

(10) STRESS PHYSIOLOGY AND IMPACT OF STRESS ON CORONARY ATHEROSCLEROTIC HEART DISEASES

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ABSTRACT:

Large number of epidemiological studies including Framingham's study have documented that stress is an important risk factor of Atherosclerotic coronary heart disease. Even and above our day to stresses related to home and job we have witnessed major acute stressful events i.e. earth quack, tsunami, flood, terrorist attacks, civil war, riots, nuclear blasts.... Historical point of view Hans Selye a father of the study of stress, established relationship between chronic stress and effects on the body. He described three stages of stress response as "General Adaptation Syndrome" [GAS]. The three stages are 1] Alarm: "Fight or Flight" reaction: body mobilizes resources to combat threat; activates the sympathetic nervous system 2] Resistance: Enhanced ability to fight stressor via moderate physiological arousal; ability to withstand additional stressors (e.g., infection) is reduced. 3] Exhaustion: Depletion of resources brings on diseases and disorders (e.g., chronically high heart rate and blood pressure increase chances of heart attack and stroke). Stress activates the *hypothalamus-pituitary-adrenal axis*, a group of structures that help the body cope with stress. The hypothalamus activities the pituitary gland, which in turn releases hormones that stimulate the adrenal glands to release the stress hormones epinephrine, nor epinephrine, and cortisol. There is release of catecholamine epinephrine (adrenaline), nor epinephrine (noradrenalin) with stimulation of Sympathetic Nervous System. Incidentally majority of studies are epidemiological. Recently there more studies explaining the pathophysiological mechanism how the stress causes CHD. Endocrinal abnormalities especially hypothalamo-pituitary-adrenal (HPA) axis, and inhibited sex steroid result an elevated waist/hip circumference ratio (WHR) and visceral obesity, combined with insulin resistance is hall mark of metabolic basis of CV disease. Insulin resistance and other risk factors dependent on the hyperinsulinemia following insulin resistance are associated with dyslipideamia i.e. increase LDL cholesterol and triglyceride and decrease, are hallmark or culprit of atherosclerosis. Chronic stress is associated with reduced physical activity and sedentary life style further induces a state of insulin resistance. When beta cells are no longer able to compensate for insulin resistance by adequately increasing insulin production, impaired glucose tolerance appears, characterized by excessive postprandial hyperglycemia. Impaired glucose tolerance may evolve into overt diabetes another risk factor of CHD.. Because all these conditions are also accompanied by the presence of an oxidative stress, oxidative stress one of the pathogenic mechanism linking the stress insulin resistance with dysfunction of both beta cells and endothelium, eventually leading to overt

diabetes and cardiovascular disease. There is evidence that chronic stress may induce a chronic inflammatory process culminating in atherosclerosis. These increased oxidative stress and inflammatory events, caused by stress, may account for the approximately 40% of atherosclerotic patients with no other known risk factors. A heightened state of cardiovascular activity, injured endothelium, and induction of adhesion molecules on endothelial cells to which recruited inflammatory cells adhere and translocate to the arterial wall. Shedding of adhesion molecules and the appearance of cytokines, and APRs in the blood are early indicators of a stress-induced APR and may be predictors of future cardiovascular disease. The most important things are 1] stress is everywhere and each and every one are exposed to stress 2]CHD is multi factorial disease and stress is one modifiable risk factor. Stress management interventions studies have further supporting the fact such successful intervention of stress management is associated with up 74% reduction in cardiac events

INTRODUCTION:

Stress, is defined as a mismatch between perceived demands and perceived capacities to meet those demands .Physiologically Stress is “non specific response to stimuli”. The response carry series of neural endocrinal response for physical survival. In physics and engineering point of view, there are actually two words stress and strain .Stress is an external force applied to an object and strain is the changes in the object in response to force. Let us take example. Suppose I hit a hammer on a steel vessel, it will generate hump on the vessel. So the hitting on a vessel with a hammer is stress and the hump is strain. But now suppose I hit my small hammer on a rubber tire of a car. Nothing will happen similar if I hit an hammer on air filled rubber tube, nothing will happen due to elastic properties. Now let et me begin with conclusive remark ,if we want be free from effects of stress we have to become elastic means flexible, adaptable and ready to change in the era of ever changing environment . This is the principal of survival of fittest.

