



UNDERSTANDING **STRESS** RESILIENCE &  
ROLE OF STRESS ADAPTOGENS



**UNDERSTANDING STRESS RESILIENCE**



**ROLE OF STRESS ADAPTOGENS**



**Dr. VARSHA KHATRY**

MBBS, Diploma in Aesthetic Medicine (Apollo Hyderabad),  
Fellowship in Aesthetic Medicine, (Ernst-Moritz-Arndt-  
Universität Greifswald, Germany)



# ROADMAP

**INTRODUCTION**

STRESS RELATED FACTS/MAGNITUDE OF IMPACT  
COMMON STRESSORS: CONSEQUENCES

VICIOUS CYCLE

STRESS  
MANAGEMENT/  
RESILIENCE

ROLE OF STRESS  
ADAPTOGENS



## STRESS: INTRODUCTION

- A condition arising from external physical or mental overload.
- Makes a person feel tormented, nervous, anxious or otherwise less capable of full and normal response to environmental demands.

*Reference: Chandrashekhar K et al. A Prospective, Randomized Double-Blind, Placebo-Controlled Study of Safety and Efficacy of a High-Concentration Full- Spectrum Extract of Ashwagandha Root in Reducing Stress and Anxiety in Adults Indian J Psychol Med. 2012 Jul-Sep; 34(3): 255–262.*





## STRESS: CONSEQUENCES

- Stress is a growing concern in contemporary society<sup>1</sup>
- Stress is an inevitable component in human life<sup>2</sup>
- Prolonged exposure:<sup>3</sup>
  - Unbalances mental and physiological state of a person
  - May lead to depression, hypertension, cardiac diseases and metabolic disorders
- Such conditions are rapidly increasing in prevalence and emerging as major diseases in India<sup>3</sup>
- Currently an increasing fraction of the population is seeking medical help to overcome stress<sup>3</sup>

### References

1. Rothbard N. *Work and Family Stress and Well-Being: An Examination of Person-Environment Fit in the Work and Family Domains. Organizational Behavior and Human Decision Processes.* 1999;77(2):85-129.
2. (K.S. Han / *International Journal of Nursing Studies* 39 (2002) 539-548)
3. Chandrashekhar K et al. *A Prospective, Randomized Double-Blind, Placebo-Controlled Study of Safety and Efficacy of a High-Concentration Full- Spectrum Extract of Ashwagandha Root in Reducing Stress and Anxiety in Adults Indian J Psychol Med.* 2012 Jul-Sep; 34(3): 255-262.



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# FACTS PREVALENCE MAGNITUDE

## INDIA<sup>1</sup>

- According to the Asia Pacific edition survey **April 2014**
- Stress # 1 lifestyle risk factor
- Ranks above physical inactivity and obesity

## GLOBAL<sup>2</sup>

- The Stress in America, survey results show that adults continue to report high levels of stress and many report that their stress has increased over the past year – American Psychological Association.
- Stress levels in the workplace are rising with 6 in 10 workers in major global economies experiencing increased workplace stress - The Regus Group



- China (86%) has the highest rise in workplace stress – The Regus Group
- Almost 80% of American workers feel stress on the job and nearly half seek help on how to manage stress. And 42% say their co-workers need such help – American Institute of Stress
- It is also top health concern for U.S. teens (9th and 12th grade), which could have serious long-term health implications – American Psychological Association.
- On a scale of 1 to 10 adults report their stress level is 4.9 compared with 5.2 in 2011, 5.4 in 2010 and 2009, 5.9 in 2008 and 6.2 in 2007.



#### References

1. <http://www.towerswatson.com/en-IN/Press/2014/05/Indian-employers-rank-stress-as-1-lifestyle-riskfactor2>.  
(K.S. Han / *International Journal of Nursing Studies* 39 (2002) 539–548)
2. <https://www.apa.org/news/press/releases/stress/2012/full-report.pdf>



## FACTS PREVALENCE MAGNITUDE - GLOBAL



Stress



Inactivity



Obesity



Tobacco



Presenteeism



Nutrition



Substance abuse

	1	2	3	4	5	6
Asia pacific						
China						
India						
SE asia						
Sing						
US						

Reference: <http://www.towerswatson.com/en-IN/Press/2014/05/Indian-employers-rank-stress-as-1-lifestyle-riskfactor>

## STRESS AND LIFESTYLE DISEASES



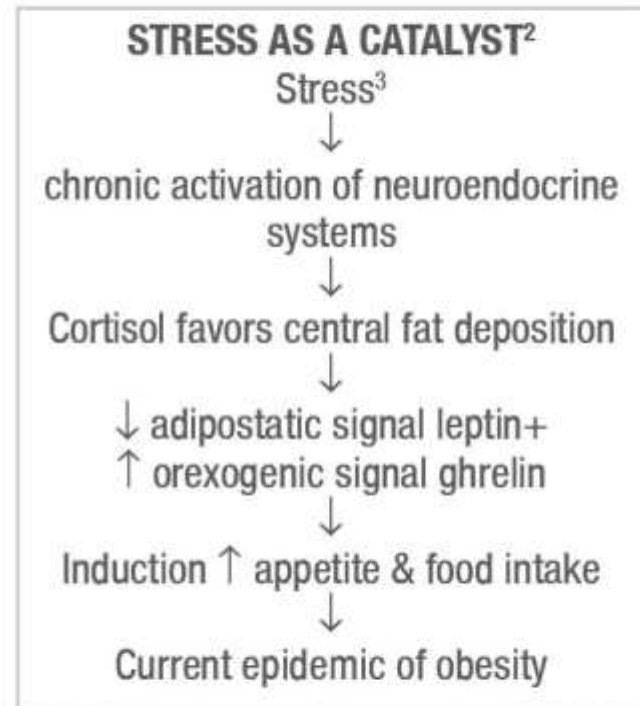
# STRESS-RELATED AILMENTS: DIABETES-CHD-OBESITY IN INDIAN POPULATION

## VULNERABILITY OF INDIANS

- Increased predisposition to diabetes and premature CAD in Indians has been attributed to the “Asian Indian Phenotype”<sup>1</sup>

The “stress” genes which have been selected under pressure in ancient environments may have not adapted to the rapid environmental changes of today.<sup>2</sup>

*CHD:Coronary heart disease; CAD:Coronary artery disease*



## References

1. Mohan V et al: *Epidemiology Of Type 2 Diabetes. Diabetes Indian J Med Res* 2007; 125(Mar):217-230.
2. *Economic volatility increasing more stress-related illness on Indian workers: Regus* – Accessed at: [http://www.indiaonline.com/article/news/economic-volatility-increasing-more-stress-related-illness-on-indian-workers-regus-5836576284\\_1.html](http://www.indiaonline.com/article/news/economic-volatility-increasing-more-stress-related-illness-on-indian-workers-regus-5836576284_1.html) on 11 Dec 2014.
3. Salam R and Reetu K. *Stress and hormones. Indian J EndocrinolMetab.* 2011 Jan-Mar; 15(1): 18–22.

