

## Key FAQ's for Physicians

### **What are Allostasis and Allostatic Load?**

**Allostasis:** The body's adaptive responses to external challenges - maintaining stability through change. The body actively copes with a challenge by expending energy and attempting to return to its initial state. Allostasis is an extension of the concept of homeostasis and represents the adaptation process of complex physiological systems to the physical, psychosocial, and environmental challenges associated with stress.

**Allostatic Load (AL):** When the physiological systems involved in allostasis do not shut off when not needed, or do not become active when needed. AL is the resulting cumulative effect on the body of either being overwhelmed by too many challenges or meeting challenges less efficiently. High AL leads to dysregulation of major physiological systems and ultimately to disease onset and mortality.

### **What research has been published in peer reviewed journals?**

Research in allostasis and allostatic load is exponentially increasing. In 2006 there were 95 peer reviewed publications, worldwide. Below is one book that reviews the research up to 2004 and a few seminal articles that support the use of AL as a diagnostic tool.

Allostasis, Homeostasis, and the Costs of Physiological Adaptation". Cambridge University Press (2004). Edited by: Jay Schulkin.

T.E.Seeman, B.S.McEwen, J.W.Rowe, and B.H.Singer. "Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging". Proc.Natl.Acad.Sci.USA (2001) Apr 10; 98(8): 4770-5

E.M.Maloney, B.M.Gurbaxani, J.F.Jones, C.L.deSouza, C.Pennachin, B.N.Goertzel. "Chronic fatigue syndrome and high allostatic load". Pharmacogenomics April; 7(3): (2006) 467-73

J. Stewart. "The detrimental effects of allostasis: allostatic load as a measure of cumulative stress". J.Physiol.Anth.(2006). Jan;25(1). 133-45.

"Allostasis, Homeostasis, and the Costs of Physiological Adaptation". Cambridge University Press (2004). Editor: J.Schulkin

B.S. McEwen. "Protective and damaging effects of stress mediators". New England J. Med. 338 (1998): 171-179.

B.S.McEwen, E.Stellar. "Stress and the individual: Mechanisms leading to disease". Arch.Int.Med. 153(1993): 2093-3101.

C.H.Johnston-Brooks. "Chronic stress and illness in children: the role of allostatic load". Psychosom.Med. Sept-Oct (1998) Vol.60 (5): 597-603

### **What clinical study data were used to create the Allostatix Load Diagnostic Test?**

In each of the studies below ongoing blood and biometric testing was accompanied by extensive interviews, conducted by nursing staff, with individuals several times during the period of study. Disease onset and mortality were measured and documented, by individual, and by diagnosed disease category.

#### **MacArthur Studies of Successful Aging**

Population: healthy 70-79 year olds  
Sample size used in creating diagnostic test: 1,189  
Period of study: 7 years  
Outcomes tracked: significant disease onset, death

See NIH site for MacArthur Studies details:

<http://www.nia.nih.gov/ResearchInformation/ScientificResources/StudyInfo.htm?id=56>

#### **CARDIA Study**

Population: healthy 18-30 year olds  
Sample size used in creating diagnostic test: 1,200  
Period of study: 20 years  
Outcomes tracked: significant disease onset, death

See NIH site for CARDIA Study details:

<http://www.nhlbi.nih.gov/resources/deca/descriptions/cardia.htm>

### **How do you create an Allostatic Load from the data?**

Typically allostatic load has been calculated using results of most (or all) of the following blood and biometric measures:

*Cardiovascular system functioning:* homocysteine, apoA, apoB, systolic bp, diastolic bp, heart rate

*Metabolic system functioning:* total cholesterol, hdl, ldl, gly. hemoglobin, waist/hip ratio, bmi, triglycerides, fasting glucose

*SNS/ANS functioning:* heart rate variability (LF/HF power)

*Immune/inflammatory system functioning:* IL-6, CRP, fibrinogen, albumin

*Renal functioning:* creatinine

*Lung functioning:* peak flow

*Hypothalamic Pituitary Axis functioning:* DHEA-S

There have been a variety of algorithms created to combine these data and produce an AL diagnostic score. Highly complex, non-linear statistical methods have been used to create the Allostax Load™ score.

**How predictive of morbidity and mortality is the Allostax Load™**

Application of the analytic methods to the MacArthur and CARDIA study databases has yielded PPV, NPV, ROC, Specificity and Sensitivity values given below:

Predicting serious disease onset:

PPV	81%
NPV	79%
Area under ROC curve	0.83
Sensitivity	0.93
Specificity	0.55

Predicting mortality:

PPV	80%
NPV	88%
Area under ROC curve	0.89
Sensitivity	0.95
Specificity	0.60