

Lifestyle, Stress and Cortisol Response: Review II

— Lifestyle —

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Abstract

To prevent lifestyle related diseases, it is important to modify lifestyle behavior. The control of mental stress level and prevention of mental stress-related diseases have become one of the most important problems in Japan. To check mental stress level objectively during the early stage of stress-related diseases and determine appropriate coping methods, it is necessary to design a useful index for mental stress. Cortisol is a steroid hormone secreted by the adrenal cortex. This is an essential hormone to human survival, and plays a key role in adaptation to stress. In another review, we concluded that cortisol appears to be an adequate index for mental stress.

However, lifestyle factors such as alcohol drinking, smoking, lack of exercise etc., are strongly associated with mental stress. Thus, in this review, we focus on the relationship between cortisol and lifestyle.

The present findings suggested that lifestyle factors; smoking, alcohol drinking, exercise, sleep and nutrition are strongly associated with cortisol levels, and it may be impossible to determine whether alterations in cortisol levels are due to mental stress.

It was suggested that those lifestyle effects on not only mental stress itself but also cortisol levels should be considered, when assessing mental stress by cortisol levels.

Key words: lifestyle, cortisol, each health practice, preventive medicine, mental stress

Introduction

There have been many epidemiological and experimental studies which discussed the relationship between cancer, obesity and diabetes etc. and individual health practices; smoking, alcohol drinking, food and stress. To prevent disease, it is important to modify lifestyle behavior. The prevention of mental stress-related diseases has become an important concern recently. To allow mental stress level to be determined objectively during the early stage of stress-related diseases and design appropriate coping methods, it is necessary to have a useful mental stress index. Following the pioneering work by Hans Selye¹⁾, the pituitary-adrenal system has been viewed as central to human adaptation to changes in the internal and external environment. In another review, it was suggested that cortisol appears to be an adequate index for mental stress (review I). Cortisol is a major steroid hormone secreted by the adrenal cortex and is a possible candidate as an index for mental stress²⁻⁴⁾.

Daily stress is known as an important factor in various kinds of disease such as cancer, cardiovascular diseases, obesity, diabetes etc., although the mechanisms of the effects in these conditions are not clear. Poor lifestyle factors such as alcohol drinking, smoking, lack of exercise etc., are strongly associated with mental stress⁵⁻⁶⁾.

Thus, in this review, we focus on the relationship between cortisol and lifestyle.

1. Smoking

Nicotine has been shown to be a potent stimulator for the release of several hypothalamic-pituitary-adrenal (HPA) hormones⁸⁾. The HPA appears to be a prime endocrine target of nicotine action⁸⁾.

Injection of nicotine results in elevated serum levels of cortisol^{9,10)}. However, some studies have indicated nicotine had no or only a slight effect on cortisol levels^{11,12)}.

The basal level of cortisol was reported to be higher in smokers than in non-smokers¹³⁻¹⁵⁾. The elevation of cortisol level has been reported to be dependent on the number of cigarettes smoked per day¹⁶⁻¹⁸⁾, although contradictory findings have also been reported¹⁹⁾. Cigarette smoking is considered to induce frequent release of hormones that in turn lead to an altered responsiveness of the endocrine axes⁸⁾. Cigarette smoking is a potent and acute stim-

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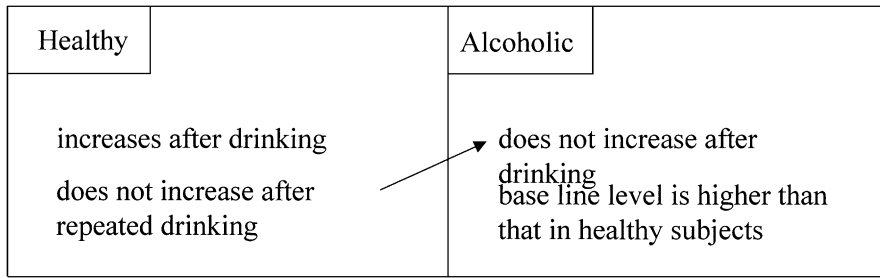


Fig. 1 The relationship between alcohol drinking and cortisol level.

ulus for various hormonal axes in healthy smokers.

After a smoking cessation trial, although the basal level was not different, the level of cortisol decreased in smokers who succeeded in cessation^{20,21}. This was consistent with the observation that increasing the level of nicotine was associated with the rise in the cortisol level. However, gender-related differences have also been reported²²⁻²⁴, and these differences are thought to be due to sex hormones.

We was suggested that acute and chronic smoking generally increased cortisol levels, because smokers showed higher cortisol levels than non-smokers, especially after a high dose of smoking, which showed higher levels of cortisol, and quitting smokers showed decreased cortisol levels compared with smoking duration. The conflicting findings were thought to show the individual differences of adrenal responses, physical stress response, metabolism and other various hormone effects¹⁹.