In context to stress and strain, physiological point of view stress has two meanings.

1] Stress is a condition in the external environment that makes unusual demands on the organism, such as threat, failure. Homeostasis point of view external environment is constantly changing. And if anything in this universe is eternal than is change and if organism has to survive it must adapt to change. So the stress and inevitable.

2] Strain is an internal condition as part of a response to a stressful situation. If an organism i.e. human being under stress, and body reacts in several ways.

Stresses are inevitable .It can be physical i.e. trauma, illness mental i.e. loss of job dear one,, infection ,it can be both i.e. major surgery ,failure in examination ,divorce .Historical point of view mind well the real stresses the human kind has faced over the evolution are different from what we face to days. Our ancestors have to face the stresses almost every minute. The stresser were life threatening i.e. attacks by wild animals ,from predators of same species fighting for prey and survival of self ,offspring.....The inbuilt stress response is meant for such a life threatening stimuli. The purpose of the response was very simple *the survival*. In such

situation there were only two options either fight or flight. So this fight and flight response is in built response to any perceived life threatening situations. It activates the *hypothalamus-pituitary-adrenal axis*, a group of structures that help the body cope with stress. The hypothalamus activities the pituitary gland, which in turn releases hormones that stimulate the adrenal glands to release the stress hormones epinephrine, nor epinephrine, and cortisol. There is release of catecholamine epinephrine (adrenaline), nor epinephrine (noradrenalin) with stimulation of Sympathetic Nervous System.

Physiological Stress Response :

[A] Immediate effects of stress

Arousal of Sympathetic Nervous system

Epinephrine and norepinephrine released

Time: 2 to 3 seconds

Effects are forceful pumping of heart .Tachycardia

More blood flow to vital organ i.e. brain, heart and exercising muscle

Increase alertness

Papillary dilation

[B] Intermediate effects of stress

Adrenal medulla

Epinephrine and norepinephrine
release from

Time: 20 to 30 seconds

Effects same as above

[C] Prolonged effects of stress

ACTH -Glucocorticoids,
various metabolic processes

Increase blood glucose and fatty acids to supply fuels to heart, brain and skeleton muscles

- Time: minutes, hours, days, or weeks

Physiologic Changes	
Autonomic nervous system	
Musculoskeletal system	
Psychoneuroendocrine system	
Limbic system	
Acute Changes	
Increased	Decreased
Respiration	Lipid metabolism
Heart rate	Bowel / bladder function
Blood pressure	Immune meditation
Muscle tension	Blood flow to extremities
Corticosteroid release	
Platelet aggregation	
Cardiac Symptoms	
Anxiety	
Angina	
Arrhythmia	
Myocardial infraction	
Sudden cardiac death	

Now in context to clinical science, if we ask the patient about having stress at home or at job place .meaning of stress is simple. It can be at home marital problems, close relative suffering from illness i.e. cancer, schizophrenia, near dyeing, divorce or job related stress i.e., conflicts with bosses, promotion related problems

Just as physician qualitatively rate the extent of heart murmurs, psychologists and physiologists have a variety of ratings schemes for evaluating stress. Given that the complaint is entirely subjective, one either relies totally on the patient's self-report or else applies generally agreed upon rules for how stressful a given event is for most people. Alternatively, one can observe subjects during exposure to a stressor and then measure physiological and/or behavioral responses. Some researchers feel that the focus should not be on major life stressors but rather the daily hassles in life (rush hour traffic, job stress and marital conflicts).

Some important life events considered as severe stress

Death of partner

Divorce

Separation from partner

Jail sentence

Death of close family member

Injury or illness to yourself

Marriage – your own.

