Is Alcohol a Toxin which Directly Elicits the Stress (Fight or Flight) Response? Part I

—— Evidence from Alcohol's Effect on Physiological Functioning ——

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(Received October 6, 1997)

ABSTRACT

Over 50% of adult males in Japan identify the consumption of alcohol as a major means of stress relief. Evidence reviewed in the current paper suggests that rather than decreasing stress, the consumption of alcohol may actually be *increasing* stress hormone and neurotransmitter secretion. The anabolic and catabolic changes elicited by stress and extreme stress are reviewed and evidence for the effect of alcohol on these functions is considered. The evidence largely supports the premise that the brain reacts to alcohol as a noxious toxin and responds with the full "fight or flight response." Continuous alcohol consumption is likely to result in the same detrimental effects on health as long-term stress. If further research supports this premise, societies which encourage the consumption of large amounts of alcohol may want to reconsider this social sanction.

INTRODUCTION

The current paper grew out of the clinical observation that the effect of drinking alcohol appeared to be particularly damaging during times of high stress. Yet, when people are under stress, one of the most highly predictable behaviors is alcohol consumption. For example, in Japan the major form of stress release for men is going out with colleagues to bars and drinking large amounts of alcohol. The author will present evidence that suggests that alcohol directly elicits the "flight or flight response", a complex set of physiological responses which are meant to insure the survival of the organism during times of danger.

ALCOHOL & THE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) AXIS

It has been shown in animals that alcohol exposure can activate the adrenocortical axis and increase glucocorticoid secretion (Ellis 1966; Mendelson and Stein 1966; Jenkins and Connolly 1968; Stokes 1973; Kakihana and Moore 1976; Kakihana 1979; Majumdar et al. 1981; Guaza et al 1983; Zgombick and Erwin 1988; Wand 1989).

Single doses of alcohol administered to alcohol-naive animals activate the hypothalamic-pituitary-adrenal (HPA) and the sympatho-adrenal (SA) axes. If blood alcohol concentrations (BACs) reach 100 mg / 100 mL or more, the HPA axis is activated consistently (Eskay et al. 1993). The SA axis has been found to be less responsive (Vogel et al. 1986; Patel and Pohorecky 1989).

Acute and chronic alcohol consumption in animals thus appears to activate the stress axis, resulting in continuously or intermittently elevated glucocorticoids which are adrenal steroid hormones secreted in response to various stressors. In general, most data in humans point to the same conclusion (Eskay et al. 1993). As Sapolsky (1993) has pointed out, these hormones are essential for successful adaptation to acute physical and psychological stress, however, chronic overexposure to glucocorticoids can result in a number of problems when catabolic activity is continuously activated and anabolic activity is suppressed over long periods of time.

IS ALCOHOL A STRESSOR WHICH ELICITS THE STRESS RESPONSE?

The term stress has been used to identify a variety of environmental challenges which threaten the homeostasis and the health of an organism. The common stressors include heat, cold, physical injury, exercise, pathogens, and various psychological states such as fear and anxiety. These stressors trigger the stress response/activation of the HPA axis which results in increases in the output of epinephrine and various pituitary hormones. The catecholamines, opiate neuropeptides, and glucocorticoids subsequently secreted by the adrenal gland enable the organism to deal with the stressor by mobilizing energy reserves, increasing cardiovascular tone, and decreasing sensitivity to pain.

The effects of alcohol on the human body and nervous system are complex, however, the current paper will suggest that *part* of this effect stems from the fact that alcohol itself acts as a stressor. It is indeed paradoxical that when under stress, people often turn to a drug which may itself elicit the stress response and increase stress hormone and neurotransmitter activity. The irony may lie in the fact that the relief which people initially feel from stress may stem, in part, from the euphoria and pain-suppression which are components of the brain's attempt to deal with the stressor.

Support for this premise that alcohol itself elicits the "fight or flight response" will begin with a review of the components of the stress response ("fight or flight response"), their adaptive value, and potential negative consequences.