2. Alcohol (Fig. 1)

Ethanol may stimulate the basal function of the HPA axis involved in centrally mediated stress responses^{25,26}. Many studies have shown that acute and short-term ethanol injection in normal subjects causes increases in cortisol level²⁷⁻³³. Some of these studies indicated that the elevation of the plasma cortisol level showed parallel changes with the blood ethanol curve²⁸⁻³⁰. A number of studies have demonstrated activation of the HPA axis associated with an increase in plasma cortisol levels after administration of high doses of ethanol, but not low doses of ethanol³¹⁻³³.

It has also been shown that repeated alcohol injection did not produce any elevation in cortisol level in normal subjects³⁴⁻³⁸. Other studies indicated that increases in cortisol levels induced by

acute injection were observed only in non-drinkers who had symptoms of alcohol intolerance, but not in heavy drinkers or in alcoholic patients³⁹. It is also well established that long-term alcohol consumption induces endocrine abnormalities, especially in the HPA axis²⁶.

Three independent studies of investigators examined cortisol levels in Asian subjects who either did or did not show alcohol-induced flushing⁴⁰⁻⁴². Approximately 50% of certain Asian groups are ALDH² deficient⁴⁰⁻⁴². ALDH² deficiency is very uncommon among other non-Mongolian ethnic groups⁴⁰⁻⁴². These studies demonstrated higher levels of cortisol following an alcohol challenge in Asians who experience alcohol-induced flushing.

In healthy people, the cortisol levels increase after drinking and do not increase after repeated drinking, but in alcoholics, the cortisol levels do not increase after drinking and basal levels of cortisol are higher than those in healthy people. Thus, it was suggested that adequate alcohol-drinking people showed normal adrenal responses but heavy and chronic alcohol drinking abnormal effect on adrenal responses. In Asians, alcohol-induced flushing should be considered.

3. Nutritional balance — obesity and malnutrition — (Fig. 2)

There is little evidence to support an important relationship between the mental state or behavior of obese patients and their hormone levels. Nutrition plays a role in determining the endocrine abnormalities often found in obesity or malnutrition.

Obese subjects show increased cortisol production and metabolism⁴³⁻⁴⁷. The Cortisol excretion rate is positively correlated with body mass index⁴⁵. In contrast, some studies indicated nor-

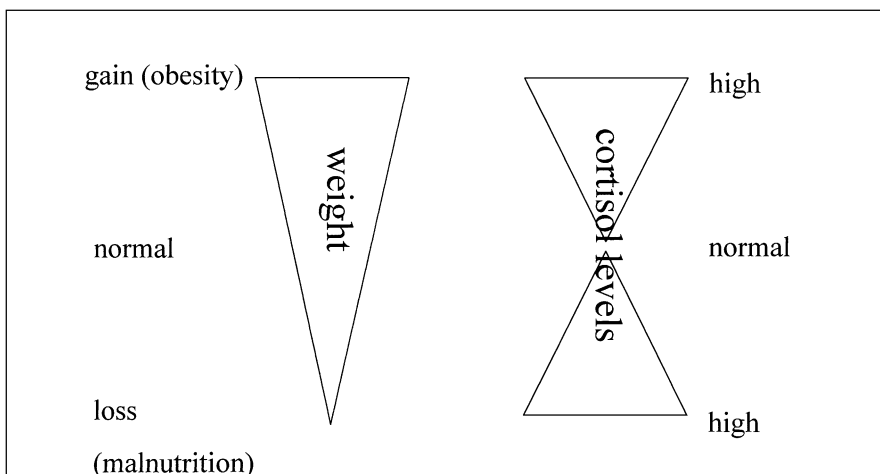


Fig. 2 The relationship between cortisol levels and obesity or malnutrition.

mal plasma cortisol levels and circadian rhythm in obese subjects and concluded there was no correlation between plasma levels of cortisol and weight of obese subjects^{48,49}.

Nutritionally deprived subjects generally show increased plasma levels of cortisol⁵⁰⁻⁵⁵. Energy deficiency causes marked changes in the metabolic and endocrine state of the human body⁵⁰⁻⁵⁵. Obese patients, after periods of starvation or reduced caloric intake or weight loss, have been reported to show either increased or normal plasma levels of cortisol^{43,44,56}. Malnutrition is associated with decreased responsiveness of the HPA axis, and these abnormalities are restored after nutritional rehabilitation⁵⁷⁻⁶¹. These tendencies have been observed in both children and elderly subjects. Children with protein-calorie malnutrition have been shown to have raised of plasma cortisol levels^{53,55}.

It is suggested that both extreme weight gain and loss are related to the rise of cortisol levels⁴³⁻⁴⁷. These might be caused by marked changes in the metabolic and endocrine abnormalities of human body⁵⁰⁻⁵⁵, because following body weight becoming normal, cortisol levels also return to normal^{43,44,56}.

4. Sleep

The circadian rhythms of cortisol are known to be slightly affected by acute modifications in the sleep-wake cycle such as sleep deprivation or and abrupt disruption of the sleep-wake schedule. Some studies have shown that the cortisol concentration is influenced by sleep itself⁶²⁻⁶⁵. However, it is difficult to distinguish between the effects of sleep and the natural circadian rhythm.

