

# Cardiovascular Manifestations of Posttraumatic Stress Disorder

Updesh Singh Bedi, MD and Rohit Arora, MD, FACC, FAHA, FACP, FSCAI,

Posttraumatic stress disorder (PTSD) involves the onset of psychiatric symptoms after exposure to a traumatic event. PTSD has an estimated lifetime prevalence of 7.8% among adult Americans, and about 15.2% of the men and 8.5% of the women who served in Vietnam suffered from posttraumatic stress disorder (PTSD)  $\geq 15$  years after their military service. Physiological responses (increase in heart rate, blood pressure, tremor and other symptoms of autonomic arousal) to reminders of the trauma are a part of the DSM-IV definition of PTSD. Multiple studies have shown that patients suffering from PTSD have increased resting heart rate, increased startle reaction, and increased heart rate and blood pressure as responses to traumatic slides, sounds and scripts. Some researchers have studied the sympathetic nervous system even further by looking at plasma norepinephrine and 24-hour urinary norepinephrine and found them to be elevated in veterans with PTSD as compared to those without PTSD. PTSD is associated with hyperfunctioning of the central noradrenergic system. Hyperactivity of the sympathoadrenal axis might contribute to cardiovascular disease through the effects of the catecholamines on the heart, the vasculature and platelet function. A psychobiological model based on allostatic load has also been proposed and states that chronic stressors over long durations of time lead to increased neuroendocrine responses, which have adverse effects on the body. PTSD has also been shown to be associated with an increased prevalence of substance abuse. With this review, we have discussed the effects of PTSD on the cardiovascular system.

**Key words:** posttraumatic stress disorder ■ cardiovascular disease ■ norepinephrine ■ military ■ hypertension

© 2007. From the Department of Internal Medicine (Bedi, resident; Arora, professor of medicine, professor of physiology and biophysics, chairman of cardiology, associate chairman of medicine for research), Rosalind Franklin University of Medicine & Science/Chicago Medical School, North Chicago, IL. Send correspondence and reprint requests for *J Natl Med Assoc.* 2007;99:642–649 to: Dr. Rohit Arora, Professor of Medicine, Professor of Physiology and Biophysics, Chairman of Cardiology, Associate Chairman of Medicine For Research, Rosalind Franklin University of Medicine & Science/Chicago Medical School, Chicago, IL; phone: (847) 688-1900 ext. 84503; fax: (224) 610-2940; e-mail: rohit.arora@va.gov

## INTRODUCTION

Posttraumatic stress disorder (PTSD) involves the onset of psychiatric symptoms after exposure to a traumatic event. Physiological response to reminders of the trauma is a part of the DSM-IV<sup>1</sup> definition of PTSD. The common physiological responses include increase in heart rate, blood pressure, tremor and other symptoms to autonomic arousal.

The estimated lifetime prevalence of PTSD among adult Americans was 7.8% in the National Comorbidity Survey, with the lifetime prevalence in women being more than twice as compared to men (10.4% vs. 5%).<sup>2</sup> According to the National Vietnam Veterans Readjustment Study (NVVRS) which was conducted in the late 1980's, nearly 0.5 million Vietnam veterans (15.2% of the men and 8.5% of the women who served in Vietnam) suffered from PTSD  $\geq 15$  years after their military service.<sup>3</sup>

Hyperarousal as a symptom of PTSD was studied by Dobbs and Wilson, who studied 21 war veterans (eight of whom were “decompensated” and suffering from combat neurosis and severe PTSD, and the other 13 had combat experience but were “compensated”) and compared them with 10 university students who had no combat experience. They were exposed to war-like sounds and flashing lights to represent explosions, while their heart rates, respiratory rates and EEGs were measured. The “decompensated” war veterans were so aroused and upset that no psychophysiological data could be recorded from them. The “compensated” war veterans not only had a higher baseline heart rate and respiratory rate but also showed a greater change to the stimulus.<sup>4</sup>

## Physiological Markers

The various physiological markers which have been studied in PTSD patients include heart rate, blood pressure, muscle activity (with electromyography), electrodermal activity (EDA), electroencephalography and peripheral temperatures. Heart rate and EDA are the most commonly studied parameters and point towards the involvement of the sympathetic nervous system.<sup>5</sup> Some researchers have studied the sympathetic nervous system even further by looking at plasma norepinephrine<sup>6</sup> and

24-hour urinary norepinephrine and cortisol<sup>7</sup> and found them to be elevated in veterans with PTSD, as compared to those without PTSD. Also, people suffering from PTSD show a greater physiological reactivity to events that remind them of the trauma, as compared to people who have suffered similar traumas but do not meet the criterion of PTSD. This has been shown in multiple studies on combat veterans,<sup>8-10</sup> sexual assault victims<sup>11</sup> and survivors of motor vehicle accidents.<sup>12,13</sup>

## Effects on Physical and Cardiovascular Health

Boscarino<sup>14</sup> looked at the prevalence of chronic diseases among Vietnam veterans and found that 67.5% of veterans with PTSD suffered from chronic diseases, as compared to 48.6% of veterans without PTSD [odds ratio (OR)=2.19]. They also reported that PTSD patients had a higher prevalence of circulatory disorders (OR=2.24); abnormal 12-lead, resting electrocardiogram results (OR=2.20); prolonged QRS durations (OR=5.02); arrhythmias (OR=2.26); and myocardial infarctions (MIs) (OR=4.46).<sup>15</sup> One of the hypotheses forwarded to explain this difference is that patients with PTSD have a higher prevalence of chronic disorders because of disturbances in the sympathoadrenal and the HPA axis, leading to abnormalities in the neuroendocrine system and chronically activated norepinephrine levels and decreased basal cortisol levels, increased number of lymphocyte glucocorticoid receptors, greater suppression of cortisol to dexamethasone, and more sensitized pituitary glands. These changes weaken the immune system, making the body more susceptible to chronic diseases. Also, chronic exposure to stress leads to hormonal and endocrine abnormalities, which in themselves may be related with some diseases; e.g., chronically elevated catecholamines and sympathetic activity may lead to higher incidence of arteriosclerosis.<sup>16</sup> Other studies including the NVVRS have also found an increased incidence of physical and cardiovascular symptoms in populations suffering from PTSD.<sup>17,18</sup> A study comparing war veterans with PTSD and those without PTSD came to the conclusion that the veterans who had PTSD had an increased risk of MI and atrioventricular conduction problems.<sup>19</sup>

