (4). In 1984, Jensen (5) reported that 63% of married alcoholic men and 10% of controls had sexual dysfunction, especially lack of sexual desire.

Use of ethanol might cause gonadal disorders, including structural testicular changes and a decrease in testicular and serum levels of T, which might be involved in the hypogonadism and feminization phenotype. Ethanol and its metabolite acetaldehyde cause a reduction in LH binding to Leydig cells, an inhibition of the enzymes responsible for the formation of sex hormones (7, 8).

Van Thiel et al. (9) demonstrated that ethanol acts as a Leydig cell toxin. Moreover, ethanol increases the metabolic clearance rate of T concomitant with an increase in hepatic 5α-reductase activity and increases conversion of androgens into estrogens. Sperm cells might be selectively affected by various substances throughout the process of spermatogenesis to spermiogenesis (10).

Both acute and chronic alcohol intoxication result in dose-dependent suppression of plasma T levels in normal men (11, 12). Alcohol-induced suppression of male T is due to a direct effect on the biosynthetic processes in the testes (13–16). Increased LH levels after alcohol-induced suppression of T in men (11, 12) and male monkeys (17) is consistent with established mechanisms of negative feedback of LH secretory activity.

Alcohol seems to exert a dual effect on the hypothalamic–pituitary–gonadal axis by directly inhibiting testicular steroidogenesis and by blocking the release of LH-releasing hormone/LH from the hypothalamic–pituitary axis (18).

In human semen, ethanol produces a significant decrease in the percentage of motility, straight-line velocity, and curvilinear velocity of sperm. Alcohol causes a significant decrease in the number of spermatozoa with normal morphology and an increase in irreversible tail defects (19).

The sperm of ethanol-consuming animals exhibit alterations in their spermatozoa concentration, abnormal motility and morphology, and a decrease of the fecundation capability (20). It has been reported that ethanol abusers might exhibit sperm alterations, such as changes in the count, morphology, and viability of the spermatozoa (21–23). Alcohol exerts a dose-related toxic effect on testicular function. Spermatogenesis disruption and a primary testicular insuffi-

Received September 30, 2004; revised and accepted April 25, 2005.
Reprint requests: K. R. Muthusami, M.Phil., Institute Of Laboratory Medicine, Kovai Medical Center and Hospital, Avanashi Road, Coimbatore 641 014, India (FAX: 0091-442-2627782; E-mail: muthusamikr@yahoo.co.in).

ciency and compensatory increase of FSH and LH secretion have been observed in alcoholics (24, 25).

A reduction in sperm concentration and in the percentage of spermatozoa with normal morphology has been detected in chronic alcoholics and in smokers. The above modifications suggest a synergistic or additive effect of both toxic habits on male reproductive function. Men who wish to procreate should be specifically warned of this matter (26).

Drinking alcohol is considered a common social entertainment. In the present study, reproductive function in chronic alcoholics was assessed to know the effects of alcoholism on reproductive function. The intent of the study was also to help physicians treating alcoholics to have a better idea of these patients' reproductive function.

MATERIALS AND METHODS

Subjects

This study was conducted at the Kasthuriba Gandhi Memorial Deaddiction Center in Coimbatore city, Tamil Nadu, India. We screened a total of 1,300 alcoholics who had reported to the Kasthuriba Gandhi Memorial Deaddiction Center and 300 nonalcoholic nonsmoking volunteers (as controls) from Coimbatore city. The study population consisted of 66 nonsmoking alcoholics, aged 36.6 ± 5.7 years (mean ± SD). Alcoholics consuming drugs like diazepam, pethidine, cannabis, and marijuana along with alcohol were excluded from the study. The control population consisted of 30 normal healthy persons aged 35.0 ± 6.1 years.

All subjects were examined by a physician before inclusion in the study. Personal interviews were conducted with all alcoholic and control subjects to obtain relevant clinical data: age, sex, domicile (urban vs. rural dwelling), marital status, diet, history of alcohol consumption, infertility status, past medical illness and treatment, history of smoking, sexual urgency and frequency, and premarital and extramarital sexual history. Sexual function (e.g., erectile function, libido potency, frequency of ejaculation) was also noted in the questionnaire.