PHYSIOLOGICAL IMPACT OF STRESS

During a crisis the brain appears to act to insure the survival of the organism by causing 1) maximum mobilization of the body's resources (generally catabolic or activation of energy expending functions) (Table 1) and by 2) by suppressing all immediately non-essential bodily functions (anabolic / energy conserving functions) (Table 2). As mentioned earlier, though these two reactions are immediately adaptive, both components can prove maladaptive if stress becomes continuous (see Sapolsky

Table 1 Effects of stress hormones on energy mobilization and other functions during crisis, the possible adaptive effect, and possible consequence of long-term activation.

Effect of Stress Hormones	**Possible Adaptive Advantage**	**Potential Long-Term Consequence**
1-1 Sudden surge in blood pressure	Enables us to flee or fight	Stroke, heart attack, blindness, glaucoma
1-2 Increase in heart rate	Enables us to flee or fight	Stroke or heart attack
1-3 Change in respiration	Enables us to flee or fight	Asthma, other respiratory disorders
1-4 Increase in muscle tension	Enables us to flee or fight	Tension headaches Stiff neck, shoulders Muscle tremors (result of continuous tension)
1-5 Increase in clotting ability of the blood	Not bleed to death if injured	Increased risk of stroke
1-6 Increased protein-degradation	Necessary energy to flee or flight	Atrophy of muscle, skin, and fat tissue
1-7 Increased blood glucose levels	Necessary energy to flee or flight	Diabetes
1-8 Increased calcium levels in blood	Important for coagulation of blood; Essential role in ion balance and enzyme activation; Essential for functioning of heart, muscles, cell membrane permeability	Fragile bones Calcified kidney stones Osteoporosis Skeletal atrophy
1-9 Pain suppression	Able to respond despite injury	Negative impact on mood and pleasure
1-10 Saliva thickens	Not choke on saliva during rapid respiration	Dry mouth
1-11 Evacuation of bowels or bladder	Unnecessary weight may slow flight	Frequent urination or diarrhea
1-12 Sweating	Possibly facilitated holding weapon or climbing tree or rock to escape (during past evolution)	Sweaty palms, feet
Nishio, 1997.		

1992 for a detailed and elegant discussion of this process). Table 1 lists some of the potential consequences of the mobilization of the organism's resources. In some vulnerable people, these can prove to be immediately fatal. For example, an elderly person may suffer a heart attack or stroke at the time of occurrence of extreme stress. Following the acute period, problems may also arise when stress continues unabated for long periods of time.

Table 2 Physiological functions suppressed during stress & possible consequences of this suppression.

Activity Suppressed	Possible Consequence of Long-Term Suppression
2-1 Energy storage	Fatigue, myopathy
2-2 Tissue repair	Slow wound healing
2-3 Digestion	Ulcers Colitis Nausea Stomach cramps
2-4 Growth	Stunted growth, dwarfism
2-5 Replacement of calcium in bones	Osteoporosis
2-6 Inflammatory processes blocked	Increased susceptibility to disease
2-7 Immune system	Increased risk of infection, disease, cancer
2-8 Reproductive functions	Menstrual problems Impotency & Infertility Lower sperm counts in males Decreased sexual interest
2-9 Appetite suppression	Weight loss Risk of anorexia Loss of appetite
Nishio, 1997.	

1. FUNCTIONS ACTIVATED DURING STRESS, THE POSSIBLE LONG-TERM CONSEQUENCES OF ACTIVATION, AND THE EFFECT OF ALCOHOL

As previously mentioned, alcohol has been found to activate the HPA axis. Each of the consequences of catabolic activation and anabolic suppression which have been found to occur following continuous stress and which were listed in Tables 1 and 2 are examined below to determine if this condition has been found following alcohol consumption. Though some clinical data will be presented, the clinical data is badly confounded due to the fact that 1) people tend to drink when under stress and 2) heavy drinking itself often creates high levels of stress through its impact on relationships, functioning at work, health, etc. Thus, though clinical evidence will be presented, more weight needs to be given to animal studies and controlled studies with human subjects.