A greater prevalence of cardiovascular risk factors, angina pectoris and type-A behavior was found by Falger et al. in their study on World War II veterans suffering from PTSD.<sup>20</sup> Smoking and rates of other adverse health practices were higher, and effort tolerance was lower in veterans suffering from PTSD, as compared to those without PTSD in a study conducted by Shalev et al.<sup>21</sup> The poor health outcomes and increased cardiovascular mortality and morbidity in PTSD may be related to the increased anxiety, panic, anger and hostility seen in PTSD.<sup>22</sup> Phobic anxiety has been linked with an increased risk for cardiovascular morbidity and mortality, especially sudden coronary death.<sup>23</sup> Hostility has been isolated as a very strong

factor linking type-A personality with cardiovascular disease.<sup>24</sup> Hostile behavior is a behavioral pattern seen in patients with PTSD; hence, it could be one of the mediators of cardiovascular disease in PTSD patients. It could be related to the increased sympathetic activity seen in these patients, leading to increased sympathetically mediated cardiovascular response and decreased parasympathetic response to stimulation.

Shalev et al. showed that the cardiac reserve was low and the effort tolerance decreased in patients with PTSD.<sup>21</sup> Burn patients with PTSD have been shown to have a decreased tolerance to pain,<sup>25</sup> and a correlation between chronic pain and PTSD has also been proposed. PTSD patients have higher rates of somatic complaints as compared to patients without PTSD.<sup>26</sup>

## Effects of Hyperactivity of the Sympathoadrenal System

Hyperactivity of the sympathoadrenal axis might contribute to cardiovascular disease through the effects of the catecholamine on the heart, the vasculature and platelet function. Platelet secretion of products such as platelet factor 4, beta-thromboglobulin and serotonin is responsible for platelet aggregation, and production of thromboxane A2 and platelet activating factor cause vasoconstriction. Platelet function is modified by increased levels of circulating catecholamines (>4 nmol/L). Catecholamines act upon the alpha-2a receptors on the platelet membranes and can cause increased platelet aggregation, secretion of various products by the platelets and also increase the action of other agonists on platelet function.<sup>27</sup> Thus, changes in platelet function brought on by a hyperfunctioning sympathoadrenal system might increase the chances of cardiovascular mortality and morbidity. Multiple studies have also found elevated catecholamines levels in people with essential hypertension.<sup>28</sup>

## Relationship of Mental Stress with Cardiovascular Disease and Arrhythmias

The effects of stress on cardiovascular system have been looked at and show that stressors, such as lack of control on the job, increase coronary heart disease (OR=1.93).<sup>29</sup> High levels of stress at job are also associated with increases in ambulatory blood pressure at work (systolic by 6.8 mmHg and diastolic by 2.8 mmHg) and left ventricular mass index.<sup>30</sup> On following the carotid intima-media thickness with ultrasound, it was found that people with higher job stresses had 48% greater atherosclerotic progression than others.<sup>31</sup> Chronic stress has also been linked with increased levels of plasminogen activator inhibitor-1, thus increasing the chances of fibrin deposition by decreasing spontaneous fibrinolysis.<sup>32</sup>

Activation of the autonomic nervous system and sympathetic activity may play a major role in causing ar-

rhythmias in early phase of myocardial ischemia (phase 1a).<sup>33</sup> Tavazzi et al. performed programmed ventricular stimulation under control and mental arithmetic (psychological stress) in 19 patients with recent uncomplicated MI. They found that during mental stress the blood pressure increased, mean ventricular refractory period decreased by 8 ms and unsustained ventricular tachycardia ( $\geq 6$ ) was induced in seven patients (as compared to in two patients during control conditions). During mental stress, ventricular fibrillation was evoked by double and triple extra-stimuli (one patient each). Thus, they came to the conclusion that in uncomplicated post-MI patients, mental stress can cause electrophysiological modifications that might lead to the appearance of life-threatening arrhythmias.<sup>34</sup> Follick et al. also found that self-reported mental stress was associated with a higher incidence of ectopic beats in a prospective study following post-MI patients over one year.<sup>35</sup> Also, psychological stress has been associated with increased incidence of cardiac events. Jiang et al. studied 126 patients with documented CAD and subjected them to mental stress and exercise stress-testing. Patients with baseline mental stress-induced ischemia were associated with subsequent higher rates of adverse cardiac events (OR=2.8) independent of age, baseline LVEF and history of previous MI.<sup>36</sup>

## Allostatic Load

McEvan and Stellar<sup>37</sup> have proposed a psychobiological model that explains how potential stressors could lead to physical disease. Allostasis is a state in which the physiological systems of the body fluctuate to meet demands from external forces. Most of the allostatic responses involve the sympathetic nervous system and the HPA axis. These are activated whenever the body experiences a challenge such as infection or danger and are shut down when the danger passes away. They extended the concept of allostasis over time and suggested that chronic stressors over long durations of time lead to increased neural or neuroendocrine responses, which have adverse effects on the body (“allostatic load”). They proposed “allostatic load” as the factor responsible for increased “wear and tear” of the body, thus increasing the chances of developing disease. The increased number and chronicity of the various disease-enhancing factors which occur in a PTSD patient may lead to enhanced disease processes over a period of time. In an analysis of the MacArthur Studies of Successful Aging data, an attempt was made to quantify allostatic load by looking at systolic blood pressure, overnight urinary cortisol and catecholamine excretion, waist-to-hip ratio, glycosylated hemoglobin, ratio of serum high-density lipoprotein (HDL) in the total serum cholesterol concentration, serum concentration of dehydroepiandrosterone sulfate and serum HDL cholesterol concentration. They came to the conclusion that people with higher allostatic loads

at baseline were more likely to have declines in physical and cognitive functioning and a higher incidence of cardiovascular disease.<sup>38</sup>