## STRESS TRIGGERING DIABETES IN DEVELOPING NATIONS

- People in urban environment are exposed to high levels of stress and tend to have higher levels of the hormone cortisol.<sup>1,2</sup>
- Associated with an increasing prevalence of disorders of glucose metabolism and other unfavourable metabolic parameters.<sup>1,2</sup>
- Stress has been known to precipitate diabetic ketoacidosis.<sup>3</sup>
- Diabetes distress- commonly associated with poor control.<sup>3</sup>



### References

1. Kann PH et al. Alterations of Cortisol Homeostasis May Link Changes of the Sociocultural Environment to an Increased Diabetes and Metabolic Risk in Developing Countries: A Prospective Diagnostic Study Performed in Cooperation With the Ovahimba People of the Kunene Region/ Northwestern Namibia. *J Clin Endocrinol Metab.* 2014 Dec 18.
2. <http://timesofindia.indiatimes.com/city/delhi/Chronic-stress-may-lead-to-diabetes/articleshow/24891207.cms>
3. Kalra S et al. The dirty dozen of diabetes. *Indian J Endocrinol Metab.* 2013 May;17(3):367-9. 10



## STRESS AND DIABETES: CASE CONTROL CROSS-SECTIONAL STUDY IN 1,403 INDIANS

- Stress scoring system- Presumptive Stressful Life Events<sup>#</sup>
- Stress score >1 Std. deviation- considered as having stress
- Mean stress score = 348 ( $\pm 147.7$ )  
- Odds Ratio is 10.5 (1.3-90.7) ( $p=0.03$ )
- Risk of metabolic syndrome varies from 1.2 to 2.1- fold for more severe stress<sup>^</sup>
- Study evidence that, stress in stressful life events is a significant risk factor for development of diabetes

*<sup>#</sup>Score for each stressful event and total score for each individual is calculated.*

*<sup>^</sup>Depressive symptoms or very stressful life events.*

### References

1. Majji SM et al. Prevalence of diabetes mellitus and role of stress in diabetes in rural Pondicherry –
2. An union territory of India. Global J Med Public Health. 2012; 1(5) September- October 2012;40 -46.



## STRESS AND CHD (1/2)

- Prospective studies have implicated emotional distress as a risk factor for the development of CHD<sup>1,2,3</sup>
- There is an overwhelming evidence for both<sup>4</sup>
  - Deleterious effects of stress on the heart
  - Vulnerability and resilience factors play a role in amplifying or dampening those effects



### References

1. Rozanski A, Blumenthal JA, Davidson KW, et al. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice. *J Am Coll Cardiol* 2005; 45 : 637–51.
2. Todaro JF, Shen B, Niaura R, et al. Effect of negative emotions on frequency of coronary heart disease (The Normative Aging Study). *Am J Cardiol* 2003; 92 : 901–6.
3. Stansfeld SA, Fuhrer R, Shipley M, et al. Psychological distress as a risk factor for coronary heart disease in the Whitehall II study.
4. Dimsdale JE. Psychological Stress and Cardiovascular Disease *J Am Coll Cardiol*. 2008;51(13):1237-1246

## STRESS AND AMI: INDIA (2/2)

Risk factor	Interheart (AMI)
Apolipoprotein A/B ratio	49.2
Hypertension	17.9 (history)
Smoking	35.7
Diabetes history	9.9
High waist-hip ratio	20.1
<b>Psychosocial stress</b>	<b>32.5</b>
Regular physical activity	12.2
Diet/diet score	13.7
Lack of alcohol intake	6.7
Cardiac causes	-

*AMI: Acute myocardial infarction*



*Reference: Gupta R et al. Regional variations in cardiovascular risk factors in India: India heart watch. World J Cardiol 2012 April 26; 4(4): 112-120.*

States	Male (%)	Male rank	Female (%)	Female rank
Punjab	30.3	1	37.5	1
Kerala	24.3	2	34	2
Goa	20.8	3	27	3
Tamil nadu	19.8	4	24.4	4
Andhra pradesh	17.6	5	22.7	10
Sikkim	17.3	6	21	8
Mizoram	16.9	7	20.3	17
Himachal pradesh	16	8	19.5	12
Maharashtra	15.9	9	18.1	13
Gujarat	15.4	10	17.7	7
Haryana	14.4	11	17.6	6
Karnataka	14	12	17.3	9
Manipur	13.4	13	17.1	11
India	12.1	14	16	15
Uttarakhand	11.4	15	14.8	14
Arunachal pradesh	10.6	16	12.5	19
Uttar pradesh	9.9	17	12	18
Jammu and Kashmir	8.7	18	11.1	5
Bihar	8.5	19	10.5	29
Nagaland	8.4	20	10.2	22
Rajasthan	8.4	20	9	20
Meghalaya	8.2	22	8.9	26
Orissa	6.9	23	8.6	25
Assam	6.7	24	7.8	21
Chhattisgarh	6.5	25	7.6	27
West bengal	6.1	26	7.1	16
Madhya pradesh	5.4	27	6.7	23
Jharkhand	5.3	28	5.9	28
Tripura	5.2	29	5.3	24

## PREVALENCE OF OBESITY: INDIA

Stress induces increased appetite and food intake thus leading to increased risk of obesity.<sup>2</sup>



### References

1. [http://www.jmn.org/viewimage.asp?img=JMedNutrNtraceut\\_2012\\_1\\_1\\_37\\_94634\\_b1.jpg](http://www.jmn.org/viewimage.asp?img=JMedNutrNtraceut_2012_1_1_37_94634_b1.jpg)
2. Salam R and Reetu K. Stress and hormones. *Indian J EndocrinolMetab.* 2011 Jan-Mar; 15(1): 18–22.