Experimental Design

The study included two subject groups, controls and alcoholics. Subjects in the control group were volunteers who were free from any disease and who had never consumed alcoholic drinks and who had never smoked. Subjects in the alcoholic group were nonsmokers who had consumed a minimum of 180 mL of alcohol (brandy and whisky, both 40%–50% alcohol content) per day for a minimum of 5 days per week in the past year.

Seminal Parameters

Semen samples were collected after at least 48 hours but no more than 7 days of sexual abstinence. The semen sample was collected by masturbation and delivered to the laboratory within ½ hour from the time of collection. After liquefaction, semen appearance, volume, consistency, pH, fructose, and sperm motility, concentration, viability, and morphology were analyzed as per the criteria of the World Health Organization (27). Motility was expressed as percentages of rapid progressively motile, slow or sluggishly motile, nonprogressively motile, and immotile sperm. Sperm viability was expressed as percentages of live and dead sperm, and sperm morphology was expressed as percentages of sperm with normal morphology, head-defective morphology, neck-defective morphology, and tail-defective morphology.

Male Fertility Hormones

Ten milliliters of venous blood was collected, and 5 mL of blood was transferred into a clean conical centrifuge tube with no anticoagulant. Serum was separated and stored at −20°C until use. The remaining 5 mL of blood was added to a Vacutainer tube containing ethylenediaminetetraacetic acid, and the complete hemogram in the blood was analyzed with Cell Dyn 1700 (Abbott Laboratories, Abbott Park, IL).

The routine biochemical parameters were analyzed with Hitachi 912 (Roche Diagnostics, Penzberg, Germany). Serum levels of FSH, T, E_2, P, and PRL were measured by the electro-chemiluminescence immunoassay method (Elecsys 1010; Roche Diagnostics), and LH was analyzed by ELISA (Cobas Core II; Roche Diagnostics). All the results were expressed in conventional units.

The results for both groups are expressed as mean ± SD. The results were analyzed statistically with commercial software (SPSS for Windows 7.5.1; SPSS, Chicago, IL). Student's *t*-test was used to determine the degree of significance for the various mean variables obtained. Semen nonparametric values (liquefaction, appearance, volume, consistency, pH, and fructose) were analyzed with the χ^2 test.

RESULTS

For alcoholics, the mean number of days of alcohol consumption per week was 6.1 ± 1.1, for a mean period of 4.5 ± 2.9 consecutive years. The mean volume of alcohol consumption was 441.1 ± 323.9 mL/day.

No significant differences were found between alcoholics and controls for any of the routine biochemical parameters (blood glucose, creatinine, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol, total bilirubin, total protein, albumin, albumin/globulin ratio, γ glutamyl transferase, alkaline phosphatase, and serum glutamate pyruvate transaminase). Neither were any significant differences found between the two groups for any of the hematologic parameters (hemoglobin, total white blood corpuscle count, differential white blood corpuscle count, platelet count, total red blood corpuscle count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and packed cell volume).

TABLE 1

Fertility hormone levels in controls and alcoholics.

Hormone	Controls (n = 30)	Alcoholics (n = 66)	*t* value
FSH (mIU/mL)	4.60 ± 1.94	7.41 ± 4.16	4.512[a]
LH (mIU/mL)	4.69 ± 2.43	7.22 ± 3.07	4.329[a]
PRL (ng/mL)	19.33 ± 5.03	18.37 ± 12.40	0.536 (NS)
T (ng/mL)	5.88 ± 2.07	4.41 ± 1.03	3.714[a]
E_2 (pg/mL)	34.28 ± 12.39	52.35 ± 28.71	4.306[a]
P (ng/mL)	0.71 ± 0.25	0.52 ± 0.20	3.737[a]

Note: Values are expressed as mean ± SD. NS = nonsignificant.
[a] $P<.001$.