## PTSD and Heart Rate Variability

Heart rate varies around a mean value, depending upon inputs from the sympathetic and parasympathetic nervous system, and this variation is referred to as heart rate variability (HRV). On power spectrum analysis, the contribution of high frequency (HF, which reflects the vagal activity), low frequency (LF, which is affected by both sympathetic and parasympathetic activity) and very low frequency (VLF) components of total variance of heart rate can be assessed. Cohen et al. found that patients with PTSD at rest had higher heart rates, lower HRV with higher LF components and lower HF components than controls, pointing towards a reduced resting parasympathetic tone and increased sympathetic activity. However, in contrast to other studies which found an increased physiological reactivity to trauma, they did not find any significant changes in autonomic activity (as measured by HR, HF and LF) when the PTSD patients were asked to recount traumatic events. Based on this, they suggested that PTSD is a state of chronic autonomic hyperstimulation, which prevents the autonomic system from responding to further stimuli.<sup>39</sup> The theory that chronic behavioral and psychosocial stressors lead to changes in the autonomic nervous system function was tested by looking at civil servants in the Whitehall II study population. Low employment grade was found to be linked with low HRV, which is a measure of the cardiac parasympathetic function. Low HRV was also associated with adverse behaviors such as smoking, alcohol, poor diet and decreased exercise, and showed strong linear associations with various components of the metabolic syndrome, such as systolic blood pressure, HDL cholesterol, triglycerides, waist circumference, and fasting and two-hour postload glucose levels, thus suggesting that low social position and the stressors associated with it might lead to a chronically impaired autonomic system, which is associated with increased coronary risk factors.<sup>40</sup> Breathing techniques (Sudarshan Kriya yoga) by increasing the parasympathetic drive and calming the stress response system and neuroendocrine release of hormones may decrease anxiety and posttraumatic stress.<sup>41</sup>

## Effects on Heart Rate and Blood Pressure

In many studies on war veterans, the baseline heart rate has been found to be elevated in the veterans suffering from PTSD, as compared to the veterans who did not meet the criterion for PTSD. Blanchard proposed that this could be either because these veterans are in a permanent state of “sympathetic overdrive” or it could represent an “experimental artifact” because the veterans were aroused in expectation of the coming psychophysi-

ological assessment.<sup>42</sup> Mcfall et al. looked at this issue by studying just the baseline heart rates, systolic and diastolic blood pressures, and norepinephrine and epinephrine levels over an extended period (with any psychophysiological stimuli) and did not find any significant differences among veterans with PTSD and those without it.<sup>43</sup> Some other studies,<sup>44,45</sup> however, found that veterans with PTSD had significantly elevated baseline cardiovascular responses. Buckley et al.<sup>46</sup> conducted a meta-analysis looking at 34 studies and 2,670 subjects and compared the basal heart rates and blood pressures of patients with PTSD with those of normal subjects. They found that the resting heart rates in PTSD patients were on an average 5 beats per minute faster than normal subjects. The effect on blood pressure was not as pronounced, with an average difference of 1–5 mmHg noted between subjects suffering from PTSD and those not. They also noted that studies with the most chronic PTSD samples showed the largest differences in basal heart rates, indicating that long-standing PTSD leads to structural and functional changes<sup>47</sup> and cardiovascular adaptation to the repeated stress responses. This repeated cardiac reactivity to stress has been shown to increase atherosclerosis and increase the incidence of coronary artery disease.<sup>48,49</sup> Also, studies have found a correlation between higher resting heart rate with early mortality from cardiovascular diseases.<sup>50</sup> Effects of long-standing elevations in diastolic blood pressure of even 5 mmHg have been associated with an increased probability of stroke and coronary artery disease in hypertensive populations.<sup>51</sup>

This basal increase in cardiovascular activity can be explained by  $\geq 3$  hypotheses.<sup>52</sup> Firstly, systemic changes in cardiovascular function might result from the cardiovascular responses to repeated stress which occurs in PTSD patients. It has been shown in multiple studies that patients with PTSD have increased cardiovascular responsiveness to stimuli reminiscent of the initial trauma, and that increased norepinephrine and epinephrine release occurs during such episodes, suggesting towards the involvement of the autonomic nervous system in bringing about the increased heart rates and blood pressure during periods of stress. Structural and functional changes in the cardiovascular system might result from such repeated autonomic activity. Chronic sympathetic activation can lead to downregulation of the beta-adrenergic receptors in the heart and peripheral vessels which increases peripheral resistance and hence blood pressure.<sup>53,54</sup>

The second hypothesis is that this increased baseline cardiovascular activity can be explained by emotional priming or anticipatory anxiety. If exposure to stimuli reminiscent of trauma occurs just before the study, then the threshold for subsequent responses is lowered, and this is referred to as emotional priming, whereas anticipatory anxiety occurs because the patients are awaiting exposure to stimuli that will remind them of the trauma.<sup>55</sup>

Ambulatory monitoring has been used to negate the influence of these two factors on the cardiovascular activity; however, the results of these studies have not been consistent, with some studies showing increase<sup>56–58</sup> in basal cardiovascular activity, whereas others do not.<sup>20,42,59</sup>

The third hypothesis looks at the other variables such as smoking and alcohol consumption. PTSD has been linked with an increased rate of smoking<sup>60</sup> and alcohol consumption.<sup>2</sup> Smoking has been linked to cardiovascular morbidity and mortality, and alcohol has been associated with increased blood pressure and heart rates.<sup>61,62</sup> Thus, the basal increase in heart rate seen in PTSD patients could be because of the increased consumption of alcohol and smoking in this population