1-1 INCREASE IN BLOOD PRESSURE

An increase in blood pressure occurs in response to stress in order to enable us to either flee or fight. Possible consequences of this increase may be stroke, heart attack, high blood pressure, glaucoma, and blindness.

Alcohol consumption has been found to be a major risk factor for high blood pressure (MacMahon 1987). Epidemiologic studies have suggested that heavy drinking is not only a risk factor for hypertension but also for hemorrhagic stroke. The

relationship between these diseases and alcohol appears to be dose-dependent. That is, the more alcohol consumed, the higher the risk (Arria and Van Thiel 1992). After a thorough review of epidemiologic studies on the relationship between alcohol consumption and the risk of hypertension, MacMahon (1987) concluded that studies conducted on general population samples demonstrated an increase in blood pressure with increases in alcohol consumption with this finding being independent of age, body weight, and cigarette smoking. Further evidence supporting the conclusion that alcohol consumption increases blood pressure is the finding in hypertensive patients that a decrease in blood pressure occurs over time with abstinence from alcohol (Klatsky 1990). MacMahon (1987) found that the risk for hypertension among people drinking an average of three to four drinks per day was 50 percent higher than nondrinkers and 100 percent higher for people consuming an average of six to seven drinks per day.

A large followup study of women who had normal blood pressure at the start of the study showed that an average of two to three drinks per day was associated with a 40 percent increase in the risk for hypertension compared with nondrinkers (Witteman et al. 1990). Together, the available data suggests that in men, 11 percent to 30 percent of hypertension cases can be attributed to heavy alcohol consumption (Arria and Van Thiel 1992).

1-2 HEART RATE INCREASE

Heart rate increases during times of stress. This can prove immediately fatal as in the elderly person who suffers a heart attack or stroke when severely shocked or frightened, or these consequences can occur when the heart rate is elevated over a long period of time due to continuous stress.

The findings of the action of alcohol on heart rate have not produced consistent findings (Friedman 1992). Heart rate has been found to increase (Juchems and Klobe 1969), not change (Dixon 1970; Ahmed et al 1973), or merely show a transient, inconsistent increase (Grollman 1942). Representative findings include the following. In a study by Friedman et al. (1974) 5 alcoholic and 5 nonalcoholic subjects received a 3-hour infusion of 15%, by volume, of alcohol, resulting in an average peak blood alcohol concentration of 176 milligrams per deciliter (mg/dl). Heart rate tended to increase progressively, averaging 11 beats per minute above the baseline value 1 hour after the infusion had stopped. This change was not observed in all subjects and the change in heart rate was not shown to be caused by the subjects' pretreatment heart rate, blood alcohol concentration, or history of alcohol use.

In the Juchems and Klobe (1969) study, 14 healthy individuals displayed a significant increase in pulse rate following the ingestion of 1 to 2 grams per kilogram of alcohol. At an average blood alcohol concentration of 39 mg/dl, the rate increased by 5 beats per minute; at 85 mg/dl, the maximal increase in rate of 10 beats per minute was observed. No further increase was observed despite increases in the level of blood alcohol. After considering these results, Friedman (1992) concluded that the slight heart rate-enhancing effects that may follow alcohol ingestion appear to be related to

alcohol's action on the nervous system and the adrenal gland.

1-3 CHANGES IN RESPIRATION

Another change which aids fighting or fleeing during danger is the change which occurs in respiration. Low-to-moderate doses of alcohol have been found to increase the respiration rate, however, it should be noted that large anesthetic, and/or toxic doses decrease the respiration rate (Kinney and Leaton 1995).

1-4 INCREASES IN MUSCLE TENSION

During times of danger muscles tense to prepare for fighting or fleeing. Long terms muscle tension can result in tension headaches, stiff neck and shoulder muscles, and muscle tremors. Chronic tension headaches are recognized as one of the common signs/symptoms of alcohol problems seen in the primary care setting (Bradley 1994).

1-5 INCREASED CLOTTING ABILITY OF THE BLOOD

In times of danger, the clotting ability of the blood generally *increases* presumably to prevent the organism from bleeding to death if severely injured. This increased clotting ability over the long-term can carry with it the risk of ischemic stroke.