**VARIOUS STRESSORS**

**STRESS**



## WORK-RELATED STRESS-CAUSES (1/3) INDIA VS. OTHER REGIONS









Parameters	India	APAC	USA	EMEA
Unclear or conflicting job expectations	40%	29%	36%	33%
Inadequate staffing (lack of support, uneven workload or performance in group)	38%	41%	52%	49%
Lack of work/life balance (excessive workloads and/or long hours)	38%	32%	24%	28%
Organizational culture	32%	31%	33%	31%
Low pay (or low increases in pay)	29%	37%	38%	28%
Technologies that expand availability during non-working hours (e.g., mobiles, notebooks)	27%	16%	8%	9%
Lack of supervisor support, feedback and not living up to their word	26%	23%	23%	22%
Lack of technology, equipment and tools to do the job	18%	18%	13%	15%
Fears about job loss, too much change	16%	16%	20%	22%
Fears about benefit reduction/loss (e.g., lower value or loss of health care coverage, reduction in retirement benefits)	12%	16%	11%	7%

Reference: <http://www.towerswatson.com/en-IN/Press/2014/05/Indian-employers-rank-stress-as-1-lifestyle-risk-factor>

## WORK-RELATED STRESS-CAUSES (2/3)

Fear of layoff, pay cut and work pressure push more employees into depression

What troubles employees most  
(Stress is taking a heavy toll on workers these days)

<b>Work stress</b>	62.14	
Job insecurity/Dissatisfaction	17.14	
Difficulties in <b>peer relationships</b>	6.43	
Survivor syndrome	4.29	
<b>Redundancy</b> , actual or treat	4.28	
Difficulties with the line mgmt.	2.86	
<b>Sexual harassment</b>	1.43	
Change in the work roles	1.43	
Figures in %		
<i>Source: PPC Worldwide; based on a study for the Oct '11 to Oct '12 period</i>		



Reference: [http://articles.economictimes.indiatimes.com/2012-10-20/news/34606588\\_1\\_work-stressmental-stress-economic-slowdown](http://articles.economictimes.indiatimes.com/2012-10-20/news/34606588_1_work-stressmental-stress-economic-slowdown)

## WORK-RELATED STRESS: CONSEQUENCES (3/3)

### INDIA<sup>1</sup>

- Absenteeism damaging productivity as well as worker's well-being- 56%\*
- Family and friends notice they are stressed by work- 49%
- Stress damaging their co-worker's personal relationships- 53%

### GLOBAL DATA<sup>2</sup>

- Australian employees are absent for an average of 3.2 working days each year through stress. This workplace stress costs the Australian economy approximately \$14.2 billion – Medibank.
- An estimated 442,000 individuals in Britain (2007/08) believed that they were experiencing work-related stress at a level that was making them ill – Labour Force Survey.

*\*Survey, canvassing the opinions of >20,000 senior executives & businessmen*

#### References

1. [http://www.indiaonline.com/article/news/economic-volatility-increasing-more-stress-related-illness-on-indian-workers-regus-5836576284\\_1.html](http://www.indiaonline.com/article/news/economic-volatility-increasing-more-stress-related-illness-on-indian-workers-regus-5836576284_1.html)
2. <http://www.gostress.com/stress-facts/>



## WORK-FAMILY STRESS / WORK-LIFE IMBALANCE-INDIA

- Work and family: two life domains-potent sources of stress
- Recent socio-economic trends indicate that, work and family are becoming increasingly stressful.

Cost-cutting and down sizing have heightened work demands and reduced job security.



Rise of dual-earner couples has intensified the struggle to manage family responsibilities



Weakened family relations

*Reference: Rothbard N. Work and Family Stress and Well-Being: An Examination of Person-Environment Fit in the Work and Family Domains. Organizational Behavior and Human Decision Processes. 1999;77(2):85-129.*

## SOCIAL STRESS BY INCOME GROUP

	Low income (n = 20)	Middle income (n = 25)	High income (n = 14)	Total (n = 59)
	%	%	%	%
Children's future	75%	48%	43%	56%
Child's marriage	40%	8%	7%	19%
Dowry	15%	4%	0%	7%
Family conflict	60%	48%	43%	51%
Joint family stress	15%	36%	29%	27%
Mother or Daughter in law stress	0%	20%	14%	12%
Personal health concern	35%	44%	71%	47%
Financial stress	35%	44%	71%	47%
Job stress	25%	36%	36%	32%
Family health concern	45%	28%	7%	29%
Burden of family care	25%	20%	7%	19%
Loss of family member	10%	24%	50%	25%
Old age	15%	24%	43%	25%
Diabetes distress	35%	16%	29%	25%
Interpersonal abuse	10%	24%	21%	19%
Loneliness	20%	24%	7%	19%
Alcoholic Husband	5%	12%	7%	8%

Reference: Mendenhall E et al. Stress and Diabetes in Socioeconomic Context: A Qualitative Study of Urban Indians Soc Sci Med. 2012 December ; 75(12): 2522-2529

## TRAVEL STRESS: THE ONS'S LATEST REPORT

Data from 60,000 people, 91.5 percent of them commuters:

- Commuters demonstrated statistically significant lower scores on all measures of well-being
- Each of the personal well-being measures decreased with each successive minute of travel
- Levels of anxiety increased with each minute

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*ONS:Office for National Statistics*



Reference: <http://www.dailymail.co.uk/news/article-2557564/Its-official-Commuting-work-makes-miserablespending-half-hour-bus-worst-way-travel.html#ixzz3LabbxiNU>



## TRAVEL STRESS: CONSEQUENCES (2/2)

The ONS's latest report

- Commuters are less likely to take exercise or eat home cooked meals
- Being more likely to suffer from insomnia and joint pain.
- Such bodily ailments could impact on mental health

*Reference: <http://www.dailymail.co.uk/news/article-2557564/Its-official-Commuting-work-makes-miserablespending-half-hour-bus-worst-way-travel.html#ixzz3LabbxiNU>*