Night workers are known to adapt only partially to the nocturnal schedule⁶⁶. The cortisol levels were low during the night shift, suggesting that night shift itself represents a high stress level. Circadian rhythms of cortisol were fundamentally maintained even during the night shift. However, the cortisol concentration in the morning, at the end of the night shift, was significantly lower than that during the day shift⁶⁷.

Alterations in cortisol levels could only be demonstrated in the evening following a night of sleep deprivation⁶⁸⁻⁷¹. Sleep deprivation results in an elevation in the cortisol level the following evening⁶⁸⁻⁷⁰. The effects of total sleep deprivation on HPA

function correspond to the absence of these immediate responses to sleep-wake transitions. During the month of Muslim fasting (Ramadan), many people alter their sleeping habits and stay awake most of the night. Thus, Ramadan is a period of sleep deprivation. Four of 10 subjects showed alterations in the cortisol rhythm during the last 2 weeks of Ramadan⁷¹.

Irregular sleep, such as sleep deprivation and shift work, effects on the circadian cortisol rhythms. However, the findings were not inconsistent, because it is difficult to distinguish between the effects of sleep and the natural circadian rhythm, and there are few studies that examined the relationship between the quality of sleep, sleeping hours and cortisol levels.

5. Physical exercise (Table 1)

Many factors are involved in individual variability in cortisol responses related to physical exercise. In this review, we categorized three factors, "Intensity of exercise and duration of exercise, Environmental effects and Type of sports" (Training, competition and performance level).

Intensity of exercise

The cortisol response to exercise is determined by threshold intensity⁷²⁻⁸¹. The serum level of cortisol is known to increase when a certain workload is exceeded^{72,73}. Cortisol increases during exercise if the intensity of the exercise exceeds 60% of maximal VO_2^{\max} after more than 1 h⁷⁴. However, conflicting observations were reported in some studies⁷⁵⁻⁸⁰. No increase in blood cortisol level after exercise at workloads above 70% of VO_2^{\max} ⁸¹. In short, cortisol levels are not increase correspondent to the workloads. These findings suggested that only intensity of exercise might not affect the measurement of cortisol responses.

Types of sport

Competition

In tennis players, cortisol levels in blood were shown to be elevated 15 min before the match⁸². In elite rowers, high anticipatory levels of cortisol were detected during an international competition⁸³.

Table 1 The relationship between exercise and cortisol reaction

Factors		Cortisol reaction
Intensity of exercise	VO2max over 70%	No change
	over 60%	↑
Types of sports	Competition	
	Tennis players	No change (increase 15 min before a match)
	Rowers	↑
	Training	
	Weightlifting	↑
	Runners	↑
	Swimmers	↑
Performance level	Weightlifting	↑ (positively related to performance level)
	Rowers	↑ (positively related to performance level)
	Environmental effect hot temperature	↑ (compared to cold temperature)
	High altitude	↑

↑: Means that cortisol level increases after exercise (including competition and training)

Training effects

Previously, cortisol was identified as a hormonal marker of training stress⁸⁴. Recent studies have indicated endocrine changes in endurance sportsman during a training year⁸⁵⁻⁸⁸. Lukaszewska et al. reported increases in cortisol in adolescent males after a weightlifting session⁸⁵. Barron et al. observed that athletes who were overtrained had impaired cortisol and elevated basal cortisol levels compared to a control group of runners⁸⁸. Stray-Gundersen et al. also reported a significant elevation in cortisol levels in recreational runners subjected to two weeks of normal training superimposed with four hard interval sessions per week⁸⁹. However, Flynn et al. concluded that the response of cortisol to training stress was unclear and, therefore, they doubted its usefulness as a marker of training stress⁹⁰.

Performance level

Kraemer et al. demonstrated that cortisol showed no differences due to training experience or strength classifications in junior weightlifters⁹¹. A longitudinal study of rowers demonstrated a parallel increase in rowing performance and blood cortisol level⁹². Elevated cortisol level in rowers reflects the increased functional capacity of the corresponding endocrine systems⁹². Resting cortisol concentrations declined more slowly during the morning in amenorrheic athletes than they do in regularly menstruating athletes and sedentary women⁹³.

Environmental effects

It was demonstrated that changes in secretory activity in response to exercise were not only closely correlated with muscular work intensity, but were also influenced by thermal stress^{94,95}.

It was shown that thermal stress caused increases in cortisol levels⁹⁶⁻⁹⁹. During swimming, the concentrations of cortisol are higher when the environment is hot^{98,99}. Dulac et al. found that cortisol concentrations in blood were significantly increased during long-distance swimming in cold water⁹⁸.

Serum cortisol level increases in response to exercise at moderated altitude⁹⁹⁻¹⁰¹. Guillard et al. observed increased urinary excretion of cortisol during mountaineering between 4,800 and 7,100 m¹⁰². Strassman et al. reported that a 46-km mountain race (between 1,900 and 3,300 m) tripled serum concentrations of cortisol¹⁰³.