Chronic, heavy alcohol consumption decreases the number of platelets (Sullivan and Herbert 1964), inhibits clotting, and reduces the release of thromboxane, a hormone-like substance. Alcohol appears to have a profound effect on the clotting ability of the blood by decreasing the levels of circulating platelets, a condition known as thrombocytopenia (Ballard 1989). Thrombocytopenia occurs in 3 to 43 percent of nonacutely ill, well-nourished chronic alcoholics, and 14 to 81 percent of acutely ill, hospitalized alcoholics. There appears to be a direct and immediate effect of alcohol on the platelets (Lindenbaum and Hargrove 1968). The opposite condition, thrombocytosis, may occur as platelet levels rebound and exceed normal levels 1 to 3 weeks after someone with thrombocytopenia begins to abstain from alcohol. Even alcoholics who have platelet counts within the normal range experience an increase in these levels after withdrawal from alcohol, and the height of their rebound usually exceeds the rebound thrombocytosis of patients with thrombocytopenia (Ballard 1993). Many researchers have suggested that thrombocytosis increases the risk of thrombotic disorders which involve blood clots. This suggests that the binge drinker who suddenly abstains may be at particular risk. The mechanism of platelet hyperactivity during alcohol withdrawal has not been explained.

Gorelick (1989) has shown that heavy drinking (greater than 60 grams/four drinks per day) is related to increased risk for stroke. Epidemiologic studies also suggest that moderate drinking increases the risk of stroke (Camargo 1989). There are various types of strokes and alcohol consumption results in a fourfold increase in the incidence of hemorrhagic stroke (the hypertension induced by alcohol is a major risk factor for subarachnoid hemorrhage) while the relationship appears to be J-shaped for ischemic stroke (Gorelick 1989; Klatsky et al 1989). It should be noted that the protective effect

of moderate amounts of alcohol was not found for Japanese populations (Camargo 1989). This difference has been explained by alcohol's effect on the blood itself in that moderate alcohol consumption reduces the viscosity of blood by increasing the anticlotting activity of platelets (Veenstra et al. 1990). Although this result is found with moderate levels of consumption, with higher alcohol consumption, the risk of ischemic stroke increases linearly. Thus at moderate levels of alcohol consumption, there may be a higher likelihood of hemorrhages and hemorrhagic stroke due to the thinning of the blood, but a lower likelihood of the formation of clots which are usually associated with ischemic stroke (Arria and Van Thiel 1992).

A decrease in the blood's ability to clot may contribute, positively or negatively, to blood-related disorders such as heart attack or stroke. Moderate consumption (fewer than 2 drinks per day) of alcohol by people with coronary artery disease appears to reduce the occurrence of heart attacks caused by clogging of an artery on the way to the heart by a blood clot (Moore and Pearson 1986). It has been proposed that in moderate amounts alcohol may be cardioprotective by exerting an anticlotting effect on the blood. However, it is well documented that excess alcohol consumption is associated with an increased risk of thromboembolic disease such as the type of stroke which results when blood clots block arteries and veins. This may be related to the rebound thrombocytosis observed after the cessation of drinking or may be related to the enhanced platelet function which may be attributable to the influx into blood circulation of newly formed platelets with increased functional activity (Ballard 1993).

Although alcohol appears to stimulate many of the same responses as stress, one of the contradictions appears to be in the clotting ability of the blood. In times of danger, the blood generally thickens, thus protecting the organism against excessive blood loss. However, many studies have found that alcohol appears to thin the blood. This may relate to the action of secretagogs. As Sapolsky (1992) has pointed out, different stressors trigger different combinations of secretagog release. For example, hemorrhage stimulates the secretion of CRF, vasopressin, oxytocin, and catecholamines (Plotsky et al. 1985a), hypotension stimulates only CRF (Plotsky et al. 1986), and insulin-induced hypoglycemia only stimulates the secretion of vasopressin (Plotsky et al 1985b). It is thus possible that the thinning of the blood in response to alcohol is a stressor-specific response pattern which is somehow initially adaptive. This blood thinning may possibly stem from the brain's attempt to speed the removal of a toxin (alcohol) from circulation.