## PTSD after Significant Cardiovascular Events and Trauma

Some small studies have shown that 8–16% of patients develop symptoms suggestive of PTSD post-MI.<sup>63–65</sup> Bennet et al., looking at post-MI patients, suggested that negative affect, fear at the time of MI, low levels of social support and inability to describe one's emotions (alexithymia) are some of the factors that predict the chances of developing PTSD post-MI.<sup>66</sup> Up to 12% of pediatric patients who underwent cardiac surgery developed PTSD, with length of stay in the ICU (>48 hours) being a strong predictor of subsequent development of PTSD.<sup>67</sup> In another study looking at adult patients postcardiac surgery, 4.2% had PTSD prior to surgery, and the number rose to 18.2% six months postsurgery.<sup>68</sup> Following cardiothoracic surgery, patients who had developed PTSD showed lower psychosocial functioning and life satisfaction.<sup>69</sup> Some patients who have significant coronary events subsequently may develop PTSD, and this may have a potential role in reinfarctions and mortality.<sup>70</sup>

## Role of Noradrenaline

It has been hypothesized that the symptoms seen in patients suffering from PTSD and other anxiety disorders might be related to increased noradrenergic responsiveness. The behavioral manifestations of catecholamine administration (or those observed in patients with pheochromocytomas) are similar to the ones which are seen in PTSD patients, who suffer from chronic symptoms of hyperarousability, are irritable, have an exaggerated startle response and decreased sleep. The increase in heart rates and blood pressures that occurs when patients with PTSD are reminded of the trauma also occurs with catecholamine administration. These findings along with the fact that increased release of catecholamines occurs under stress points to the fact that alterations in the catecholaminergic system might be related to PTSD.

It has been shown that stress, anxiety and fear are associated with increased plasma and urinary norepinephrine, epinephrine and their metabolites such as 3-methoxy-4-hydroxy-phenylethylene-glycol<sup>71,72</sup> (MHPG)

in healthy humans; e.g., epinephrine levels have been shown to increase two-fold during public speaking and norepinephrine levels three times during physical exercise.<sup>73</sup> It was shown in public speakers that epinephrine and norepinephrine levels were elevated prior to and during the speech and were associated with an increase in heart rate and electrocardiogram (ECG) abnormalities. The increased heart rate and ECG changes could be prevented by administration of beta-blockers.<sup>74</sup>

Kardiner noticed that some war veterans exhibited symptoms such as increased heart rate, blood pressure, diaphoresis, dizziness, vertigo and nausea, which pointed towards hyperresponsiveness of the sympathetic system in these patients.<sup>75</sup> Kolb hypothesized that in PTSD there occurred a “conditioned emotional response” to the original traumatic event, and subsequently when the patient was exposed to events reminding him of the original trauma, there occurred an exaggerated physiological response mediated through the adrenergic systems.<sup>76</sup> Multiple studies have shown that patients suffering from PTSD have an increased baseline heart rate,<sup>10,77-79</sup> increased heart rate and blood pressure response to traumatic slides, sounds and scripts<sup>4,78,80-83</sup> and increased startle reaction.<sup>84</sup> Some studies<sup>82,83,85</sup> have not found an increase in the basal heart rate of patients with PTSD; however, an increase in reactivity to reminders of the trauma has been a consistent finding.<sup>86</sup>

## Plasma and Urinary Norepinephrine and Epinephrine

Studies have also looked at plasma and urinary epinephrine and norepinephrine, which are peripheral measures of the noradrenergic system. Studies have not shown an increase in the resting plasma norepinephrine;<sup>42,87</sup> however, they have shown an increase in plasma epinephrine<sup>83</sup> and norepinephrine in response to traumatic reminders in PTSD patients. An increase in 24-hour urinary epinephrine and norepinephrine has also been demonstrated in patients with PTSD, as compared to patients with schizophrenia, major depression and normal subjects. In fact, an increase in the norepinephrine–cortisol ratio has been found to be more specific for patients with PTSD. This increase in the norepinephrine/cortisol ratio occurs because of an increase in the urinary norepinephrine as well as a decrease in the urinary cortisol levels found in these patients.<sup>88</sup> Not only do patients with PTSD have greater and longer durations of increase in plasma epinephrine levels as compared to controls, but also, the increases in epinephrine levels are greater when these patients are exposed to trauma-relevant stimuli as compared to trauma-irrelevant stimuli.<sup>83</sup> These studies point towards an increased responsiveness of the sympathoadrenal system in patients with PTSD.

## Peripheral Norepinephrine Receptor Function

Studies have shown a decrease in the number of platelet adrenergic alpha-2 receptors in patients with PTSD.<sup>89</sup> It has also been shown that the alpha-2 receptor complex is uncoupled and hence is less efficient in patients with PTSD.<sup>90</sup> A decrease in basal as well as stimulated cyclic adenosine 3'-5'-monophosphate (cAMP)<sup>91</sup> and monoamine oxidase<sup>92</sup> (MAO) activity has been observed in patients suffering from PTSD, as compared to healthy controls. MAO degenerates catecholamines; hence, decreased MAO activity correlates with higher systemic norepinephrine and epinephrine levels. This downregulation of receptors as well as their decreased responsiveness point towards chronically high norepinephrine levels bringing about these compensatory changes.

## Pharmacological Studies

The fact that in patients with PTSD, anxiety, flashback and other symptoms of autonomic arousal have been associated with an increased noradrenergic activity has therapeutic implications. These symptoms respond well to drugs that reduce noradrenergic function. Propranolol is a beta-blocker and hence antagonizes the sympathetic system. It has been studied in Vietnam veterans<sup>93</sup> and abused children<sup>94</sup> with PTSD and has shown to reduce the number of nightmares, recollections of trauma, hypervigilance, insomnia, startle responses, angry outbursts and other arousal symptoms. Clonidine is a centrally acting alpha-2 agonist that reduces central adrenergic activity by reducing the activity in the locus coeruleus. It has also been shown to reduce nightmares, improve sleep, decrease explosiveness and reduce hyperalertness and other symptoms of sympathetic activity.