Cortisol increased to levels above the normal range, particu-

larly during indoor running with an internal focus of attention¹⁰⁴. Vigorous exercise can have a beneficial effect on mood, but the environment and setting in which it occurs and the attentional focus appear to exert mediating effects.

Competition and training include both mental and physical stress effects⁸²⁻⁸³. In general, physical activity was associated with increase of cortisol levels⁸²⁻⁸³. However, there were many confounding factors such as the intensity of exercise, type of sports (competition, training effects and performance levels) and environmental effects⁷²⁻¹⁰⁴. When the physical activity, mental stress and cortisol levels are examined, it is necessary to consider how hard, how long, how many times subjects exercise.

Other considerable effects

The elevation of cortisol levels has also been suggested to be caused by the stress of blood collection⁴. Lower cortisol stress responses have been consistently shown in females compared to males¹⁰⁵. Personality and other traits may influence how stressful situations are appraised and may, thus, have predictive value for understanding individual differences in emotional and physiological responses to apparently identical situations¹⁰⁶⁻¹⁰⁸. More insight into individual differences in cortisol reactivity is needed.

Conclusion

Lifestyle factors such as alcohol drinking, smoking, lack of exercise etc., are strongly associated with cortisol levels, which are widely accepted to be related to various types of mental stress⁸⁻¹⁰⁸.

Cortisol responses to mental stress have been found to differ between individuals, but the sources of these differences are far from clear. Under these conditions, it may be impossible to determine whether the observed alterations in cortisol are due to mental stress. Based on the findings of a number of previous studies related to lifestyle and cortisol, it is suggested that lifestyle factors are strongly associated with change in cortisol levels. Lifestyle effects on not only mental stress itself but also cortisol levels should be considered, when assessing mental stress using cortisol levels. It is necessary to improve the more comprehensive mental stress index survey including lifestyle and other strong effects such as gender, age and character.

References

- 1) Selye H. A syndrome produced by diverse bicuous agents. *Nature* 1936; 138: 72.
- 2) Brien TC. Free cortisol in human plasma. *Horm. Metab. Res.* 1980; 12: 643-650.
- 3) Slaunwhite WR, Lockie GN, Back N, Sandberg AA. Inactivity in vivo of transcortin-bound cortisol. *Science* 1962; 135: 1062-1063.
- 4) Kirschbaum C, Hellhammer DH. Salivary cortisol in psychological research: an overview. *Neuropsychobiology* 1989; 22: 150-169.
- 5) Simonsick EM. Personal health habits and mental health in national probability sample. *Am. J. Prev. Med.* 1991; 7(6): 425-437.
- 6) Paffenbarger RS Jr, Lee IM, Leung R. Physical activity and personal characteristics associated with depression and suicide in American college men. *Acta. Psychiatr. Scand.* 1994; Suppl 377: 16-22.
- 7) Ezo S, Morimoto K. Behavioral lifestyle and mental health status of Japanese factory workers. *Preve. Med.* 1994; 23: 98-105.
- 8) Kirschbaum C, Wust S, Strasburger CJ. Normal cigarette smoking increases free cortisol in habitual smokers. *Life Sci.* 1991; 50: 435-442.
- 9) Gilbert DG, Meliska CJ, Plath LC. Noise stress does not modulate effects of smoking/nicotine on beta-endorphin, cortisol, ACTH, glucose, and mood. *Psychopharmacology-Berl.* 1997; 130: 197-202.
- 10) Pickworth WB, Baumann MH, Fant RV, Rothman RB, Henning-