The negative impact at higher doses may be related to other components of the stress response elicited by alcohol which may contribute to stroke. Other components of the stress response which might increase the risk of strokes include increased blood pressure (greater turbulence at branches of blood vessels increases risk of cholesterol chunks breaking off and entering the blood stream), increased protein in the blood, and constriction of certain blood vessels for the redirection of blood during stress.

1-6 INCREASED PROTEIN DEGRADATION

Another adaptive response of the body during stress is the breaking down of stored sources of energy in order to fuel the emergency response. If this process continues for a prolonged period, atrophy of body tissues may begin to occur including the atrophy of muscles, skin, and fat tissues.

The balance between protein formation and protein destruction is affected by chronic alcohol abuse with evidence indicating that protein synthesis is decreased and protein destruction is increased (Preedy and Peters 1992; Marsano and McClain 1991). Alcoholics with liver disease seem to have higher requirements for dietary protein because of the increased demand for amino acids to be broken down in muscle gluconeogenesis (Marsano 1993).

Degenerative changes of the heart and skeletal muscle may result from chronic alcohol consumption (Rubin 1989; Arria and Van Thiel 1992).

1-7 INCREASED BLOOD GLUCOSE LEVELS

When challenged by a stressor, the level of glucose in the blood increases as the body tries to supply energy to the necessary areas of the body and brain. It has been found that in individuals with adequate diets, one of the metabolic effects of alcohol may be to cause abnormally high levels of blood glucose (Kinney and Leaton 1995). The development of diabetes have been found to be enhanced by alcohol use (National Institute on Alcohol Abuse and Alcoholism [NIAAA] 1990).

1-8 INCREASED BLOOD CALCIUM LEVELS

During times of stress, the level of calcium in the blood increases. This most likely occurs for a number of reasons. Calcium plays an essential role in ion balance and enzyme activation as well as being essential for the functioning of the heart, muscles, and for cell membrane permeability. During stress, calcium is taken from the bones and further storage of calcium in bones is blocked. If stress continues for a long period of time, this can lead to fragile bones, calcified kidney stones, osteoporosis, and skeletal atrophy.

Alcohol intoxication causes a transitory elevation in parathyroid hormone levels, with resultant high levels of calcium in the blood. When alcohol use is prolonged, serum parathyroid levels remain elevated (Griffiths, Parantainen, and Olson 1993). Laitinen et al. (1991) found that parathyroid hormone levels rose in nonalcoholic men administered 60 grams of alcohol daily (equivalent to approximately 5 standard drinks per day) for 3 weeks. Parathyroid hormone levels returned to normal within 1 week following the cessation of alcohol consumption. In alcoholics, persistent parathyroid hormone changes may develop into secondary hyperparathyroidism. This is thought to be a result of a number of metabolic factors including the reduced synthesis of the steroid sex hormone testosterone (Wright et al 1991) which subsequent leads to decreased activity of osteoblasts (Adler 1992; Van Thiel and Lester 1974). Alcohol also stimulates the secretion of cortisol, a corticosteroid that regulates several metabolic func-

tions (Rico 1990; Rico et al 1985). It has been shown that excess levels of cortisol in the blood may result in decreased bone mineral content (Laitinen et al. 1992). All of these factors, by promoting bone resorption and elevated blood calcium levels, may lead to secondary hyperparathyroidism.

The alcoholic is at risk for at least three significant metabolic bone disorders, among them osteoporosis (Griffiths, Parantainen, and Olson 1993). The mechanism of development of osteoporosis in the alcoholic is unclear, but one of the factors involved in alcohol-related osteoporosis may be the fact that alcoholics have high levels of corticosteroids in their blood. It has been found that corticosteroids can induce bone loss (Ortoft and Oxlund 1988). Laitinen and colleagues (1992) demonstrated decreased bone formation with normal bone resorption in a group of long-term alcoholics during alcohol intoxication; bone formation returned to normal during the 2-week period following cessation of drinking.