Muthusami. Male fertility profile in alcoholism. Fertil Steril 2005.

Male Fertility Hormones

Regarding the correlation between libido and T, alcoholics showed decreased libido due to decreased levels of T, but controls showed no significant decrease in libido and T. It was also found that 71% of alcoholics and 7% of controls had erectile impotence.

Alcoholics showed a statistically significant increase in FSH ($P<.001$) and LH ($P<.001$) levels compared with controls. Prolactin ($P<.536$) did not show any statistically significant change in alcoholics compared with controls (Table 1).

The mean T ($P<.001$) and P ($P<.001$) levels in the alcoholic group showed statistically significant decreases compared with the control group. The mean E_2 ($P<.001$) level in alcoholics showed a statistically significant increase compared with controls.

Seminal Parameters

In the alcoholic group, sperm count ($P<.001$), percentage of rapid progressively motile sperm ($P<.001$), percentage of live sperm ($P<.001$), and percentage of morphologically normal sperm ($P<.001$) were statistically significantly decreased compared with the control group (Table 2).

The percentages of slow progressively motile sperm ($P<.001$), nonprogressively motile sperm ($P<.001$), immotile sperm ($P<.001$), dead sperm ($P<.001$), head-defective sperm ($P<.001$), neck-defective sperm ($P<.001$), and tail-defective sperm ($P<.022$) were all statistically significantly increased compared with the control group. Chi-square values for semen appearance, pH, viscosity, liquefaction, and fructose between controls and alcoholics did not show any statistical significance.

TABLE 2

Seminal parameter values in controls and alcoholics.

Seminal parameter	Controls (n = 30)	Alcoholics (n = 66)	*t* value
Semen volume (mL)	2.17 ± 0.712	1.56 ± 0.79	3.761[a]
Sperm count ($\times 10^6$/mL)	132.97 ± 89.02	51.99 ± 44.71	4.719[a]
Rapid progressively motile sperm (%)	56.10 ± 8.72	30.38 ± 15.82	10.229[a]
Slow progressively motile sperm (%)	21.48 ± 2.76	29.02 ± 8.37	6.571[a]
Nonprogressively motile sperm (%)	2.50 ± 1.07	4.10 ± 2.21	4.782[a]
Immotile sperm (%)	20.17 ± 8.25	35.91 ± 13.01	7.161[a]
Live sperm (%)	80.80 ± 6.29	60.20 ± 16.61	8.783[a]
Dead sperm (%)	19.20 ± 6.29	39.77 ± 16.62	8.767[a]
Morphologically normal sperm (%)	82.00 ± 9.76	67.17 ± 16.73	5.447[a]
Head-defective sperm (%)	11.30 ± 7.81	18.27 ± 9.43	3.791[a]
Neck-defective sperm (%)	4.27 ± 2.70	9.05 ± 5.82	5.493[a]
Tail-defective sperm (%)	2.43 ± 1.68	5.56 ± 5.02	2.347[b]

Note: Values are expressed as mean ± SD. NS = nonsignificant.
[a] $P<.001$.
[b] $P<.01$.

Muthusami. Male fertility profile in alcoholism. Fertil Steril 2005.

DISCUSSION

It is evident from the report of the physician and from the biochemical and hematologic analysis that all the alcoholics and controls in this study were free from diabetes mellitus, hypertension, renal failure, liver failure, anemia, malnutrition, and chronic infections.

Sexual disorders have been reported frequently in chronic alcoholics. The present study on decreased libido and erectile impotence is supported by the studies of Mulligan et al. (28), Rosen (29), and Gumus et al. (6), which showed that high levels of blood alcohol cause reduced sexual stimulation, inability to enjoy orgasm, and retarded ejaculation. Whalley (4) reported that 54% of hospitalized alcoholic men and 24% of healthy controls had erectile impotence. Jensen (5) reported that 63% of married alcoholic men and 10% of controls had sexual dysfunction due to lack of sexual desire.