- field JE. Endocrine responses during acute nicotine withdrawal. *Pharmacol. Biochem. Behav.* 1996; 55: 433–437.
- 11) Andersson K, Eneroth P, Arner P. Changes in circulating lipid and carbohydrate metabolites following systemic nicotine treatment in healthy men. *Int. J. Obes. Relat. Metab. Disord.* 1993; 17: 675–680.
 - 12) Stalke J, Harder O, Bahr V, Hensen J, Scherer G, Oelkers W. The role of vasopressin in the nicotine induced stimulation of ACTH and cortisol in men. *Clin. Investig.* 1992; 70: 218–223.
 - 13) Baron JA, Comi RJ, Cryns V, Brinck-Johnsen T, Merger NG. The effect of cigarette smoking on adrenal cortical hormones. *J. Pharmacol. Exp. Ther.* 1994; 272: 151–155.
 - 14) Field AE, Colditz GA, Willett WC, Longcope C, McKinlay JB. The relation of smoking, age, relative weight, and dietary intake to serum adrenal steroids, sex hormones, and sex hormone-binding globulin in middle-aged men. *J. Clin. Endocrinol. Metab.* 1994; 79: 1310–1316.
 - 15) Handa K, Kono S, Ishii H, Imanishi K, Arakawa K. Relationship of alcohol consumption and smoking to plasma cortisol and blood pressure. *J. Hum. Hypertens.* 1994; 8: 891–894.
 - 16) Haak T, Jungmann E, Raab C, Usadel KH. Elevated endothelin-1 level after cigarette smoking. *Metabolism* 1994; 43: 267–269.
 - 17) Gilbert DG, Meliska CJ, Williams CL, Jensen RA. Subjective correlates of cigarette-smoking-induced elevations of peripheral beta-endorphin and cortisol. *Psychopharmacology* 1992; 106: 275–281.
 - 18) Seyler E Jr, Fertig J, Pomerleau O, Hunt D, Parker K. The effects of smoking on ACTH and cortisol secretion. *Life Sci.* 1984; 34: 57–65.
 - 19) Hautanen A, Manttari M, Kupari M, et al. Cigarette smoking is associated with elevated adrenal androgen response to adrenocorticotropin. *J. Steroid Biochem. Molec. Biol.* 1993; 46: 245–251.
 - 20) Meliska CJ, Stunkard ME, Gilbert DG, Jensen RA, Martinko JM. Immune function in cigarette smokers who quit smoking for 31 days. *J. Allergy Clin. Immunol.* 1995; 95: 901–910.
 - 21) Frederick SL, Reus VI, Ginsberg D, Hall SM, Munoz RF, Ellum G. Cortisol and response to dexamethasone as predictors of withdrawal distress and abstinence success in smokers. *Biol. Psychiatry* 1998; 43: 525–530.
 - 22) Meliska CJ, Gilbert DG. Hormonal and subjective effects of smoking the first five cigarettes of the day: a comparison in males and females. *Pharmacol. Biochem. Behav.* 1991; 40: 229–235.
 - 23) Pomerleau CS, Garcia AW, Pomerleau OF, Cameron OG. The effects of menstrual phase and nicotine abstinence on nicotine intake and on biochemical and subjective measures in women smokers: a preliminary report. *Psychoneuroendocrinology* 1992; 17: 627–638.
 - 24) Law MR, Cheng R, Hackshaw AK, Allaway S, Hale AK. Cigarette smoking, sex hormones and bone density in women. *Eur. J. Epidemiology* 1997; 13: 553–558.
 - 25) Wand G, Froehlich J. Alterations in hypothalamo-hypophyseal function by ethanol. In: McCleod R, Muller E, eds, *New York: Springer-Verlag; Neuroendocrine Perspectives*; 1990: 45–122.
 - 26) River C, Vole W. Interaction between ethanol and stress on ACTH secretion. *Alcohol Clin. Exp. Res.* 1988; 12: 206–210.
 - 27) Ida Y, Tsujimaru S, Nakamura K, 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.
 - 28) Jeffoate WJ, Platts P, Ridout M, Hastings AG, MacDonald I, Selby C. Endocrine effects of ethanol infusion in normal subjects: modification by naloxone. *Pharmacol. Biochem. Behav.* 1980; 13: 145–148.