## Correlation with Increased Substance Abuse

Sixty-to-80% of patients suffering from PTSD are known to suffer from concurrent substance abuse problems,<sup>95,96</sup> such as the use of alcohol, opiates, marijuana and other central depressants. In a study, it was found that 48% of veterans with PTSD were heavy smokers (>25 cigarettes per day), as compared to 28% of veterans without PTSD.<sup>97</sup> Another longitudinal study found that increases in PTSD were associated with increases in smoking and alcohol consumption.<sup>98</sup> It may be because these patients have a hyperactive central sympathetic system, and these agents, which depress the central adrenergic activity, produce temporary relief to patients suffering from PTSD. Also, they have a deficiency of endogenous opiates, and substance abuse with opiates not only provides relief from the PTSD symptoms by decreasing the central sympathetic drive but also replenishes the endogenous opioid system. This makes it particularly difficult to deal with the problem of substance abuse in these patients because they not only have to

deal with the withdrawal symptoms, but there is a danger of exacerbating the PTSD symptoms.<sup>99</sup>

## CONCLUSION

Components of PTSD include hyperarousability and physiological reactivity to events reminiscent of the original trauma. These patients have increased sympathoadrenal activity, as evidenced by increased baseline heart rate; increased heart rate and blood pressure response to traumatic slides, sounds and scripts; increased startle reaction; and increased plasma epinephrine, nor-epinephrine and 24-hour urinary norepinephrine. Hyperactivity of the sympathoadrenal axis might contribute to cardiovascular disease through the effects of the catecholamines on the heart, the vasculature and platelet function. A psychobiological model based on allostatic load has also been proposed and states that chronic stressors over long durations of time lead to increased neural or neuroendocrine responses that have adverse effects on the body. PTSD has also been shown to be associated with an increased prevalence of substance abuse, which has its own adverse biological effects.

## REFERENCES

- Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Text rev. Washington, DC: American Psychiatric Association; 2000.
- Kessler RC, Sonnega A, Bromet E, et al. Posttraumatic stress disorder in the National Comorbidity survey. *Arch Gen Psychiatry*. 1995;52:1048-1060.
- Schlenger WE, Kulka RA, Fairbank JA. The prevalence of post-traumatic stress disorder in the Vietnam generation: a multimethod, multisource assessment of psychiatric disorder. *J Trauma Stress*. 1992;5:333-363.
- Dobbs D, Wilson WP. Observations on Persistence of War Neurosis. *Dis Nerv Syst*. 1960;21:1-6.
- Blanchard EB, Buckley TC. Psychophysiological assessment of posttraumatic stress disorder: posttraumatic stress disorder: a comprehensive text. Allyn and Bacon; 1999:248-266.
- Blanchard EB, Kolb LC, Prins A. Psychophysiological responses in the diagnosis of posttraumatic stress disorder in Vietnam veterans. *J Nerv Ment Dis*. 1991;179:99-103.
- Mason JW, Giller EL, Kosten TR, et al. Urinary free-cortisol level in post-traumatic stress disorder patients. *J Nerv Ment Dis*. 1986;174:145-149.
- Blanchard EB, Kolb LC, Taylor A, et al. Cardiac response to relevant stimuli as an adjunct in diagnosing post-traumatic stress disorder: replication and extension. *Behav Ther*. 1989;20:535-543.
- Keane TM, Kaloupek DG, Blanchard EB, et al. Utility of psychophysiological measurements in the diagnosis of post traumatic stress disorder: results from a Department of Veterans Affairs Cooperative study. *J Consult Clin Psychol*. 1998;6:914-923.
- Pitman RK, Orr SP, Foa DF, et al. Psychophysiological assessment of post traumatic stress disorder imagery in Vietnam combat veterans. *Arch Gen Psychiatry*. 1987;44:970-975.
- Griffin MG, Resick PA, Mechanic MB. Psychophysiological and nonverbal assessment of peritraumatic dissociation in rape victims. Paper presented at the 10th annual meeting of the International Society for traumatic stress studies, 1994, Chicago, IL.
- Blanchard EB, Hickling EJ, Buckley TC, et al. The psychophysiology of motor vehicle accident related post-traumatic stress disorder: replication and extension. *J Consult Clin Psychol*. 1996;64:742-751.
- Blanchard EB, Hickling EJ, Taylor AE, et al. The psychophysiology of motor vehicle accident related post traumatic stress disorder. *Behav Ther*. 1994;25:453-467.
- Boscarino JA. Diseases Among Men 20 Years After Exposure to Severe Stress: Implications for Clinical Research and Medical Care. *Psychosom Med*. 1997;59(6):605-614.
- Boscarino JA, Chang J. Electrocardiographic abnormalities among men 20 years after severe stress. *Ann Behav Med*. 1999;19:S146.
- Boscarino JA, Katkin E, eds. Cardiovascular Reactivity to Psychological Stress and Disease. Washington, DC: American Psychological Association; 1993.
- McFarlane AC, Atchison M, Rafalowicz E, et al. Physical symptoms in post-traumatic stress disorder. *J Psychosom Res*. 1994;38(7):715-726.
- Wagner D, Heinrichs M, Ehler U. Prevalence of Symptoms of Posttraumatic Stress Disorder in German Professional Firefighters. *Am J Psychiatry*. 1998;155:1727-1732.
- Boscarino JA, Chang J. Electrocardiogram abnormalities among men with stress-related psychiatric disorders: implications for coronary heart disease and clinical research. *Ann Behav Med*. 1999;21:227-234.
- Falger PRJ, Op den Velde W, Hovens JE. Current posttraumatic stress disorder and cardiovascular risk factors in Dutch resistance veterans from World War II. *Psychother Psychosom*. 1992;57:164-171.
- Shalev AY, Bleich A, Ursano RJ. Posttraumatic stress disorder: somatic comorbidity and effort tolerance. *Psychosomatics*. 1990;31:197-203.
- Schnurr PP, Jankowski KM. Physical health and post traumatic stress disorder: review and synthesis. *Semin Clin Neuropsychiatry*. 1999;4(4):295-304.
- Hayward C. Psychiatric illness and cardiovascular disease risk. *Epidemiol Rev*. 1995;17(1):129-138.
- Goldstein MG, Niaura R. Cardiovascular death, Part I: Coronary artery disease and sudden death, In Soudemire A, eds. Psychological factors affecting medical conditions. Washington, DC: American Psychiatric Press; 1995:19-37.
- Perry SW, Cella DF, Falkenberg J. Pain perception in burn patients with stress disorders. *J Pain Sympnt Manag*. 1987;2:29-33.
- Solomon Z, Miculincer M. Combat stress reaction, post-traumatic stress disorder and somatic complaints among Israeli soldiers. *J Psychosom. Res*. 1987;31:131-137.
- Anfossi G, Trovati M. Role of catecholamines in platelet function: pathophysiological and clinical significance. *Eur J Clin Invest*. 1996;26:353-370.
- Goldstein DS. Plasma catecholamines and essential hypertension: an analytical review. *Hypertension*. 1983;5:86-99.
- Bosma H, Marmot MG, Hemingway H, et al. Low job control and risk of coronary heart disease in Whitehall II (prospective cohort) study. *BMJ*. 1997;314:558-565.
- Schnall PL, Schwartz JE, Landsbergis PA, et al. Relation between job strain, alcohol, and ambulatory blood pressure. *Hypertension*. 1992;19:488-494.
- Everson SA, Lynch JW, Chesney MA, et al. Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study. *BMJ*. 1997;314:553-558.
- Raikkonen K, Lassila R, Keltikangas-Jarvinen L, et al. Association of chronic stress with plasminogen activator inhibitor-1 in healthy middle-aged men. *Arterioscler Thromb Vasc Biol*. 1996;16:363-367.
- Zaza A, Schwartz PJ. Role of the autonomic nervous system in the genesis of early ischemic arrhythmias. *J Cardiovasc Pharmacol*. 1985;7(suppl 5):S8-S12.
- Tavazzi L, Zotti AM, Rondanelli R. The role of psychologic stress in the genesis of lethal arrhythmias in patients with coronary artery disease. *Eur Heart J*. 1986;7(suppl A):99-106.
- Follick MJ, Gorkin L, Capone RJ, et al. Psychological distress as a predictor of ventricular arrhythmias in a post-myocardial infarction population. *Am Heart J*. 1988;116:32-36.
- Jiang W, Babyak M, Krantz DS, et al. Mental stress-induced myocardial ischemia and cardiac events. *JAMA*. 1996;276:1651-1656.
- McEwan BS, Stellar E. Stress and the individual: Mechanisms leading to disease. *Arch Intern Med*. 1993;153:2093-2101.
- Seeman TE, Singer BH, Rowe JW, et al. Price of adaptation—allostatic load and its health consequences: MacArthur studies of successful aging. *Arch Intern Med*. 1997;157:2259-2268.
- Cohen H, Benjamin J, Geva AB, et al. Autonomic dysregulation in panic disorder and in post-traumatic stress disorder: application of power spectrum analysis of heart rate variability at rest and in response to recollection of trauma or panic attacks. *Psychiatry Res*. 2000;96(1):1-13.