The present study showed increased FSH levels in alcoholics. It is the direct toxic effect of alcohol on the testis that leads to decreased seminiferous tubular function. The FSH elevation is due to the absence of testicular feedback regulation at the pituitary level.

The present results correlate with those of Gumus et al. (6), who reported that serum FSH levels are higher in chronic alcoholics. Similar findings have been reported by Van Thiel et al. (30), who found that FSH levels increased in alcohol-fed animals. The decreased total sperm count in semen found in the present study is also confirmed by Lindholm et al. (24), who found increased FSH levels in alcoholics with severe spermatogenesis disruption.

Because alcohol enters into the testis directly, causing decreases in spermatogenesis and T synthesis, it causes the increased level of LH found in chronic alcoholics. The results of this study are supported by those of Heinz et al. (31), Sengupta et al. (32), and Bannister and Lowosky (7), who found that LH levels were increased in chronic alcoholics.

In the present study, the decreased T and increased LH levels in alcoholics suggest that the major effect of alcohol on plasma T in humans is exerted on the testis at a peripheral site rather than on the hypothalamic–pituitary axis at a central site. This finding is supported by those of Mendelson et al. (11), Gordon et al. (33), Lester and Van Thiel (34), and Van Thiel et al. (35), who reported that decreased T levels were accompanied by increased LH levels in alcoholics.

The present study demonstrates that alcohol does not produce any change in PRL levels. This shows that alcohol in the chronic state acts at the peripheral testis level rather than at the central hypothalamic–pituitary level. Contrary to this, Ching and Lin (36) reported that alcohol could increase dopamine stores in the median eminence. An increased dopamine signal from hypothalamic neurons might have suppressed PRL secretion by the pituitary lactotrophs. Decreased plasma T levels, as found in the present study, correlate with study results from Van Thiel (37) and Ida et al. (38).

In alcoholics, decreased T levels are due to decreased synthesis of T in the testis or to increased metabolic clearance of T. Increased metabolic clearance of T by the stimulation of aromatase, a key enzyme in the conversion of T to E_2, leads to an increase in E_2 levels. The statistically significant increase of E_2 levels in chronic alcoholics in the present study is supported by the findings of Van Thiel et al. (39), Gordon et al. (40), Van Thiel et al. (34), and Emanuele et al. (41).

Decreased P levels in chronic alcoholics are due to decreased action or synthesis of 3β hydroxysteroid dehydrogenase, a rate-limiting enzyme for the conversion of pregnenolone to P. It is evident that the sites of alcohol-induced inhibition in the steroidogenic pathway observed in vitro are the reactions from pregnenolone to P by the nicotinamide adenine–dependent 3β-hydroxysteroid dehydrogenase/oxosteroid isomerase and from androstenedione to T by the nicotinamide adenine dinucleotide phosphate–dependent 17-ketosteroid reductase (42–45).

Progesterone is the precursor for the synthesis of T. Alcohol might suppress the action of the enzyme 3β hydroxysteroid dehydrogenase responsible for the synthesis of progesterone and T. The inadequate availability of P might lead to decreased synthesis of T. It is evident from this study that alcohol induces a bidirectional effect on T reduction, by [1] decreasing the synthesis of T in testis by decreasing the progesterone, and/or by [2] enhancing T metabolism.

Because the present study finds no statistically significant changes in alcoholics' semen appearance, pH, viscosity, liquefaction, and fructose, the accessory sex organs ductuli efferentes, seminal vesicle, prostate, bulbourethral (Cowper) gland, and urethral (Littre) gland are found to have normal functions.

The decreased sperm count found in the present study is supported by Brzek (46), who found that alcohol consumption decreases semen volume, density, and motility. The abnormal sperm morphology noted in the present study is supported by Goverde et al. (23), who found that daily alcohol consumption decreases normal sperm morphology. The statistically significant decrease in sperm count in the present study is confirmed by Carlsen et al. (47), who found a significant decrease in mean sperm count, from 113 $\times$ 10^6/mL to 66 $\times$ 10^6/mL.

