From 1995 to 2005, death rates from CVD declined 26.4%. This is certainly great news, isn’t it? However, even though death rates from cardiovascular disease (CVD) have declined, the burden of disease remains high.

The 2005 overall death rate from cardiovascular disease (CVD) was 278.9 per 100,000, or roughly 1 of every 2.9 deaths in the United States. The preliminary mortality data for 2006 showed that CVD accounted for 34.2% of all deaths that year. It remains the leading cause of death in the country.

About every 25 seconds, an American will have a coronary event, and about every minute someone will die from one. As many of us know, controllable risk factors for heart disease include smoking, high blood pressure, high blood cholesterol, diabetes, being overweight or obese, and physical inactivity.

On the basis of data from the latest National Health and Nutrition Examination Survey (2), the prevalence of overweight (body mass index-for-age values at or above the 95th percentile) in children 6 to 11 years of age increased from 4.0% in 1971-1974 to 17.0% in 2003-2006. In addition, 62% of adults >18 years of age who responded to the National Health Interview Survey (3), reported no vigorous activity lasting >10 minutes per session.

The basis of these neuro-endocrine changes, from an HPA-T perspective, is a proinflammatory state which sets the stage for heart disease and one of its main progenitor conditions, metabolic syndrome, by the up-regulation of the sympathetic nervous system. This occurs chiefly through a predominance of norepinephrine over epinephrine. This is particularly true if an already stressed HPA axis is stimulated further through the actions of CRF.
Much research suggests that both hypothalamic and extrahypothalamic CRF activate the locus ceruleus in the brain, leading to an increase in norepinephrine (4). In a study by Melia (5), results showed that endogenous CRF is necessary for the induction of tyrosine hydroxylase in response to the stress paradigm and that exogenously administered CRF is sufficient for the regulation of this enzyme in non-stressed subjects. Thus, CRF is necessary to induce tyrosine hydroxylase which is the rate-limiting step in the production of catecholamines. Then, Koob, et al, showed that norepinephrine can enhance forebrain CRF activity, leading to higher activity of both norepinephrine and CRF in patients, possibly closing a feed-forward loop (6).

So when a person is stressed, there is an upregulation of catecholamines (particularly NE) and cortisol that occurs in a dance where the body is trying to balance the production of inflammatory cytokines with cortisol which attempts to turn down the gain on the inflammation. But there is a cost to the dance, particularly in light of adrenal fatigue and exhaustion. One can see these specific patterns in metabolic syndrome.

The typical pattern seen on the HPA profile in a patient with metabolic syndrome or hyperinsulinemia will show a high NE with usually a low epinephrine - indicating the decreased adrenal medullary activity noted in a study by Ward, et al (7). The researchers looked at the relationship between 24-hour urinary catecholamine excretion and serum lipid and lipoprotein levels examined among 6 male participants of the Normative Aging Study. Epinephrine excretion was positively correlated with the highdensity lipoprotein cholesterol (HDL-C) level and the ratio of HDL-C to LDL-C and inversely correlated with the triglyceride level. Their data suggested that epinephrine plays an important role in regulating lipid and lipoprotein metabolism in humans.

In addition, decreased adrenal medullary activity (adrenal stress) may contribute to the dyslipidemia (increased triglycerides and decreased HDL-C) commonly observed among the obese. This is the typical lipid pattern in metabolic syndrome. They concluded that the sympathoadrenal system, along with hyperinsulinemia, might contribute to the increased cardiovascular risk associated with the insulin resistance syndrome.

In a study by Troisi (8), the relationship of obesity to sympathetic nervous system activity was investigated. Sympathetic activity was assessed by measurement of 24-hour urinary norepinephrine excretion and level of obesity by BMI. They showed mean urinary norepinephrine excretion was higher in subjects classified as either hyperglycemic and hyperinsulinemic than the mean urinary norepinephrine excretion in normal subjects. There are many other studies looking at NE excretion and risk of metabolic syndrome and CHD. DePergola and colleagues (9) even suggested that insulin and noradrenaline cooperate independently to the development of the metabolic syndrome.
In CHD and metabolic syndrome there are typically higher levels of NE and lower levels of epinephrine, often with low levels of adrenal function. This is part of the “perfect storm” for the propagation of inflammatory mediators. In a recent article, by Szelenyi (10) it was demonstrated that the TNF-α response is in direct correlation with level of NE. Finally, Brunner, et al. (10) not only confirmed that there is relative cardiac sympathetic (NE and epi) predominance in CHD, but their group found several inflammatory markers to be strongly related to the metabolic syndrome, among them IL-6 and C-reactive protein.