 - 29) Jenkins JS, Connolly J. Adrenocortical response to ethanol in man. *Br. Med. J.* 1968; 2: 804–805.
 - 30) Merry J, Marks V. Plasma-hydrocortisone response to ethanol in chronic alcoholics. *Lancet* 1969; 1: 921–923.
 - 31) Yikahri RH, Huttunen MO, Harkonen M, Leino T, Helenius T, Liewendahl K, Karonen S. Acute effects of alcohol on anterior pituitary secretion of the tropic hormones. *J. Clin. Endocrinol. Metab.* 1978; 46: 715–720.
 - 32) Gianoulakis C, Guillaume P, Thavundayi J, Gutkowska J. Increased plasma atrial natriuretic peptide after ingestion of low doses of ethanol. *Alcohol Clin. Exp. Res.* 1997; 21: 162–170.
 - 33) Soyka M, Corig E, Naber D. Serum prolactin increase induced by ethanol—a dose-dependent effect not related to stress. *Psychoneuroendocrinology* 1991; 16: 441–446.
 - 34) Mendelson JH, Stein S. Serum cortisol levels in alcoholic and non-alcoholic subjects during experimentally induced ethanol intoxication. *Psychosom. Med.* 1966; 28: 616–626.
 - 35) Mendelson JH, Ogata M, Mello NK. Adrenal function and alcoholism I. Serum cortisol. *Psychosom. Med.* 1971; 33: 145–157.
 - 36) Schuckit MA, Risch SC, Gold EO. Alcohol consumption, ACTH level, and family history of alcoholism. *Am. J. Psychiatry* 1988; 145: 1391–1395.
 - 37) Schuckit MA, Gold EO, Risch C. Plasma cortisol levels following ethanol in sons of alcoholic and controls. *Arch. Gen. Psychiatry* 1987; 44: 942–945.
 - 38) Ireland MA, Vandongen R, Davidson L, Beilin LJ, Rouse IL. Acute effects of moderate alcohol consumption on blood pressure and plasma catecholamines. *Clin. Sci.* 1984; 66: 643–648.
 - 39) Del-Arbol JL, Aguirre JC, Raya J, Rico J, Ruiz-Requena ME, Miranda MT. Plasma concentrations of β -endorphin, adrenocorticotrophic hormone, and cortisol in drinking and abstinent chronic alcoholics. *Alcohol* 1995; 12: 525–529.
 - 40) Ho SB, DeMaster EG, Safer RB, Levine AS, Morley JE, Go VLW, Allen JI. Opiate antagonist nalmefene inhibits ethanol-induced flushing in Asians: A preliminary study. *Alcohol Clin. Exp. Res.* 1988; 12: 705–712.
 - 41) Seto A, Tricomi S, Goodwin DW, Kolodney R, Sullivan T. Biochemical correlates of ethanol-induced flushing in Orientals. *J. Stud. Alcohol* 1978; 39: 1–11.
 - 42) Goedde HW, Singh S, Agarwal DP, Fritze G, Stapel K, Paik YK. Genotyping of mitochondrial aldehyde dehydrogenase in blood samples using allele-specific oligonucleotides. *Hum. Genet.* 1989; 81: 305–307.
 - 43) Schneider BS, Hirsch J. Hypothalamic-pituitary function in obesity. in *Contemporary Metabolism*, Vol.2, Freinkel N (Ed), New York, Plenum, 1982; pp.119–144.
 - 44) Copinschi G, Delaet MH, Brion JP, Leclercq K, Hermite ML, Robyn V, Viresoro E, Van Canter E. Simultaneous study of cortisol, growth hormone, and prolactin nyctohemeral variations in normal and obese subjects: influence of prolonged fasting in obesity. *Clin. Endocrinol.* 1978; 9: 15–26.
 - 45) Fraser R, Ingram MC, Anderson NH, Morrison C, Davies E, Connell JM. Cortisol effects on body mass, blood pressure, and cholesterol in the general population. *Hypertension* 1999; 33: 1364–1368.
 - 46) Pasquali R, Biscotti D, Spinucci G, Vicennati V, Genazzani AD, Sgarbi L, Casimirri F. Pulsatile secretion of ACTH and cortisol in premenopausal women: effect of obesity and body fat distribution. *Clin. Endocrinol. Oxf.* 1998; 45: 603–612.
 - 47) Andrew R, Phillips DI, Walker BR. Obesity and gender influence