Gomathi et al. (22) and Goverde et al. (23) reported decreased sperm motility in alcoholics, which is in accordance with the findings of the present study. Goverde et al. (23) observed a significant decrease in the viability of sperm in alcoholics, and this has been confirmed by the present study. The decreased number of morphologically normal sperm and increased number of morphologically defective sperms as found in the present study are supported by the findings of Donnelly et al. (19), Gomathi et al. (22), and Nagy et al. (21), who reported that alcohol consumption decreases the number of sperm with normal morphology

and increases the number of sperm with morphological abnormalities.

CONCLUSIONS

It is evident from the results of the present study that chronic alcoholism suppresses both blood hormonal levels and reduces semen quality. In Leydig cells, alcohol decreases the male sex hormone T. Furthermore, it decreases P and increases E_2 levels in blood. Because of the suppression of blood levels of T in alcoholics, the pituitary feedback regulation is altered. The pituitary LH is increased in blood as a compensatory mechanism. At the seminiferous tubular level, alcohol decreases semen volume, total sperm concentration, motility of sperm, number of morphologically normal sperm, and viability of sperm. The pituitary FSH level in blood is increased because of the loss of seminiferous tubular function in alcoholics.

This study has proved beyond doubt that chronic alcohol consumption has a detrimental effect on male reproductive hormones and on the quality of semen, which, in turn, will make people who are addicted to alcohol impotent and sterile. Hence, men are advised to refrain from chronic alcohol consumption if they want to procreate and lead a normal sexual life.

Acknowledgments: The authors thank Drs. Nalla G. Palaniswami and Thavamani Devi Palaniswami, Chairman and Vice Chairman of the Kovai Medical Center (Coimbatore, India) for providing facilities for this study; Dr. D. Srinivasan for his help in recruiting participants from the Kasthuriba Gandhi Deaddiction Center (Coimbatore, India); Mr. Ananthan, psychologist at the Kasthuriba Gandhi Deaddiction Center, for his enthusiastic support and guidance; Mrs. R. Kavitha, biochemist, Mr. Badhuru Belli and Mrs. R. Radhamani, laboratory technologists, and all the Laboratory Medicine staff at Kovai Medical Center for their valuable assistance during the analysis; and Mr. K. Vijaykumar of Mede Systems (Coimbatore, India) and Mr. Z. M. Saifudeen, Zonal Manager, Nicholos Pirmal India, for their help in procuring the reagent kits.