Chronic stress:

Hans Selye a father of the study of stress, established relationship between chronic stress and effects on the body. The physiological and psychological response to situations that threaten or challenge us and that require some kind of adjustment. He describe three stages of stress response as "General Adaptation Syndrome" [GAS].

The three stages are

1. Alarm

"Fight or Flight" reaction: body mobilizes resources to combat threat; activates the sympathetic nervous system

2. Resistance

Enhanced ability to fight stressor via moderate physiological arousal; ability to withstand additional stressors (e.g., infection) is reduced.

3. Exhaustion

Depletion of resources brings on diseases and disorders (e.g., chronically high heart rate and blood pressure increase chances of heart attack and stroke).

In modern era the stress is different from our ancestors in two way

1] The real threats are not wild animals, predators and prey but they are different and incidentally man made. Some examples are conflicts with boss and spouse, traffic jam,

2] The stresses are regular and almost daily routine i.e. whether we can reach office in time or not...Even young student are not exception. Educational stress itself a branch of studying stress physiology.

These frequent, recurrent stresses do not put our body into relaxation and recover completely. So we are ultimately the victims of chronic stress, more dangerous than acute stress.

Typical stress response in human being is divided into three component

- Physiological component: Arousal, hormone secretion.
- Emotional Component: Anxiety, fear, grief, resentment, excitement (if stress is from challenge).
- Behavioral Component: Coping strategies (both behavioral and mental)—problem focused and/or emotion-focused.

Ultimately end result of any stressful events is depend upon coping ability and support system .individual' attitude, personality social support system also play significant role. These factors generate. Appraisal to stress in limbic system of brain.

Appraisal point of view Selye assumed that stress depended only on the intensity of the stressor while another psychologist Lazarus proposed that the stress is a result of mental processes.

Lazarus and Folkman's Theory for perceived stress and its management strategies

1] Primary Appraisal:

Is Stressor Negative?

If it is negative, does it involve harm or loss, threat, or challenge (chance to grow).

Yes

[2] Secondary Appraisal: Can I Control the Situation?

If coping resources are adequate, then consider options for coping strategy:

[A] Problem-focused coping strategies.

A response aimed at reducing, modifying, or eliminating a source of stress (e.g., if grades in a course are low, reduce work hours, change study strategy, etc.).

or

[B] Emotion-focused coping strategies.

i.e. emotional impact of the stressor (e.g., denial, religious faith, wishful thinking, humor,).

In the low grades example, you can reappraise the stressor and reduce the importance you attach to that course, that major or academic work in general.

Two major emotion-focused strategies are: MEDITATION and BIOFEEDBACK

Consider, CHANGE PRIORITIES IN LIFE : HEALTH FIRST

STRESS AND CARDIOVASCULAR EVENTS:

Cardiovascular diseases are the leading cause of death, mainly the death related to coronary atherosclerotic heart diseases i.e. myocardial infarction, sudden death, ventricular fibrillation...., Epidemiological studies have implicated stress as one of the risk factors and potentially modifiable risk factors for cardiovascular disease (CVD) but little is known about the mechanisms that underlie this connection. Individuals belonging to the Type-A personality group are those people who are more exposed to stress and present a big chance of suffering from a physical or mental disorder related to stress, i.e. hypertension, and CHD.

However, the physiological mechanisms accounting for these associations between personality traits on one hand, and cardiovascular morbidity and mortality on the other are not completely understood. Potential mechanisms are limbic and hypothalamic–pituitary–adrenal deregulations, dysfunctions of the autonomic control of the heart, altered blood platelet function, and non-compliance to medical treatments. Experimental evidence for an association between a propensity for lethal arrhythmias and signs of either increased sympathetic or reduced vagal activity has encouraged the development of quantitative markers of autonomic activity. Stress increases blood pressure, and prolonged high blood pressure can damage the heart or cause strokes, myocardial infarcts and renal events. Recently more attention is given to metabolic alteration in chronic stress and its relationship with atherosclerotic heart diseases.