1-9 PAIN SUPPRESSION

Yet another component of the "fight or flight" response is pain suppression. It has been hypothesized that this occurs in order to allow an organism to react to save itself despite serious injury. Alcohol was once used as a crude anesthetic because of its pain-killing ability before better and safer anesthetics were developed (Tabakoff, Hoffman, Petersen 1990).

1-10 THICKENING OF SALIVA

Another response during stress is the thickening of saliva which presumably occurs so that the organism will not choke on its saliva or ingest it into the lungs during rapid respiration. The water placed on the podium for public speakers is presumably to counteract this stress induced dry mouth. No data concerning alcohol's acute or chronic effects on saliva secretion was available.

1-11 EVACUATION OF BOWELS OR BLADDER

The automatic evacuation of the bowels and bladder in times of extreme danger is thought to have been adaptive by serving to increase speed of flight. Lesser levels of stress often result in more frequent need to urinate and/or diarrhea.

Chronic diarrhea is recognized as one of the common signs/symptoms of alcohol problems seen in the primary care setting (Bradley 1994).

1-12 INCREASED PERSPIRATION

The increased perspiration on hands and feet which occurs during times of stress is thought to have facilitated the holding of a weapon or the climbing of a tree or rocks during escape over the course of evolution.

It has been found that the chronic alcoholic perspires heavily (Kinney and Leaton 1995).

2. FUNCTIONS SUPPRESSED DURING STRESS, THEIR POSSIBLE LONG-TERM CONSEQUENCES, AND ALCOHOL

In addition to the catabolic (energy expending) functions activated during stress, the brain suppresses various immediately nonessential functions. However, that which is immediately adaptive can become maladaptive over the long run. The following reviews the suppressed anabolic activities, how they can become maladaptive if suppressed over the long-term, and how these activities are affected by alcohol.

2-1 ENERGY STORAGE SUPPRESSED

If energy is constantly used and those stores not replaced, the results will be fatigue and/or myopathy. In the primary care setting, fatigue is recognized as one of the possible signs/symptoms suggestive of alcohol problems (Bradley 1994).

Epidemiological studies have suggested that one of the risk factors for cardiomyopathy may be heavy drinking and that this relationship appears to be dose-dependent (higher the amount of alcohol consumed, the greater the risk). The cardinal feature of cardiomyopathy is a dilated, weakened heart muscle. This condition may result from a number of factors including infections, autoimmune disease, and toxic substances, including alcohol. However, many cases of cardiomyopathy are of unknown origin (Moushmoush and Abi-Mansour 1991). Researchers estimate that 21 percent to 32 percent of cardiomyopathy cases can be attributed to alcohol abuse (Regan 1990).

2-2 TISSUE REPAIR SUPPRESSION

Tissue repair is suppressed during times of stress as the body puts overall survival at the forefront.

As Rubin (1993) has pointed out, a bewildering variety of diseases have been linked to excess consumption of alcohol (more than 60 grams of alcohol per day) yet despite decades of research on the causes of alcohol-induced tissue injury, the pathogenesis (how they are caused) of these disorders remains elusive. Thus far an unequivocal cause and effect relationship between tissue injury and chronic alcohol abuse has not be found. The growth and replication of cells are regulated by several signaling molecules, collectively termed growth factors (Rubin 1993). The presence of alcohol has been shown to inhibit the actions of the platelet-derived growth factors on liver cells (Higashi and Hoek 1991). Rubin (1993) has suggested that such effects may account, at least in part, for the known inhibition of liver regeneration by alcohol and the retardation of growth in the fetal alcohol syndrome.

Alcohol has long been associated with liver disease which occurs not only because of direct injury to liver cells, but because alcohol also appears to perpetuate the damage by disrupting the liver regeneration (self-repair) (Diehl 1993). Data obtained from patients and from animal models (Wands et al. 1979; Duguay et al. 1982; Frank et al. 1979; Orrego et al. 1981; Diehl et al. 1990) indicates that alcohol consumption impairs liver regeneration. Though direct evidence has been sighted herein for only the liver,

alcohol may likely play a role in many diseases by slowing tissue repair through its elicitation of the stress response and the subsequent suppression of this anabolic functions.