REFERENCES

1. Boyden TW, Pamenter RW. Effect of ethanol on the male hypothalamic-pituitary-gonadal axis. Endocr Rev 1983;4:389–95.
2. Schiavi RC. Chronic alcoholism and male sexual dysfunction. J Sex Marital Ther 1990;16:23.
3. Lemere F, Smith JW. Alcohol induced sexual impotence. Am J Psychiatry 1973;130:212–3.
4. Whalley LJ. Sexual adjustment of male alcoholics. Acta Psychiatr Scand 1978;58:281–98.
5. Jensen SB. Sexual function and dysfunction in younger married alcoholics. Acta Psychiatr Scand 1984;69:543–9.
6. Gumus B, Yigitoglu MR, Lekili M, Uyanik BS, Muezzinoglu T, Buyuksu C. Effect of long-term alcohol abuse on male sexual function and serum gonadal hormone levels. Int Urol Nephrol 1998;30:755–9.
7. Bannister P, Losowsky MS. Ethanol and hypogonadism. Alcohol Alcohol 1987;22:213–7.
8. Adler RA. Clinically important effects of alcohol on endocrine function. Clinical review 33. J Clin Endcrinol Metab 1992;74:957–60.
9. Van Thiel DH, Galaver PK, Cobb CF, Santucci L, Graham TO. Ethanol, a Leydig cell toxin: evidence obtained in vivo and in vitro. Pharmacol Biochem Behav 1983;18:317–23.
10. Insler V, Lunenfeld B. Infertility: the dimension of the problem. In: Insler V, Lunenfeld B, eds. Infertility: male and female. 2nd ed. London: Churchill Livingstone, 1993.
11. Mendelson JH, Mello NK, Ellingboe J. Effects of acute alcohol intake on pituitary-gonadal hormones in normal human males. J Pharmacol Exp Ther 1977;202:676–82.
12. Valimaki MJ, Pelkonen R, Harkonen M, Ylikahri R. Hormonal changes in noncirrhotic male alcoholics during ethanol withdrawal. Alcohol Alcohol 1984;19:235–42.
13. Anderson RA, Willis BR, Oswald C, Reddy JM, Beyler SA, Zaneveld LJD. Hormonal imbalance and alterations in testicular morphology induced by chronic ingestion of ethanol. Biochem Pharmcol 1980;29:1409–19.
14. Eriksson CJP, Widenius TV, Leinonen P, Harkonen M, Ylikahri RH. Inhibition of testosterone biosynthesis by ethanol. Biochem J 1983;210:29–36.
15. Willis BR, Anderson RA Jr, Oswald C, Zaneveld LJD. Ethanol-induced male reproductive tract pathology as a function of ethanol dose and duration of exposure. J Pharmacol Exp Ther 1983;225:470–8.
16. Mello NK, Mendelson JH, Bree MP, Ellingboe J, Skupny AST. Alcohol effects on luteinizing hormone and testosterone in male macaque monkeys. J Pharmacol Exp Ther 1985;233:588–96.
17. McCann SM. Regulation of secretion of follicle-stimulating hormone and luteinizing hormone. In: Greep RO, Astwood EB, Knobil E, Sawyer WH, Geiger SR, eds. Handbook of physiology. Washington, DC: American Physiological Society, 1974:489–517.
18. Little PJ, Adams ML, Cicero TJ. Effects of alcohol on the hypothalamic-pituitary-gonadal axis in the developing male rat. J Pharmacol Exp Ther 1992;263:1056–61.
19. Donnelly GP, McClure N, Kennedy MS, Lewis SE. Direct effect of alcohol on the motility and morphology of human spermatozoa. Andrologia 1999;31:43–7.
20. Anderson RA, Willis BR, Oswald C, Zaneweld JL. Ethanol-induced male infertility: impairment of spermatozoa. J Pharmacol Exp Ther 1983;225:479–86.
21. Nagy F, Pendergrass PB, Bown DC, Yeager JC. A comparative study of cytological and physiological parameters of semen obtained from alcoholics and non-alcoholics. Alcohol Alcohol 1986;21:17–23.
22. Gomathi C, Balasubramanian K, Bhanu NV, Srikanth V, Govindarajulu P. Effect of chronic alcoholism on semen studies on lipid profiles. Int J Androl 1993;16:175–81.
23. Goverde HJ, Dekker HS, Janssen HJ, Bastiaans BA, Rolland R, Zielhuis GA. Semen quality and frequency of smoking and alcohol consumption. An explorative study. Int J Fertil Menopausal Stud 1995;40:135–8.
24. Lindholm J, Fabricius-Bjerre N, Bahnsen M, Boiesen P, Bangstrup L, Pedersen ML, et al. Pituitary-testicular function in patients with chronic alcoholism. Eur J Clin Invest 1978;8:269–72.
25. Villalta J, Ballesca JL, Nicolas JM, Martinez de Osaba MJ, Antunez E, Pimentel C. Testicular function in asymptomatic chronic alcoholics: relation to ethanol intake. Alcohol Clin Exp Res 1997;21:128–33.
26. Martini AC, Molina RI, Estofan D, Senestrari D, de Cuneo FM, Ruiz RD. Effects of alcohol and cigarette consumption on human seminal quality. Fertil Steril 2004;82:374–7.
27. World Health Organization. WHO laboratory manual for the examination of human semen and sperm-cervical mucus interaction. 4th ed. Cambridge, United Kingdom: Cambridge University Press, 1999.
28. Mulligan T, Retchin SM, Chinchilli V, Bettinger CB. The role of aging and chronic disease in sexual dysfunction. J Am Geriatr Soc 1988;36:520–4.
29. Rosen RC. Alcohol and drug effects on sexual response. Human experimental and clinical studies. Ann Rev Sex Res 1991;2:119–80.
30. Van Thiel DH, Galaver PK, Rosenblum E, Eagon YB. Effects of ethanol on endocrine cells: testicular effects. Ann N Y Acad Sci 1987;492:287–302.
31. Heinz A, Rommelspacher H, Graf KJ, Kurten I, Otto M, Baumgartner A. Hypothalamic-pituitary-gonadal axis, prolactin, and cortisol in alcoholics during withdrawal and after three weeks of abstinence: comparison with health control subjects. Psychiatry Res 1995;56:81–95.
32. Sengupta SN, Ray R, Shetty KT, Desai NG. Pituitary gonadal func-