- cortisol secretion and metabolism in man. *J. Clin. Endocrinol. Metab.* 1998; 83: 1806–1809.
- 48) Yanovski JA, Yanovski SZ, Gold PW, Chrousos GP. Differences in corticotropin-releasing hormone-stimulated adrenocorticotropin and cortisol before and after weight loss. *J. Clin. Endocrinol. Metab.* 1997; 82: 1874–1878.
 - 49) Bayliss RIS. Factors influencing adrenocortical activity in health and disease. *Br. Med. J.* 1955; 1: 495.
 - 50) Schonla MM, Shanley BC, Loening WEK, Parent MA, Coovadia HM. Plasma-cortisol and immunosuppression in protein-calorie malnutrition. *Lancet* 1972; Aug 26: 435–437.
 - 51) Malozowski S, Muzzo S, Burrows R, et al. The hypothalamic-pituitary-adrenal axis in infantile malnutrition. *Clin. Endocrinol. Oxf.* 1990; 32: 461–465.
 - 52) Alleyne GAO, Young VH. Adrenal function in malnutrition. *Lancet* 1966; 1: 911.
 - 53) Tuchinda C, Chatranon W. Blood cortisol levels in malnourished Thai children with and without acute stress. *J. Med. Ass. Thailand* 1982; 65: 82–85.
 - 54) Rao KSJ, Srikanthia SG, Gopalan C. Plasma cortisol levels in protein-calorie malnutrition. *Arch. Dis. Child* 1968; 43: 365–367.
 - 55) Castellanos H, Arroyave G. Role of the adrenal cortical system in the response of children to severe protein malnutrition. *Am. J. Clin. Nutr.* 1961; 9: 186.
 - 56) Cohen MR, Pickar D, Cohen RM, Wise TN, Cooper JN. Plasma cortisol and beta-endorphin immunoreactivity in human obesity. *Psychosom. Med.* 1984; 46: 454–462.
 - 57) Bayliss RIS. Factors influencing adrenocortical activity in health and disease. *Br. Med. J.* 1955; 1: 495.
 - 58) Saudek CD, Felig P. The metabolic events of starvation. *Am. J. Med.* 1976; 60: 117–126.
 - 59) Cahill Jr GF. Starvation in man. *Clin. Endocrinol. Metab.* 1976; 5: 397–415.
 - 60) Laundberg L, Young JB. Fasting, feeding and regulation of the sympathetic nervous system. *N. Engl. J. Med.* 1978; 298: 1295–1301.
 - 61) Palmblad J, Levi L, Burger A, et al. Effects of total energy withdrawal (fasting) on the levels of growth hormone, thyrotropin, cortisol, adrenaline, noradrenaline, T4, T3, and rT3 in healthy males. *Acta. Med. Scand.* 1977; 201: 15–22.
 - 62) Späth-schualhe E, Uthgenannt D, Voget G, Kern W, Born J, Fehm HL. Corticotropin-releasing hormone-induced adrenocorticotropin and cortisol secretion depends on sleep and wakefulness. *J. Clin. Endocrinol. Metab.* 1993; 77: 1170–1173.
 - 63) Davidson JR, Moldofsky H, Lue FA. Growth hormone and cortisol secretion in relation to sleep and wakefulness. *J. Psychiatry Neurosci.* 1991; 16: 96–102.
 - 64) Follenius M, Brandenberger G, Badasept J, Libert J, Ehrhart J. Nocturnal cortisol release in relation to sleep structure. *Sleep* 1992; 15: 21–27.
 - 65) Van Cauter E, Turek FW. Endocrine and other biological rhythms. In: DeGroot Lj ed. *Endocrinology*. Philadelphia: W.B. Saunders, 1994; 2487–2548.
 - 66) Kobayashi F, Furui H, Akamatsu Y, Watanabe T, Horibe H. Changes in psychophysiological functions during night shift in nurses. Influence of changing from a full-day to a half work shift before night duty. *Int. Arch. Occup. Environ. Health* 1997; 69: 83–90.
 - 67) Leproult R, Copinschi G, Buxton O, Cauter EV. Sleep loss results in an elevation of cortisol levels the next evening. *Sleep* 1997; 20: 865–870.
 - 68) Akerstedt T, Palmblad J, de la Torre B, Marana R, Gillberg M. Adrenocortical and gonadal steroids during sleep deprivation. *Sleep* 1980; 3: 23–30.
 - 69) Kant GJ, Genser SG, Torne DR, Pfalser JL, Mougey EH. Effects of 72 hours sleep deprivation on urinary cortisol and indices of metabolism. *Sleep* 1984; 7: 142–146.
 - 70) Horn JA. A review of the biological effects of total sleep deprivation in man. *Biol. Psychol.* 1978; 7: 55–102.
 - 71) Hadramy MS, Zawawi TH, Abdelwahab SM. Altered cortisol levels in relation to Ramadan. *Eur. J. Clin. Nutr.* 1988; 42: 359–362.
 - 72) Davis CTM, Few JD. Effects of exercise on adrenocortical function. *J. Appl. Physiol.* 1973; 35: 887–891.
 - 73) Sundsfjord JA, Strømme SB, Aakvaag A. Plasma aldosterone (PA), plasma renin activity (PRL) and cortisol (PF) during exercise. *Res. Steroids* 1975; 6: 133–140.
 - 74) Davis CTM, Few JD. Effects of exercise on adrenocortical function. *J. Appl. Physiol.* 1973; 35: 887–891.
 - 75) Brandenberger G, Follenius M. Influence of timing and intensity of muscular exercise on temporal patterns of plasma cortisol levels. *J. Clin. Endocrinol. Metab.* 1975; 40: 845–849.
 - 76) Brandenberger G, Follenius M, Hietter B. Feedback from meal-related peaks determines diurnal changes in cortisol response to exercise. *J. Clin. Endocrinol. Metab.* 1982; 54: 592–596.
 - 77) Farrell PA, Garthwaite TL, Gustafson AB. Plasma adrenocorticotropin and cortisol responses to submaximal and exhaustive exercise. *J. Appl. Physiol.* 1983; 55: 1441–1444.
 - 78) Gawell MJ, Park DM, Alaghband-Zadeh J, Rose FC. Exercise and hormonal secretion. *Postgrad. Med. J.* 1979; 55: 373–376.
 - 79) Schnabel A, Kindermann W, Schmitt WM, Biro SG, Stegmann H. Hormonal and metabolic consequences of prolonged running at the individual anaerobic threshold. *Int. J. Sports Med.* 1983; 3: 163–168.
 - 80) Stephenson LA, Kolka MA, Francesconi R, Gonzalez RR. Circadian variations in plasma renin activity, catecholamines and aldosterone during exercise in women. *Eur. J. Appl. Physiol. Occup. Physiol.* 1989; 58: 756–764.
 - 81) Cashmore GC, Davis CTM, Few JP. Relationship between increases in plasma cortisol concentrations and rate of cortisol secretion during exercise in man. *J. Endocrinol.* 1977; 72: 109–110.
 - 82) Booth A, Shelley G, Mazur A, Thorp G, Kittok R. Testosterone, and winning and losing in human competition. *Horm. Behav.* 1989; 23: 556–571.
 - 83) Snegovskaya V, Viru A. Elevation of cortisol and growth hormone levels in the course of further improvement of performance capacity in trained rowers. *Int. J. Sports Med.* 1993; 14: 202–206.
 - 84) Lukaszewska J, Biczowa B, Bobilewicz D, Wolk M, Obuchowicz-Fidelus B. Effects of physical exercise on plasma cortisol and growth hormone levels in young weight lifters. *Endocrinol. Pol.* 1976; 27: 149–157.
 - 85) Häkkinen K, Keskinen KL, Alén M, Komi PV, Kauhanen H. Serum hormone concentrations during prolonged training in elite endurance-trained and strength-trained athletes. *Eur. J. Appl. Physiol.* 1989; 59: 233–238.
 - 86) Vervoo C, Quist AM, Vermulst LJM, Erich WB, De Vries WR, Thijssen JHH. The behaviour of the plasma free testosterone/cortisol ratio during a season of elite rowing training. *Int. J. Sports Med.* 1991; 12: 257–263.
 - 87) Kirwan JP, Costill DL, Fink WJ, Mitchell JB, Houmard J, Flynn MG. Changes in selected blood measures during repeated days of intense training and carbohydrate control. *Int. J. Sports Med.* 1990; 11: 362–366.