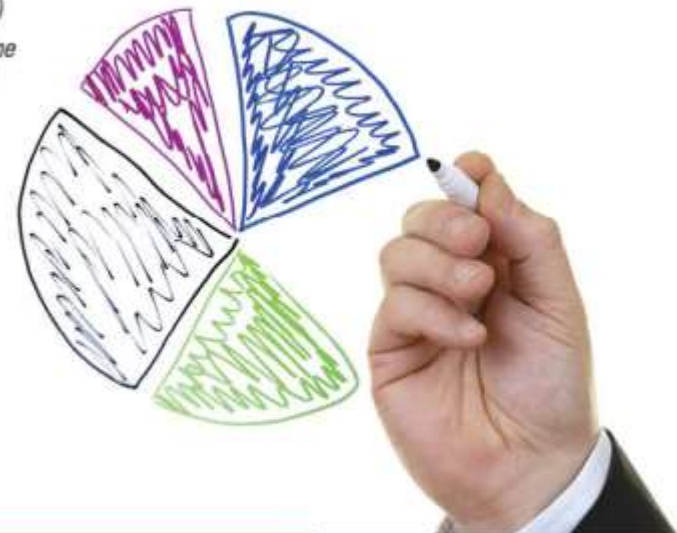


# IMPACT OF STRESS: SUMMARY

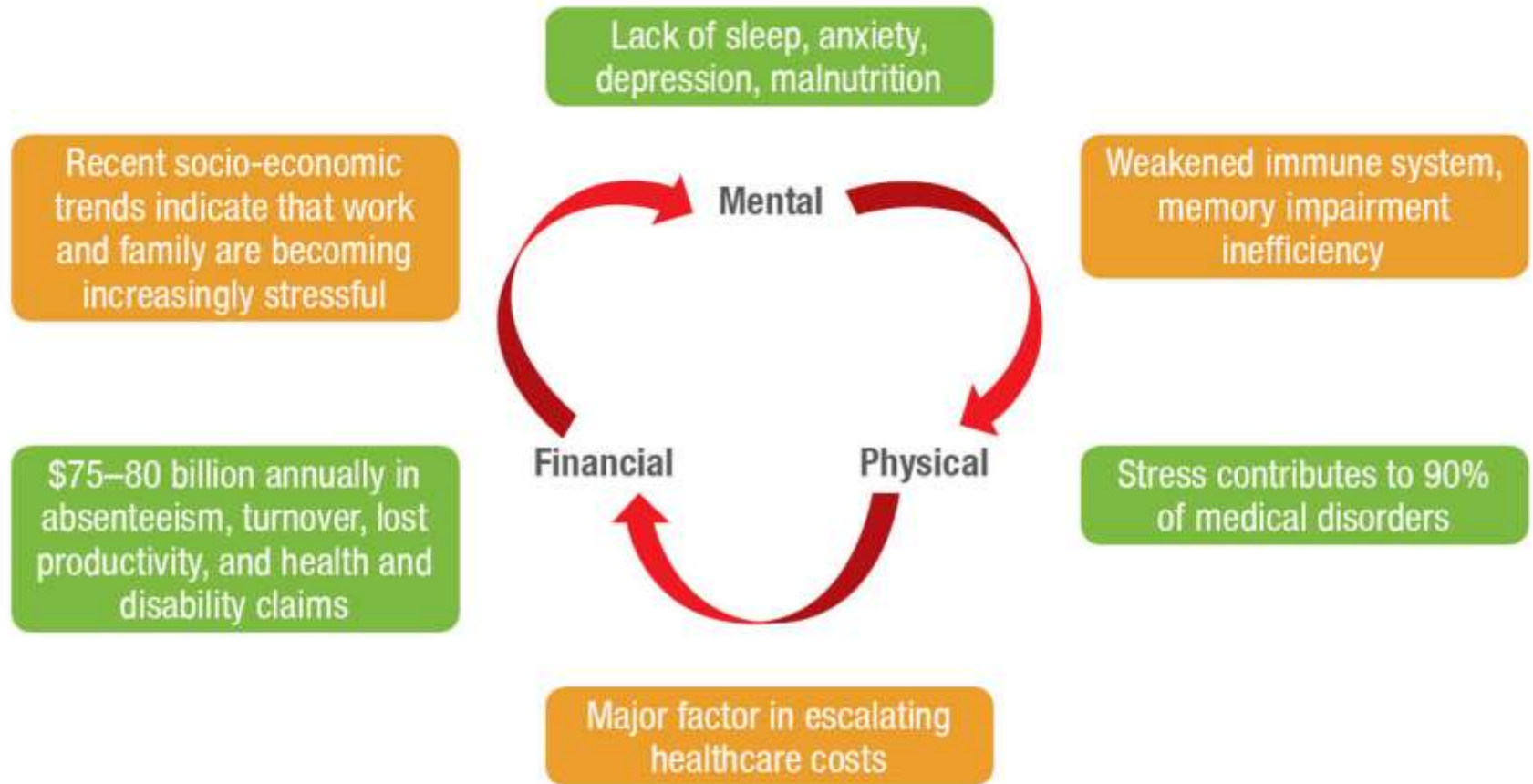
- Impact on Lifestyle Disorders
  - Increases risk of metabolic syndrome by 1.2-2 fold<sup>1</sup>
  - Population attributable risk for CHD (AMI) 32.5%<sup>2</sup>
- Impairs immune function<sup>3</sup>
- Results in memory impairments<sup>4</sup>

## References

1. Majji SM et al. Prevalence of diabetes mellitus and role of stress in diabetes in rural Pondicherry –An union territory of India. *Global J Med Public Health*. 2012; 1(5) September- October 2012;40 -46.
2. Gupta R et al. Regional variations in cardiovascular risk factors in India: India heart watch. *World J Cardiol* 2012 April 26; 4(4): 112-120.
3. Rojas IG et al. Stress-Induced Susceptibility to Bacterial Infection During Cutaneous Wound Healing. *Brain, Behavior, and Immunity* 16, 74–84 (2002)
4. Pugh CR et al. The immune system and memory consolidation: a role for the cytokine IL-1 $\beta$ . *Neuroscience and Biobehavioral Reviews* 25 (2001) 29-41



## IMPACT OF STRESS: VICIOUS CYCLE\*



*\*The New York Business Group on Health estimate*

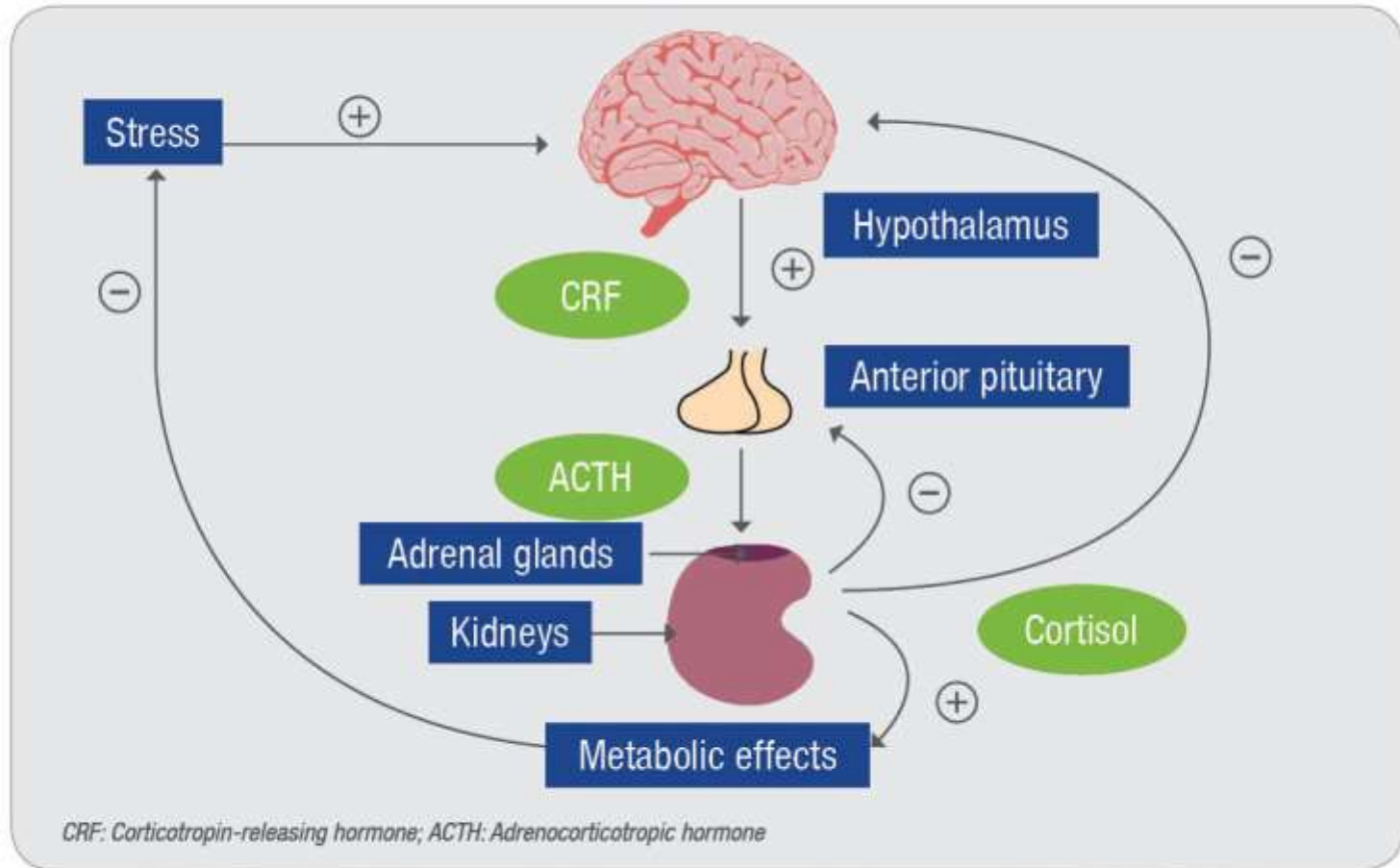
*Reference: Rothbard N. Work and Family Stress and Well-Being: An Examination of Person–Environment Fit in the Work and Family Domains. Organizational Behavior and Human Decision Processes. 1999;77(2):85-129.*