40. Hemingway H, Shipley M, Brunner E, et al. Does Autonomic Function Link Social Position to Coronary Risk? The Whitehall II Study. *Circulation*. 2005;111:3071-3077.
41. Brown RP, Gerbarg PL. Sudarshan Kriya yogic breathing in the treatment of stress, anxiety, and depression: part I—neurophysiologic model. *J Altern Complement Med*. 2005;11(1):189-201. Erratum in: *J Altern Complement Med*. 2005;11(2):383-384.
42. Blanchard EB. Elevated basal levels of cardiovascular responses in Vietnam veterans with PTSD: a health problem in the making? *J Anxiety Disord*. 1990;4:233-237.
43. McFall ME, Veith RC, Murburg MM. Basal sympathoadrenal function in posttraumatic stress disorder. *Biol Psychiatry*. 1992;31:1050-1056.
44. Gerardi RJ, Keane TM, Cahoon BJ, et al. An in vivo assessment of physiological arousal in posttraumatic stress disorder. *J Abnorm Psychol*. 1994;103:825-827.
45. Marouka M, Carlson JG, Chemtob CM. Twenty four hour ambulatory blood pressure and heart rate monitoring in combat related posttraumatic stress disorder. Unpublished doctoral dissertation, University of Hawaii.
46. Buckley TC, Kaloupek DG. A meta-analytic examination of basal cardiovascular activity in posttraumatic stress disorder. *Psychosom Med*. 2001;63:585-594.
47. Light KC, Sherwood A, Turner JR. High cardiovascular reactivity to stress: a predictor of later hypertension development. In: Turner JR, Sherwood S, Light KC, eds. Individual differences in cardiovascular response to stress. New York, NY: Plenum Press; 1992:281-293.
48. Fredrickson M, Mathews KA. Cardiovascular responses to behavioral stress and hypertension: a meta-analytic review. *Ann Behav Med*. 1990;12:30-39.
49. Manuck SB, Kaplan JR, Clarkson TB. Behaviorally induced heart rate reactivity and atherosclerosis in cynomolgus monkeys. *Psychosom Med*. 1983;45:95-108.
50. Greenland P, Davglus ML, Dyer AP, et al. Resting heart rate is a risk factor for cardiovascular and non cardiovascular mortality. *Am J Epidemiol*. 1999;149:853-862.
51. Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary artery disease. Part 2, short term reductions in blood pressure: overview of randomized drug trials in their epidemiological context. *Lancet*. 1990;335:827-837.
52. Buckley TC, Kaloupek DG. A meta-analytic examination of basal cardiovascular activity in posttraumatic stress disorder. *Psychosom Med*. 2001;63:585-594.
53. Amerena J, Julius S. The role of the autonomic nervous system in hypertension. *Hypertens Res*. 1995;18:99-110.
54. Hocking-Schuler JL, O'Brien WH. Cardiovascular recovery from stress and hypertension risk factors: a meta-analytic review. *Psychophysiology*. 1997;34:649-659.
55. Prins A, Kaloupek DG, Keane TM. Psychophysiological evidence for autonomic arousal and startle in traumatized adult populations. In: Friedman MJ, Charney DS, Deutch AY, eds. Neurobiological and clinical consequences of stress: from normal adaptation to PTSD. Philadelphia, PA: Lippincott-Raven; 1995:291-314.
56. Cohen H, Kotler M, Matar MA, et al. Power spectral analysis of heart rate variability in posttraumatic stress disorder patients. *Biol Psychiatry*. 1997;41:627-629.
57. Gerardi RJ, Keane TM, Cahoon BJ, et al. An in vivo assessment of physiological arousal in posttraumatic stress disorder. *J Abnorm Psychol*. 1994;103:825-827.
58. Muraoka RJ, Carlson JG, Chemtob CM. Twenty-four hour ambulatory blood pressure and heart rate monitoring in combat related posttraumatic stress disorder. *J Trauma Stress*. 1998;11:473-484.
59. Orr SP, Meyerhoff JL, Edwards JV, et al. Heart rate and blood pressure resting levels and responses to generic stressors in Vietnam veterans with post traumatic stress disorder. *J Trauma Stress*. 1998;11:155-164.
60. Beckham JC, Moore SD, Feldman ME, et al. Health status, somatization, and severity of posttraumatic stress disorder. *Am J Psychiatry*. 1998;155:1565-1569.
61. Kunos G, Varga K. Alcohol effects on autonomic control of the cardiovascular system. In: Zakhari S, Wassef M, eds. Alcohol and cardiovascular system. Bethesda, MD: National Institutes of Health; 1996:243-261.