- 88) Baron GL, Noakes TD, Levy W, Smith C, Millar RP. Hypothalamic dysfunction in overtrained athletes. *J. Clin. Endocrin. Metab.* 1985; 60: 803–806.
- 89) Stray-Gundersen J, Videman T, Snell PG. Changes in selected objective parameters during overtraining. *Med. Sci. Sports Exerc.* 1986; 18: S54–S55.
- 90) Flynn MG, Pizza FX, Boone JB Jr, Andres FF, Michaud TA, Rodriguez-Zayas JR. Indices of training stress during competitive running and swimming seasons. *Int. J. Sports Med.* 1994; 15: 21–26.
- 91) Kraemer WJ, Fry AC, Warren BJ, Stone MH, Fleck SJ, Kearney JT, Conroy BP, Maresh CM, Weseman CA, Triplett NT, Gordon SE. Acute Hormonal responses in elite junior weightlifters. *Int. J. Sports Med.* 1992; 13: 103–109.
- 92) Louckas AB, Mortola JF, Girton L, Yen SSC. Alterations in the hypothalamic-pituitary-ovarian and the hypothalamic-pituitary-adrenal axes in athletic women. *J. Clin. Endocrinol. Metab.* 1989; 68: 402–411.
- 93) Collins KJ, Weiner JS. Endocrinological aspects of exposure to high environmental temperatures. *Physiol. Rev.* 1968; 48: 785–839.
- 94) Hartley LH, Mason JW, Hogan RP et al. Multiple hormonal responses to prolonged exercise in relation to physical training. *J. Appl. Physiol.* 1972; 33: 607–610.
- 95) Hartley LH, Mason JW, Hogan RP et al. Multiple hormonal responses to prolonged exercise in relation to physical training. *J. Appl. Physiol.* 1972; 33: 607–610.
- 96) Galbo H, Houston ME, Christensen NJ, et al. The effect of water temperature on the hormonal response to prolonged swimming. *Acta Physiol. Scand.* 1979; 105: 326–337.
- 97) Dulac S, Quirion A, Decarufel D, et al. Metabolic and hormonal responses to long-distance swimming in cold water. *Int. J. Sports Med.* 1987; 8: 352–356.
- 98) Deligiannis A, Karamouzis M, Kouidi E, Mougios V, Kallaras C. Plasma TSH, T3, T4 and cortisol responses to swimming at varying water temperatures. *Br. J. Sp. Med.* 1993; 27: 247–250.
- 99) Bashir N, El-Migdadi F, Hasan Z, Al-Hader AA, Wezermes I, Gharaibeh M. Acute effects of exercise at low altitude (350 meters below sea level) on hormones of the anterior pituitary & cortisol in athletes. *Endocrine Res.* 1996; 22: 289–298.
- 100) Kuoppasalmi K, Naveri H, Horkonen M, Adelcreutz H. Plasma cortisol, androstenedione, testosterone and leutinizing hormone in running exercise of different intensities. *Scand. J. Clin. Lab. Invest.* 1980; 40: 403–409.
- 101) Newmark RS, Himathongkam T, Martin RP, Cooper KH, Rose LJ. Adrenocortical response to marathon running. *J. Clin. Endocrinol.* 1976; 42: 393–395.
- 102) Tabata I, Atoi Y, Miyashita M. Blood glucose concentration dependent ACTH and cortisol responses to prolonged exercise. *Clin. Physiol.* 1984; 4: 299–307.
- 103) Sutton JR. Effect of acute hypoxia on the hormonal response to exercise. *J. Appl. Physiol.* 1977; 42: 587–592.
- 104) Harte JL, Eifert GH. The effects of running, environment, and attentional focus on athletes catecholamine and cortisol levels and mood. *Psychophysiology* 1995; 32: 49–54.
- 105) Kirshbaum C, Wüst S, Hellhammer DH. Consistent sex differences in cortisol responses to psychological stress. *Psychosom. Med.* 1992; 54: 648–657.
- 106) Brandstädter J, Baltes-Götz B, Kirschbaum C, Hellhammer D. Developmental and personality correlated of adrenocortical activity as indexed by salivary cortisol: observations in the age range of 35 to 65 years. *J. Psychosom. Res.* 1991; 35: 173–185.
- 107) Pope MK, Smith TW. Cortisol excretion in high and low cynically hostile men. *Psychosom. Med.* 1991; 53: 386–392.
- 108) Bossert S, Berger M, Krieg JC, Schreiber W, Jounker M, von Zerssen D. Cortisol response to various stressful situations: relationship personality variables and coping styles. *Neuropsychobiology* 1988; 20: 36–42.