## STRESS AND GENERAL ADAPTATION SYNDROME



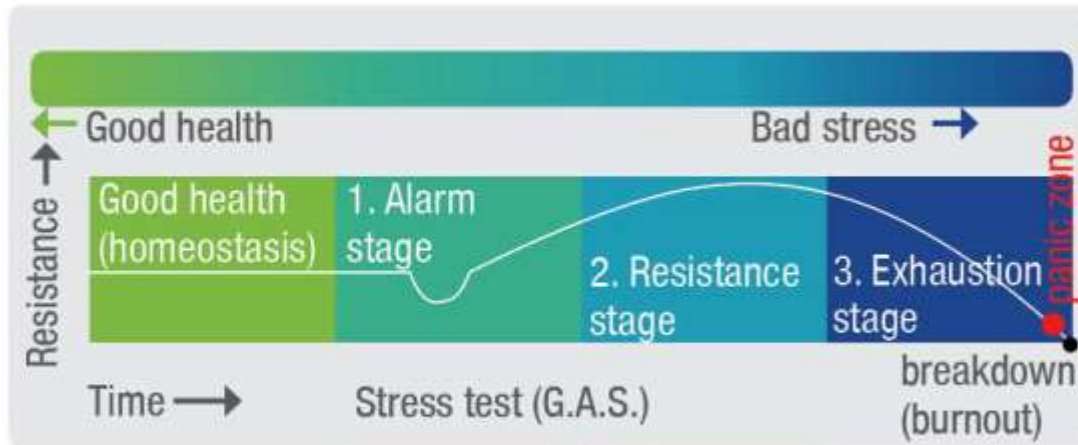
# STRESS AND THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS

Adrenal fatigue is caused by continual over stimulation of the adrenal glands from constant stress.



Reference: The Physiology of Stress: Cortisol and the Hypothalamic-Pituitary-Adrenal Axis. Available from [http://dujs.dartmouth.edu/fall-2010/the-physiology-of-stress-cortisol-and-the-hypothalamic-pituitary-adrenal-axis#.U8zqP\\_mSySo](http://dujs.dartmouth.edu/fall-2010/the-physiology-of-stress-cortisol-and-the-hypothalamic-pituitary-adrenal-axis#.U8zqP_mSySo). Cited on 23/7/2014

# GENERAL ADAPTATION SYNDROME



Fight or Flight <sup>2</sup>	Body learning to cope with the situation <sup>2</sup>	Body has used all its resources, degeneration <sup>2</sup>	
		<b>Initial symptoms<sup>2</sup></b>	<b>Untreated long-term stress<sup>2</sup></b>
		■ Muscle tension	■ Diabetes
		■ Loss of focus/ concentration	■ Depression
		■ Headaches	■ Mental health problems
		■ Increased heart rate	■ Heart/ Cardiovascular problems
		■ Having a short temper	■ Bowel/Digestive Problems
		■ An edgy personality	
		■ Irritations (Rashes, Eczema)	
		■ Loss of appetite	

## References

1. Perdrizet GA. Hans Selye and beyond: Responses to stress. *Cell Stress Chaperones*. 1997;2(4):214-19.
2. <http://www.stress.org.uk/files/combat-nutritional-stress.pdf>

## NUTRITION AND STRESS

- Subclinical or marginal deficiencies of essential micro-nutrients can lead to psychological and physiological symptoms that are related to stress.<sup>1</sup>
- Unless critical nutrients are quickly replaced, coping mechanisms further break down and emotional problems worsens.<sup>2</sup>
- Enough of the right nutrients can prevent stress, and controlling stress can, in turn, prevent nutrient deficiencies.<sup>2</sup>
- Nutrient supplements can help with management of stress.<sup>2</sup>



### References

1. *Vitamins and Minerals for Stress Adaptation*. Accessed at [http://cortisolconnection.com/ch8\\_3.php](http://cortisolconnection.com/ch8_3.php) on 28/02/2015
2. *Stress Can Cause Nutrient Deficiencies*. Accessed at [http://www.diabeteslibrary.org/View.aspx?url=stress\\_b\\_vitamins](http://www.diabeteslibrary.org/View.aspx?url=stress_b_vitamins) on 28/02/2015

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# MANAGEMENT OF STRESS

**Mediators:** Coping processes Social support Cognitive appraisal

## HEALTH STATUS

Stressful  
events



Indicators of adaptation status: somatic  
health and psychological symptoms

Psychological and physical wellbeing



*Reference: K.S. Han / International Journal of Nursing Studies 39 (2002) 539–548*



## STRESS RESILIENCE (SIMPLE)

- The ability to 'bounce back' to healthy functioning when faced with significant stressors and events
- It does not eliminate stress
- Gives strength to tackle difficult situations



Reference: <http://www.slideshare.net/pangulongdiondalusong/family-resilience>

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## MANAGEMENT OF STRESS (1/2)