If the person fails to manage stress, the person is susceptible to anxiety, fear, grief, depression. There is increasing evidence to suggest a link between sadness, depression and coronary

heart diseases. Many investigators have reported a strong correlation between depression and cardiovascular mortality. It has been noted that depression is associated with sedentary and other negative life styles, abnormal autonomic variability of heart rate and a altered platelets functions.

Stress, resulting in an uncontrollable defeat reaction, has been shown by James Henry to be followed by specific endocrine abnormalities, including sensitization of the hypothalamo-pituitary-adrenal (HPA) axis, and inhibited sex steroid . The resulting an elevated waist/hip circumference ratio (WHR). Intraabdominal, visceral fat masses--combined with insulin resistance is hall mark of metabolic basis of CV disease and are powerful risk factors for cardiovascular disease, diabetes and stroke. Endocrine chain of events during chronic stress are primary factors, followed by visceral fat accumulation, insulin resistance and other risk factors dependent on the hyperinsulinemia following insulin resistance which is associated with dyslipideamia i.e. increase LDL cholesterol and triglyceride and decrease HDL C a hallmark or culprit of atherosclerosis.

Chronic stress with reduced physical activity induces a state of insulin resistance. When beta cells are no longer able to compensate for insulin resistance by adequately increasing insulin production, impaired glucose tolerance appears, characterized by excessive postprandial hyperglycemia. Impaired glucose tolerance may evolve into overt diabetes. These 3 conditions, i.e. insulin resistance, impaired glucose tolerance, and overt diabetes, are associated with an increased risk of cardiovascular disease. Because all these conditions are also accompanied by the presence of an oxidative stress, oxidative stress one of the pathogenic mechanism linking the stress insulin resistance with dysfunction of both beta cells and endothelium, eventually leading to overt diabetes and cardiovascular disease.

Chronic stress may induce a chronic inflammatory process culminating in atherosclerosis. These inflammatory events, caused by stress, may account for the approximately 40% of atherosclerotic patients with no other known risk factors. It is argued that by activating the sympathetic nervous system, the hypothalamic-pituitary axis, and the renin-angiotensin system, stress causes the release of hormones such as catecholamines, corticosteroids, glucagon, growth hormone, and renin, and elevated levels of homocysteine, which induce a heightened state of cardiovascular activity, injured endothelium, and induction of adhesion molecules on endothelial cells to which recruited inflammatory cells adhere and translocate to the arterial wall. An acute phase response (APR), similar to that associated with inflammation, is also engendered, which is characterized by macrophage activation, the production of cytokines, other inflammatory mediators, acute phase proteins (APPs), and mast cell activation, all of which promote the inflammatory process. Shedding of adhesion molecules and the appearance of cytokines, and APRs in the blood are early indicators of a stress-induced APR and may be predictors of future cardiovascular disease.

The studies have reviewed effects of acute stressors among people facing disasters (earthquakes), Job stress, marital unhappiness, stress of caregiving ,Type A behavior pattern,

Hostility, depression found to be significantly correlated with incident of Sudden death, myocardial infarction, myocardial ischemia, wall motion abnormalities as studies by LV angiography, arrhythmias, angina... Fortunately approaches are available for stress management that can decrease patients' suffering and enhance their quality of life.