One possible explanation for the patterns typically seen in metabolic syndrome (high NE, low epinephrine and low adrenal status) which is a preamble to CHD are due to years of excursions of the blood sugar with the body using epinephrine and cortisol to help sustain euglycemia. The adrenals (particularly the adrenal cortex) consequently get worn out and the patient is then left “running” on NE, often with concomitant anxiety, sleep difficulties and/or hypertension. This situation also sets the stage for increased inflammatory status.

Those who use the Communication System Management (CSM) clinical model see the above patterns on a regular basis. Currently, medical research involving multiple neurotransmitters and particularly their inter-relationships is limited. Until the time that such research becomes available, we are left to scour the literature and see glimpses of our model as researchers work to collate the bits and pieces of the whole. With time, we at Sanesco are sure that research will bear out the veracity of the CSM model.

The discussion above gives an inkling of what the recent medical literature has to tell us about the state of the neuro-endocrine system in CHD. We believe that rebalancing the HPA-T axis is an important step in toning down the gain on the body’s sympathetic nervous system. This is done by providing adequate inhibitory NTs (serotonin and GABA) to counterbalance the NE and possibly epinephrine that are the result of ramping up of the sympathetic system. What we see clinically are products like Prolent, Lentra, and Tranquilant “standing in the gap” and in essence “cooling down” the excitatory NTs. This yields calmer patients who typically sleep better and are better able to handle the stress that can, over time, impact CHD risk.

In summary, CHD is the result of the interplay of numerous risk factors, not the least of which are increased sympathetic nervous system activity as evidenced by increased levels of NE in the urine often associated by low levels of urinary epinephrine. Concomitantly, there is often upregulation of the HPA axis with regard to adrenal function. After prolonged periods, this may lead to diminished adrenal function. The combination of these factors can lead to increased inflammation within the cardiovascular system often manifesting in higher levels of hs-CRP and fibrinogen, etc. The scenario discussed above may be part of the underlying cause of CHD - forming the antecedents and triggers that end up shaping the disease.

The prevention of CHD should be approached in a holistic and integrated manner with primary concerns centering on lifestyle and dietary choices. All risk factors should be addressed as comprehensively as possible and the underpinnings of sympathetic overdrive and inflammation must be taken into consideration as part of that comprehensive plan.
Visual and Statistical References


A Practical “Tool” For An Integrative Approach

One of the clinical “tools” available to practitioners considering the natural therapy options discussed by Dr Watkins is Sanesco’s Communication System Management (CSM) model. The CSM model is a clinical system designed to help you to assess, monitor, and correct key neurotransmitter imbalances that may be associated with your patients’ symptoms of anxiety and depression. The CSM model includes three integrated components.

- The CSM model utilizes a noninvasive lab assay measuring neurotransmitter and adrenal hormone levels to establish baseline levels of a patient’s biochemistry. Subsequent testing is used as an effective tool for monitoring treatment.

- As a model of individualized medicine, CSM includes patient-centered analysis of symptoms and lab results. With oversight by Sanesco’s Medical Board, highly trained clinical staff correlates 48 patient-reported symptoms, current dietary and lifestyle factors, supplement and medication intake, to the reported lab results; generating a comprehensive “Correlation Analysis” report. This Correlation Analysis report provides you with extensive patient specific information to help you open the window to your patient’s neuroendocrine system.

- The third component of the CSM model is using the nutraceutical supplements discussed in Dr Watkins’ monograph. Sanesco’s Targeted Nutritional Therapy products are safe and effective options for restoring some of the biochemical imbalances that may be associated with anxiety and depression, as well as other symptoms related to neuroendocrine system function.

Sanesco developed this “CSM” model in collaboration with a team of medical doctors, naturopathic doctors, nutritionists, and researchers. The goal was to provide a practical science-based individualized approach for looking at the key contributors to potential underlying causes of chronic symptoms.

Sanesco provides complimentary training to practitioners on the three components of this model through its CSM Certification Program. This exclusive program includes one-to-one interactive training sessions, live webinars, a self-tutorial library, and much more. Contact a Sanesco representative to enroll today - Call 866.670.5705 and Press “2”

The above statements have not been evaluated by the FDA. The products mentioned above are not intended to diagnose, treat, cure or prevent any disease.

Not all of the nutraceutical products mentioned in this monograph are distributed by or sold by Sanesco International. Contact a Sanesco representative for more information.