- Lifestyle changes
- Exercise
- Nutrition

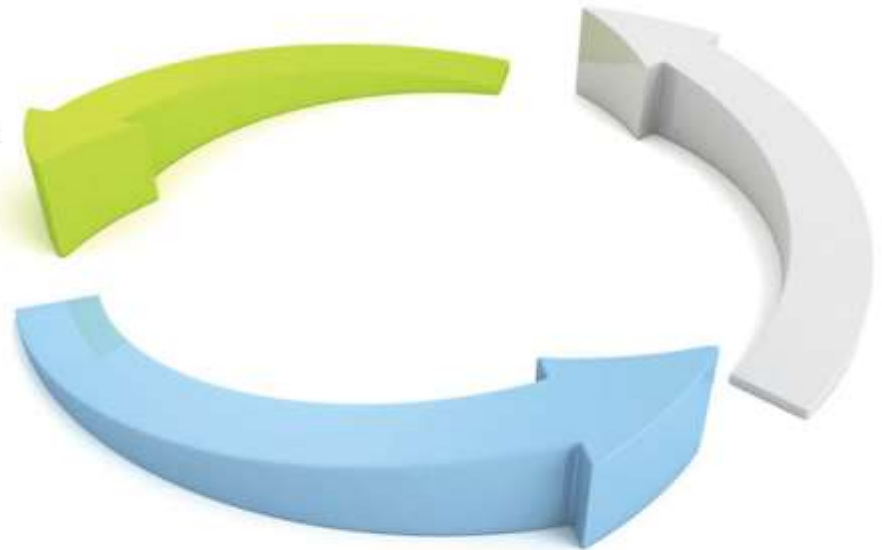


*Reference: Vinod SP and Shivakumar H. A current status of adaptogens: Natural remedy to stress. Asian Pacific Journal of Tropical Disease.2012;S480-S490.*

## MANAGEMENT OF STRESS (2/2)

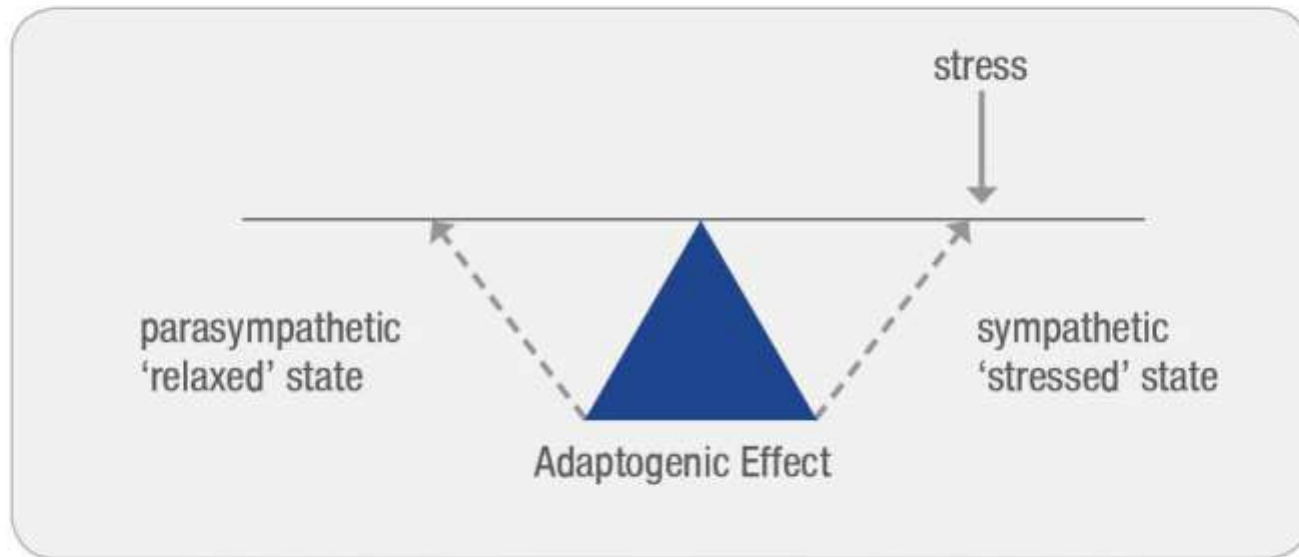
Stress adaptogens: One of the best and most powerful ways to lower excess cortisol levels, bring the body into a state of metabolic harmony and reduces the damaging effects of stress.

- Positively change stress response → prevents health problems
- Help the body to adapt by normalizing physiological processes
- Act as tonics
- Prescribed to enhance vitality
- Indicated when stress levels are high, during convalescence after or in difficult life chances (event)



< **Reference:** Vinod SP and Shivakumar H. A current status of adaptogens: Natural remedy to stress. *Asian Pacific Journal of Tropical Disease*.2012;S480-S490. >