tioning in male alcoholics in an Indian psychiatric hospital. Alcohol Alcohol 1991;26:47–51.
33. Gordon GG, Southern AL, Lieber CS. The effects of alcoholic liver disease and alcohol ingestion on sex hormone levels. Alcohol Clin Exp Res 1978;2:259–63.
34. Lester R, Van Thiel DH. Gonadal function in alcoholic men. Adv Exp Biol Med 1978;85A:399–414.
35. Van Thiel DH, Lester R, Vaitukaitis J. Evidence for a defect in pituitary secretion of luteinizing hormone in chronic alcoholic men. J Clin Endcrinol Metab 1978;47:499–507.
36. Ching M, Lin CY. Ethanol acutely reduces LH and prolactin secretion: possible involvement by dopamine. Alcohol 1994;11:105–12.
37. Van Thiel DH. Ethyl alcohol and gonadal function. Hosp Pract 1984; 11:152–8.
38. Ida Y, Tsujimaru S, Nakamaura K, Shiro I, Mukasa H Egami H, et al. Effects of acute and repeated alcohol ingestion on hypothalamic-pituitary-gonadal and hypothalamic-pituitary-adrenal functioning in normal males. Drug Alcohol Depend 1992;31:57–64.
39. Van Thiel DH, Gavaler JS, Smith WI Jr, Paul G. Hypothalamic-pituitary-gonadal dysfunction in man using cimetidine. N Engl J Med 1979;300:1012–5.
40. Gordon GG, Altman K, Southern AL, Rubin E, Lieber CS. Effect of alcohol (ethanol) administration on sex-hormone metabolism in normal men. N Engl J Med 1976;295:793–7.
41. Emanuele NV, LaPaglia N, Steiner J, Kirsteins L, Emanuele MA. Reversal of chronic ethanol-induced testosterone suppression in peripubertal male rats by opiate blockade. Alcohol Clin Exp Res 1999;23: 60–6.
42. Widenius TV, Orava MM, Vihko RK, Ylikahri RH, Eriksson CJP. Inhibition of testosterone biosynthesis by ethanol: multiple sites and mechanisms in dispersed Leydig cells. J Steroid Biochem 1987;28: 185–8.
43. Cicero TJ, Bell RD. Effects of ethanol and acetaldehyde on the biosynthesis of testosterone in rodent testes. Biochem Biophys Res Commun 1980;94:814–9.
44. Cicero TJ, Bell RD, Meyer ER, Badger TM. Ethanol and acetaldehyde directly inhibit testicular steroidogenesis. J Pharmacol Exp Ther 1980; 213:228–33.
45. Orpana AK, Orava MM, Vihko RK, Harkonen M, Eriksson CJP. Ethanol-induced inhibition of testosterone biosynthesis in rat Leydig cells: central role of mitochondrial NADH redox state. J Steroid Biochem 1990;36:603–8.
46. Brzek A. Alcohol and male fertility (preliminary report). Andrologia 1987;19:32–6.
47. Carlsen E, Giwereman A, Keiding M, Skakkebaek NE. Evidence for decreasing quality of semen during the past 50 years. Br Med J 1992;305:609–13.