62. Camargo CA, Rimm EB. Epidemiological research on moderate alcohol consumption and blood pressure. In: Zakhari S, Wassef M, editors. Alcohol and cardiovascular system. Bethesda, MD: National Institutes of Health; 1996:25-62.
63. Doerfler LA, Pbert L, DeCosimo. Symptoms of post-traumatic stress disorder following myocardial infarction and coronary artery bypass surgery. *Gen Hosp Psychiat*. 1994;185:498-506.
64. Kutz I, Shabatai H, Solomon Z, et al. Post-traumatic stress disorder in myocardial infarction patients: prevalence study. *Isr J Psychiatry Relat Sci*. 1994;31(1):48-56.
65. Bennett P, Brooke S. Myocardial infarction, intrusive memories, and post-traumatic stress disorder. *Br J Clin Psychol*. 1999;38:411-416.
66. Bennett P, Conway M, Clatworthy J, et al. Predicting post-traumatic symptoms in cardiac patients. *Heart Lung*. 2001;30(6):458-465.
67. Connolly D, McClowry S, Hayman L, et al. Posttraumatic stress disorder in children after cardiac surgery. *J Pediatr*. 2004;144(4):480-484.
68. Schelling G, Richter M, Roozendaal B, et al. Exposure to high stress in the intensive care unit may have negative effects on health-related quality-of-life outcomes after cardiac surgery. *Crit Care Med*. 2003;31(7):1971-1980.
69. Stoll C, Schelling G, Goetz AE, et al. Health-related quality of life and post-traumatic stress disorder in patients after cardiac surgery and intensive care treatment. *J Thorac Cardiovasc Surg*. 2000;120(3):505-512.
70. Pedersen SS. Post-traumatic stress disorder in patients with coronary artery disease: a review and evaluation of the risk. *Scand J Psychol*. 2001;42(5):445-451.
71. Buchsbaum MS, Muscettola G, Goodwin FK. Urinary MHPG, Stress response, personality factors and somatosensory evoked potentials in normal subjects and patients with major affective disorders. *Neuropsychobiology*. 1981;7:212-216.
72. Lader M. The peripheral and central role of the catecholamines in the mechanisms of anxiety. *Int Pharmacopsychiatry*. 1974;9:125-137.
73. Dimsdale J, Moss J. Plasma catecholamines in stress and exercise. *JAMA*. 1980;243:340-342.
74. Taggart P, Carruthers M, Sommerville W. Electrocardiogram, plasma catecholamines, and lipids and their modification by oxprenolol when speaking before an audience. *Lancet*. 1973;2(7825):341-346.
75. Kardiner A. The traumatic neuroses of war. Psychosomatic monograph II-III. National research Council, Washington, DC; 1941.
76. Kolb LC. The post traumatic stress disorder of combat: A subgroup with a conditioned emotional response. *Mil Med*. 1984;149(3):237-243.
77. Wenger MA. Studies of autonomic balance in Army Air Force personnel. *Comp Psychol Monogr*. 1984;101:1-11.
78. Blanchard EB, Kolb LC, Pallmeyer TP, et al. A psychophysiological study of posttraumatic stress disorder in Vietnam veterans. *Psychiatr Q*. 1982;54:220-229.
79. Kolb LC. The post traumatic stress disorder of combat: A subgroup with a conditioned emotional response. *Mil Med*. 1984;149(3):237-243.
80. Malloy PF, Fairbank JA, Keane TM. Validation of a multimethod assessment of posttraumatic stress disorders in Vietnam veterans. *J Consult Clin Psychol*. 1983;51:488-494.
81. McFall ME, Murburg MM, Ko GN, et al. Autonomic responses to stress in Vietnam combat veterans with post traumatic stress disorder. *Biol Psychiatry*. 1990;27:1165-1175.
82. Orr SP, Pitman RK, Lasko NB, et al. Psychophysiological assessment of posttraumatic stress disorder imagery in world war II veterans. *J Abnorm Psychol*. 1993;102:152-159.
83. Shalev AY, Orr SP, Peri T, et al. Physiologic responses to loud tones in Israeli patients with posttraumatic stress disorder. *Arch Gen Psychiatry*. 1992;49:870-874.
84. Butler RW, Braff DL, Rausch JL, et al. Physiological evidence of exaggerated startle response in a subgroup of Vietnam veterans with combat-related PTSD. *Am J Psychiatry*. 1990;147:1308-1312.
85. Orr SP, Pitman RK, Lasko NB, et al. Psychophysiological assessment of posttraumatic stress disorder imagery in world war II veterans. *J Abnorm Psychol*. 1993;102:152-159.
86. Bremner JD, Krystal JH, Southwick SM, et al. Noradrenergic mechanisms