2-3 DIGESTION SUPPRESSED DURING STRESS

Digestion is suppressed during stress and this has been shown to result in an increase in ulcers, colitis, nausea, and stomach cramps among others. Alcohol use has been found to irritate the gut's lining and inhibit the muscular contractions called peristalsis that pass food along the intestines. Acute and chronic stomach irritation by alcohol may result in gastritis and can certainly aggravate, if not cause ulcers of the stomach or duodenum. Chronic heavy drinkers may also complain of morning nausea and vomiting (Kinney and Leaton 1995).

2-4 GROWTH SUPPRESSION

The secretion of growth hormones is suppressed during times of stress. The result is particularly evident in severely abused children who may present with stunted growth or dwarfism.

Fetal alcohol exposure is the most blatant example of the deleterious impact of alcohol on normal growth, however acute and chronic alcohol exposure have also been found to inhibit the proliferation and function of cells in some adult tissues, including the liver (Diehl 1993). Both acute and chronic alcohol exposure consistently have been shown to diminish serum GH (hypothalamic-pituitary-growth hormone) and insulinlike growth factor 1 (IGF-1) in animals and humans of both sexes (Emanuelle and Emanuele 1997). Researchers are currently attempting to identify the specific mechanism by which alcohol inhibits the signals of trophic factors. Thus far, the most effective intervention for liver degeneration has been abstinence from alcohol which is associated with gradual resolution of many of alcohol's antiproliferative consequences (Orrego et al. 1981).

2-5 CALCIUM REPLACEMENT IN BONES SUPPRESSED

As mentioned earlier when considering the increase in calcium in the blood during stress, the hormones which facilitate reabsorption of calcium into bones are suppressed during stress. This can eventually result in a number of skeletal abnormalities including osteoporosis. High levels of corticosteroids in the blood of alchoholics have been suggested as a cause of this condition. As mentioned previously, long-term alcoholics demonstrate decreased bone formation with normal bone resorption during alcohol intoxication. However, bone formation returned to normal during the 2-week period following cessation of drinking (Laitinen et al. 1992).

2-6 SUPPRESSION OF INFLAMMATORY PROCESSES

People under stress are generally more susceptible to disease as the inflammatory process (part of the immune system) in the body is suppressed. The neutrophil is a type

of white blood cell that is the primary defense against bacterial invasion and a local accumulation of neutrophils usually occurs in response to such an infection. However, alcohol has been shown to decrease the number of neutrophils. Chronic alcohol intoxication, even in the absence of bacterial infection can lead to decreased numbers of neutrophils (Lindenbaum 1987). The acute administration of mildly intoxicating doses of alcohol to nonalcoholics produces a marked slowing of neutrophil movement into areas of injured skin; this effect rapidly reverses with abstinence from alcohol (Ballard 1993). Neutrophils travel to the sites of inflammation or infection by adhering to capillary walls. Alcohol directly interferes with this process and the more alcohol, the more severe the interference (McGregor et al 1974).

2-7 IMMUNE SYSTEM SUPPRESSION

Not only is the inflammatory response to infection suppressed during stress, but other immune functions as well. With suppressed immunity comes increased susceptibility to infection and cancer. In a review of research concerning alcohol's effect on immune function, Roselle (1992) found that most studies demonstrate that alcohol suppresses many different activities and cell types of the immune system. These findings are consistent with the increased susceptibility to infection observed among alcoholics. For example, alcohol may be a major contributor increasing the susceptibility to infection and hastening the course of diseases associated with AIDS (Kruger & Jerrells 1992). Chronic alcohol consumption has also been associated with increased risk of cancers of the upper digestive and respiratory tracts, and liver. A possible increased risk also exists for cancers of the large bowel and breast. Garro and Lieber (1990) concluded that the suppression of the immune response may be one way in which alcohol influences the cancer-causing process.