## ADAPTOGENIC EFFECT



# ROADMAP

INTRODUCTION

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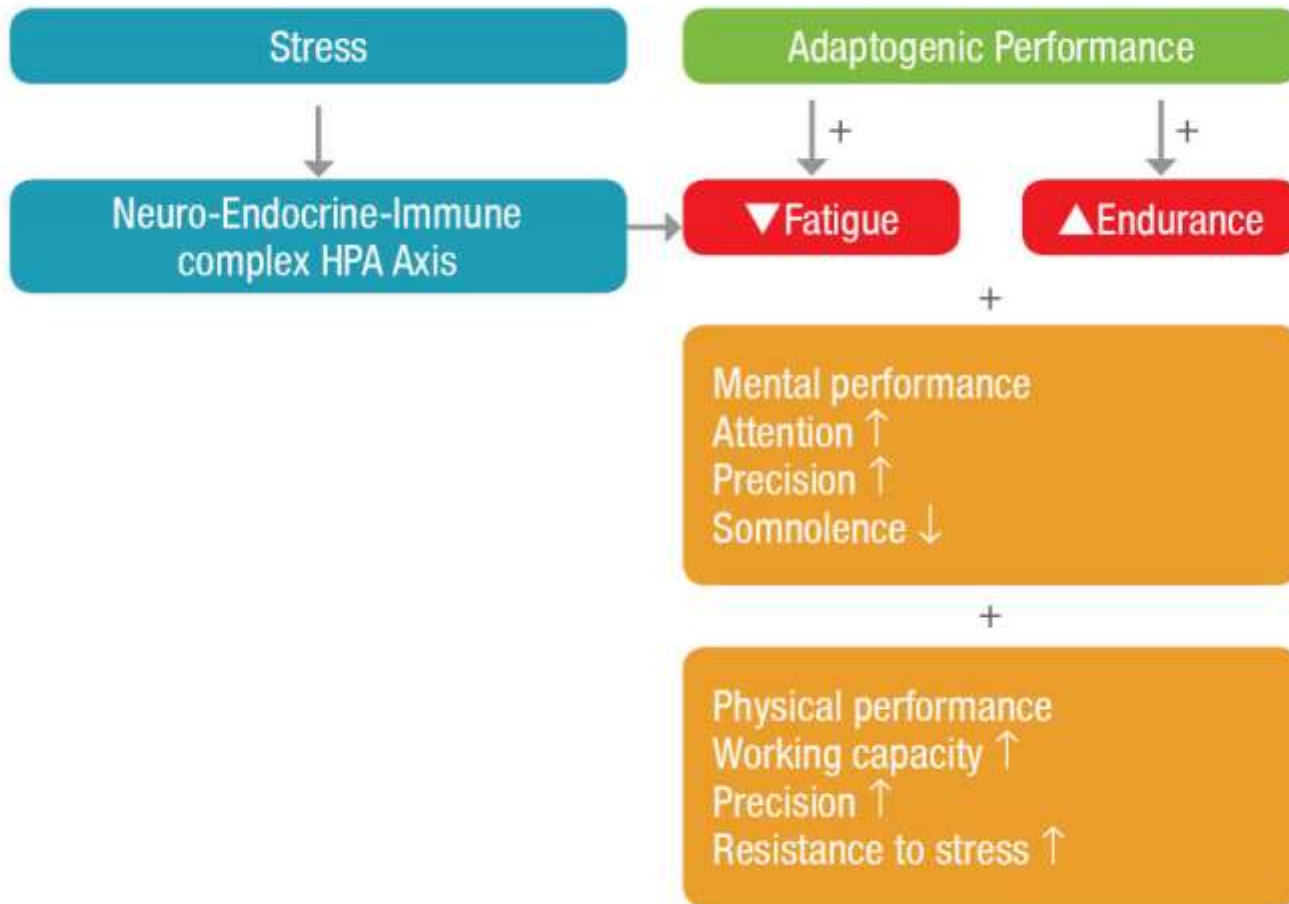
COMMON STRESSORS:  
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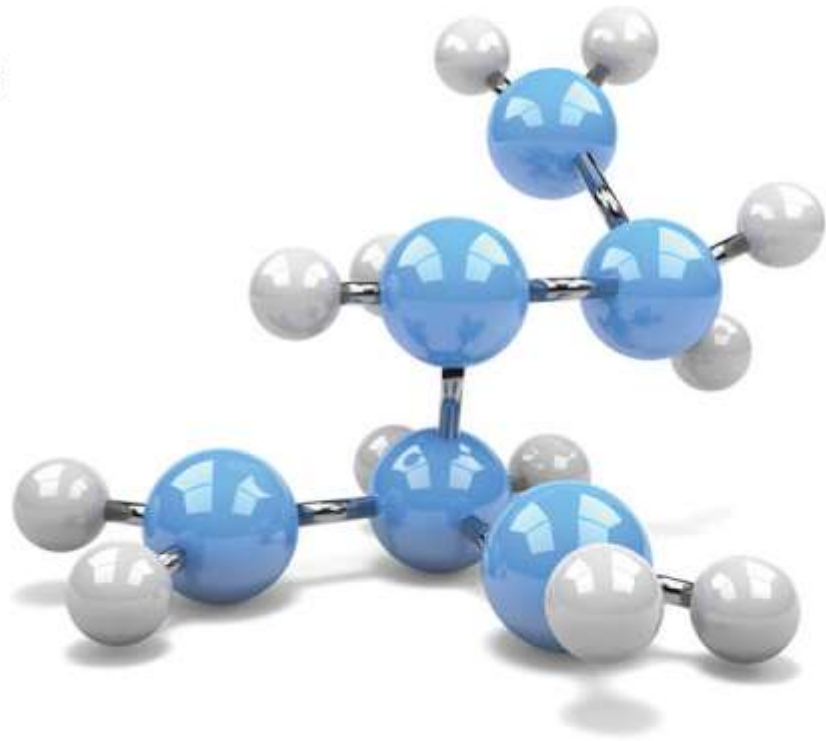
## ROLE OF ADAPTOGENS: EFFECT ON STRESS SYMPTOMS



*Reference: Vinod SP and Shivakumar H. A current status of adaptogens: Natural remedy to stress. Asian Pacific Journal of Tropical Disease. 2012;S480-S490.*

## BENEFICIAL **STRESS**-PROTECTIVE EFFECT OF **ADAPTOGENS**

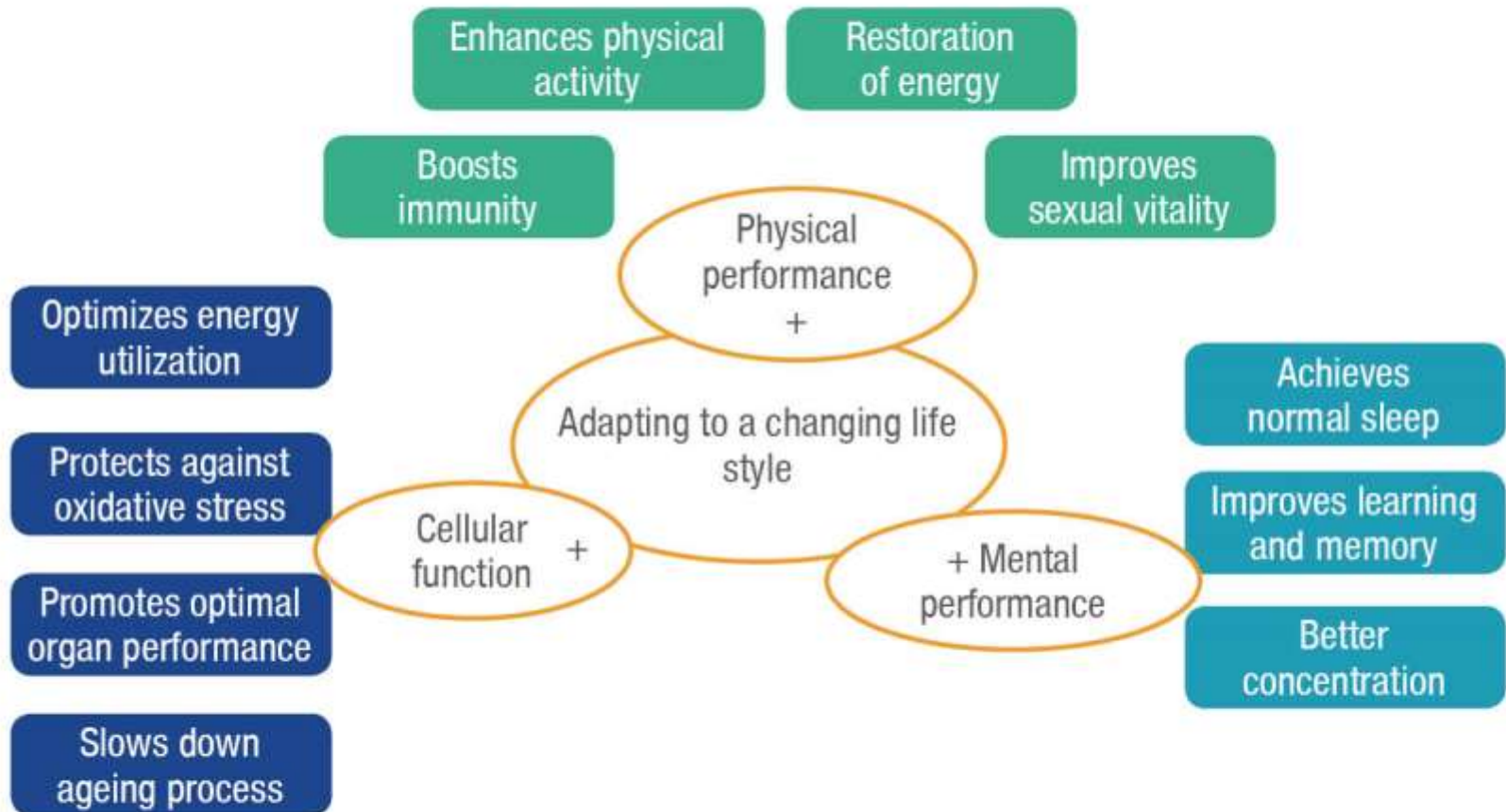
- Regulation of homeostasis via the hypothalamic pituitary-adrenal (HPA) axis
- Control of key mediators of stress response
  - Molecular chaperones
  - Stress-activated protein kinase
  - Transcription factor
  - Cortisol
  - Nitric oxide (NO)