in stress and anxiety: II. Clinical studies. *Synapse*. 1996;23:39-51.

87. Blanchard EB, Kolb LC, Prins A, et al. Changes in plasma norepinephrine to combat related stimuli among Vietnam veterans with posttraumatic stress disorder. *J Nerv Ment Dis*. 1991;179:371-373.

88. Mason JW, Giller EL, Kosten TR, et al. Elevation of urinary norepinephrine/cortisol ratio in posttraumatic stress disorder. *J Nerv Ment Dis*. 1988;176(8):498-502.

89. Perry BD, Giller EJ, Southwick SM. Altered platelet alpha-2 adrenergic binding sites in posttraumatic stress disorder (letter). *Am J Psychiatry*. 1987;144:1324-1327.

90. Perry BD, Southwick SM, Giller EL. Adrenergic receptor regulation in PTSD. Paper presented at 141st annual meeting of American Psychiatric Association, Montreal, Canada.

91. Lerer B, Ebstein RP, Shestatsky M, et al. Cyclic AMP transduction in post traumatic stress disorder. *Am J Psychiatry*. 1987;144:1324-1327.

92. Davidson J, Lipper S, Kilts CD, et al. Platelet MAO activity in posttraumatic stress disorder. *Am J Psychiatry*. 1985;142:1341-1343.

93. Kolb LC, Burris BC, Griffiths S. Propranolol and clonidine in the treatment of chronic posttraumatic stress disorders of war. In: van der Kolk BA, Posttraumatic stress disorder: psychological and biological sequelae. Washington, DC: American Psychiatric Press; 1984:97-105.

94. Famularo R, Kinscherrf R, Fenton T. Propranolol treatment for childhood posttraumatic stress disorder, acute type: a pilot study. *Am J Dis Child*. 1988;142:1244-1247.

95. Branchey L, Davis W, Lieber CS. Alcoholism in Vietnam and Korea veterans: a long term follow-up. *Alcoholism Clin Ex. Res* 1984;8:572-575.

96. Keane TM, Gerardi RJ, Lyons JA, et al. The interrelationship of substance abuse and posttraumatic stress disorder: Epidemiological and clinical considerations. *Rec De. Alcohol* 1988;6:27-48.

97. Beckham JC, Kirby AC, Feldman ME, et al. Prevalence and correlates of heavy smoking in Vietnam veterans with chronic posttraumatic stress disorder. *Addict Behav*. 1997;22(5):637-647.

98. Solomona Z, Mikulincerb M, Kotler M. A two year follow-up of somatic complaints among Israeli combat stress reaction casualties. *J Psychosom Res*. 1987;31(4):463-469.

99. Friedman MJ: Biological approaches to the diagnosis and treatment of post-traumatic stress disorder. In: *Psychotraumatology*. Everly GS, Lating JM, eds. New York, NY: Plenum Press; 1994:171-194. ■

## We Welcome Your Comments

The *Journal of the National Medical Association* welcomes your Letters to the Editor about articles that appear in the *JNMA* or issues relevant to minority healthcare. Address correspondence to [EditorJNMA@nmanet.org](mailto:EditorJNMA@nmanet.org).

## C A R E E R O P P O R T U N I T Y



### THE WILLIAM A. HARK, M.D. AND SUSANNE G. SWIFT, PROFESSOR AND CHAIR DEPARTMENT OF ORTHOPAEDIC SURGERY RUSH MEDICAL COLLEGE AND RUSH UNIVERSITY MEDICAL CENTER

Rush Medical College and Rush University Medical Center announces a search for the William A. Hark, M.D. and Susanne G. Swift, Professor and Chair, Department of Orthopaedic Surgery. Rush University is home to Rush Medical College founded in 1837 and the first medical college in the Midwest. Rush University Medical Center is the largest private academic medical center in Illinois. The Department of Orthopaedic Surgery is founded on a long tradition of excellence in clinical care, teaching and research and provides a full range of consultation, treatment and follow-up care for Orthopaedic Surgery. Department physicians are trained in all aspects of orthopaedic surgery. The Department includes a fully accredited training program in orthopaedic surgery with 22 residents and 13 fellows. The department includes seven endowed chairs and is made up of thirteen sections and a division of Spine Surgery and one of Sports Medicine.

Candidates must be board certified, with senior level rank and with qualifications to fulfill the Rush Medical College criteria for full professorial appointment. We seek a recognized leader with an outstanding academic background, experience in academic administration, and the ability to advance and develop superior programs in clinical service, education, and research endeavors related to Orthopaedic Surgery. *Rush University is an Affirmative Action Equal Opportunity Employer.* Please send nominations or letters of interest and curriculum vitas no later than July 31, 2007 to:

**Robert Higgins, M.D. ([Robert\\_Higgins@Rush.edu](mailto:Robert_Higgins@Rush.edu)),  
Rush University Medical Center  
1653 West Congress Parkway  
Chicago, Illinois 60612**