Earthquakes and CHD: Significant number of studies indicate the increase incidence of CHD event after earthquakes. Factors associated are the emotional trauma acting, injuries and loss of physical and near ones, living in cramped emergency camps, facing disrupted sleep. During the 1999 earthquake in Taiwan, 12 patients were studied with Holter monitoring. It was observed that during earthquake, increases in heart rate, HR variability itself changed, with a relative drop in high-frequency variability and an increase in the low-frequency/high-frequency ratio, denoting relative withdrawal of parasympathetic nervous system activity and an increase in sympathetic nervous system (SNS) activity. Cannon et al observed that during earthquake in Japan, blood viscosity and markers of procoagulant activity i.e. fibrinogen, von Willebrand factor, and D-dimer increased. The Northridge, California earthquake, daily numbers of deaths attributed to cardiovascular disease increased dramatically on the day of the earthquakes.. Stress Cardiomyopathy is a condition where left ventricular angiogram studies by radiological or nuclear LV angiography. The study will demonstrate wall motion abnormality characteristic of stress cardiomyopathy. Orth-Gomer et al. studied the impact of work stress and marital stress on the subsequent incidence of CAD in a cohort of Stockholm women followed for ~5 years. Marital stress was associated with a 2.9-fold increased risk of recurrent events, whereas work stress did not predict subsequent coronary events in these women.

MRFIT Multiple Risk Factor Intervention Trial found that chronic work stress and marital dissolution increased the risk of cardiovascular mortality in men who were followed for 9 years.

Provocative tests for Psychological/emotional stressor i.e. arithmetic exercise and similar activities are under way and some results are associated with elicited extensive changes in regional circulation of myocardium and almost as consistently evocative of myocardial perfusion abnormalities. The changes were not as straightforward as those with exercise as was exercise testing. 60% of CAD patients developed wall motion abnormalities during mental stress testing. Such tests can be major tool for research on stress.

Implantable defibrillators are the one more tool to access to data to correlate stress and arrhythmias. It has been observed that horrific disasters doubled the rate of ventricular arrhythmias in patients fitted with implantable defibrillators.

Studies have found that distressed caregivers had an increased risk of hypertension when followed over a 6-year period. Other reports from this group have found that caregivers have increased levels of D-dimer, a circulating procoagulant factor, more sleep disruption, and higher level of circulating plasma inflammatory cytokines.

Whether stress "caused" or "contributed to" the development of a condition of cardiovascular event is an interesting question to medical researcher. Because stress is everywhere, what is logic it do to identify a risk factor that cannot be modified like age, sex and genetics..... ? Answer is : " Stress is no different from other background cardiac risk factors such as genetics or age. There is no reason to ignore such factors, just because they are not modifiable. Stress can be modified through numerous approaches. It remains to prove that such stress modifications consistently decrease the risk for MI and cardiac death. In Duke study an interventional Stress Reduction group underwent 4 months of training in exercise or stress management versus just standard care were compared. Results showed after five years, there was 74% reduction in cardiac events.

100s of interventions for stress management are discussed in literature.

Some Interventions For Stress Management

Formal psychotherapy,

Medications,

Time management

Progressive relaxation training,

Hypnosis

Yoga and Meditation,

Regular exercise.

.....

EFFECTS OF STRESS MANAGEMENT by TM meditation:

- decreased oxygen uptake (VO₂), CO₂ output (VCO₂),
- electromyograph (EMG) improvements during dynamic exercise, respiration, lactate levels, systemic vascular resistance (SVR), heart rate,
- and increased production of the essential amino acid phenylalanine.

Endocrine and autonomic effects of stress management

- Reduced vasomotor activity.
- Improvements related to blood pressure, thrombosis, and cholesterol and triglyceride levels all can be demonstrated

Effective Stress management leads to reduced

- anxiety,
- depression,
- hostility, and
- aggression,
- better insight, reduced habit reliance,
- increased self-efficacy,
- increased empathy, and
- increased spirituality.
- chronic pain,

- insomnia,
- hypertension,
- coronary disease,
- *Shown to improve fertility.*

CONCLUSION:

When we under stress our healthy dietary habits wane away we tend to increase our weight and obesity, especially man tends to tobacco smoking, drinking alcohol, other unhealthy habits other high-risk activities, and leads to increased sedentary activity i.e. Viewing TV ...and decrease in physical exercise. This all factors aggravate the effects of stress on cardiovascular system. Just negotiating with stress by effective stress and time management leads favorable effects on development of atherosclerosis coronary heart disease.

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