*Reference: Panossian A, Wikman G Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity. Curr Clin Pharmacol. 2009 Sep;4(3):198-219. Epub 2009 Sep 1*



# ADAPTOGENIC PERFORMANCE



## KEY INGREDIENTS: BENEFITS

### Ginseng

- Increases the body's resistance to physical, chemical and biological stress
- Enhances libido and copulatory performance
- Balances cortisol
- Promotes vitality and increases resistance to stress and ageing
- Enhances physical and mental performance

### Garlic

- Anti-fatigue effect

### Green tea extracts

- L-theanine enhances calming & curative properties
- Theanine lowers cortisol levels during stress periods
- Helps the ability to learn and remember
- Diminish stress, worry, anxiety and improves concentration
- Lowers chances of heart disease and developing certain types of cancer



## KEY INGREDIENTS: BENEFITS

### Vitamins B<sub>5</sub> (Pantothenic Acid)

Protects against mental and physical stress, anxiety, trouble sleeping (insomnia), irritability, reduces signs of ageing and chronic fatigue syndrome.

### Choline Bitartrate

Anti-ageing benefits and antidote for stress

### Vitamin C (Ascorbic Acid)

- Improving physical performance and strength in the elderly
- Prevents common cold
- Antioxidant
- Improves immune system function



## KEY INGREDIENTS: BENEFITS

### L-Cystiene

Reduction of oxidative stress<sup>1,2</sup>

protect against oxidant-related up-regulation of endothelial adhesion molecules and slow down the progression of vascular damage in non-insulin dependent diabetes.

### Copper

Metabolic syndrome is significant and inversely associated with the highest quartiles of Cu intake.<sup>7</sup>

### L-carnitine

Supplementation associated with <sup>3,4,5,6</sup>

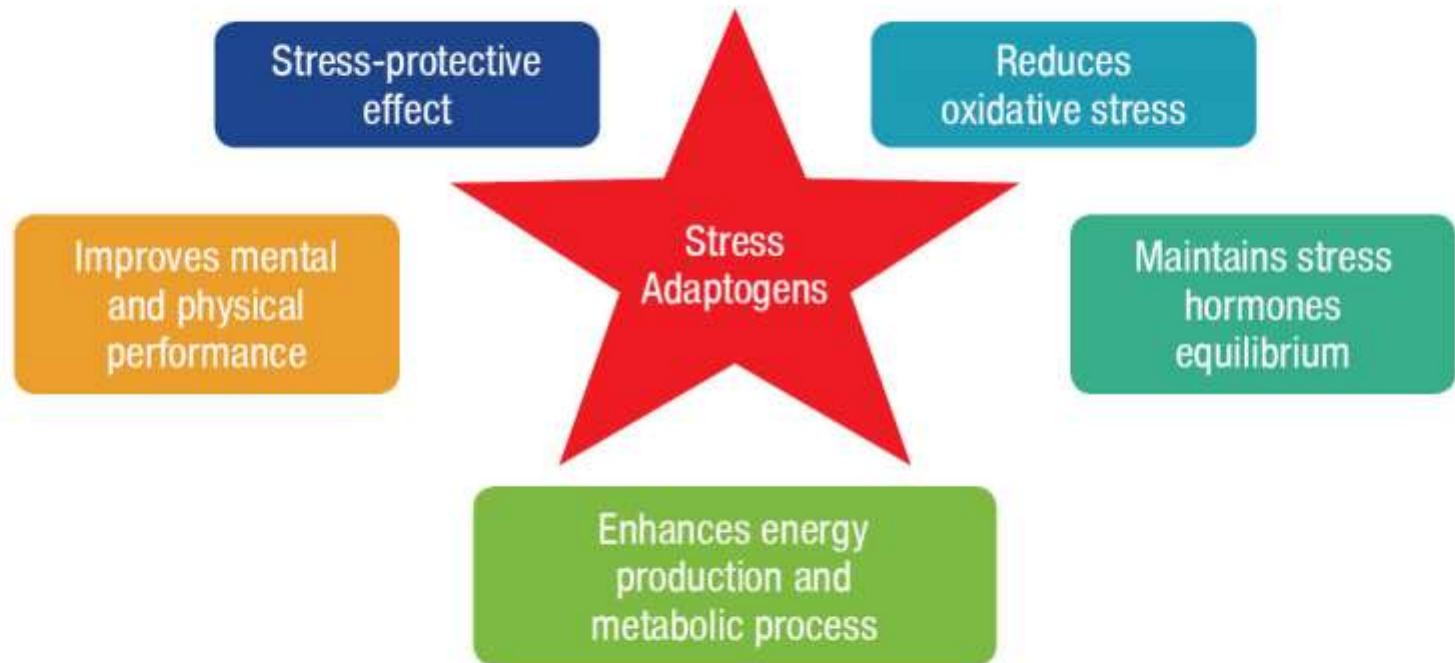
- Significant reduction in oxidative stress\*<sup>3</sup>
- Significant increase in antioxidant enzyme activities\*<sup>3</sup>
- Improvement in fatigue symptoms\*\*<sup>4</sup>
- Attenuates oxidative stress responses, enhances antioxidant status, and improves performance\*\*\*<sup>5</sup>
- Facilitates an increased capacity for physical and cognitive activity by reducing fatigue and improving cognitive functions\*\*\*\*<sup>6</sup>

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\*in CAD patients; \*\* in cancer patients; \*\*\* patients with end-stage renal disease; \*\*\*\*in centenarians

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