2-8 REPRODUCTIVE FUNCTIONS SUPPRESSED

Stress has been shown to disrupt reproductive functions resulting in menstrual problems, impotency and infertility, lower sperm counts in males, and decreased sexual interest in both males and females.

Wright, Gavalier, and Van Thiel (1991) reviewed the effects of alcohol on the male reproductive system and concluded that alcohol causes loss of libido, impotence, and sterility in males. They also concluded that alcohol produces hypogonadism by disrupting all three control points of the hypothalamic-pituitary-gonadal axis and that compensatory mechanisms that normally function to normalize gonadal function are also damaged by alcohol. In addition, they found that the alcohol-induced reduction of gonadotropin-releasing hormone secretion by the hypothalamus appears to be greater than the alcohol-induced reduction in gonadotropin secretion by the pituitary.

In a review of the effects of alcohol on neuroendocrine function in women, Mello et al. (1993) found that alcohol abuse and alcoholism are associated with a broad spectrum of disorders of reproductive function in women including amenorrhea, anovulation, luteal phase dysfunction, ovarian pathology, and hyperprolactinemia. Luteal

phase dysfunction, anovulation, and persistent hyperprolactinemia have also been observed in social drinkers. The risk of spontaneous abortion has been found to be considerably increased in women drinking alcohol. Early menopause is another possible consequence of alcohol consumption in women (Lloyd and Williams 1948).

2-9 APPETITE SUPPRESSION

An additional process suppressed during times of stress is appetite. This can result in weight loss and at its extreme can be seen operative in the vicious cycle of anorexia nervosa. It has been found clinically that chronic heavy drinkers may complain of loss of appetite (Kinney and Leaton 1995). It has also been found that when alcohol is administered in the absence of strict nutritional control, alcohol-fed animals eat less (Korsten and Wilson 1993).

SUMMARY

Experimental evidence is clear that alcohol activates the hypothalamic-pituitary-adrenal axis (HPA). Alcohol consumption appears to elicit many of the same physiological responses as stress often in experimental laboratory settings in the absence of other stressors. It is felt that the data reviewed concerning physiological responses to alcohol give support to the premise that alcohol itself is a stressor which elicits the full spectrum of the "fight or flight response." Alcohol has been shown to increase various catabolic activities including blood pressure and heart rate. Low to moderate doses increase the rate of respiration. The clotting ability of the blood decreases with alcohol ingestion and the current paper suggests that this is a stressor-specific response which is perhaps meant to help rid the circulation of the toxic substance more quickly. Also like stress, alcohol increases protein degradation, blood glucose levels, and blood calcium levels. Other functions which alcohol affects in the same way as stress are pain suppression, bowel and bladder functioning, and perspiration.

Anabolic activities also appear to be affected by alcohol in the same way as by stress. Alcohol appears to suppress energy storage, tissue repair, digestion, growth, and calcium replacement in bones. The inflammatory response and other aspects of the body's immune system as well as reproductive functions and appetite are also suppressed by alcohol.

If alcohol does, in fact, elicit the full spectrum of the stress response, this has profound implications for social policies and social attitudes concerning drinking. For example, the socially condoned practice of drinking alcohol as a way of releasing stress may be achieving the *opposite* objective physiologically. The person who drinks under stress is actually *increasing* their levels of stress hormone and neurotransmitter secretion. It is likely no coincidence that many incidences of crime, illness, and many mental breakdowns are associated with the pairing of alcohol and high levels of stress.

The implications for physical health are obvious. Alcohol negatively impacts directly many organs and systems, but it also has many indirect effects through its elicitation of the multiple components of the stress response. The impact on health may be

particularly detrimental when heavy alcohol consumption overlaps with already high levels of stress. The message is that if one is experiencing high levels of stress, it is particularly important to avoid alcohol.

The changes which occur as a result of the activation of the HPA axis affect not only the body but the mind as well. A future article will focus on the psychobiological impact of stress and whether alcohol appears to elicit the same emotional and cognitive phenomena as stress.

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