Journal of
Health Education Research & Development

Joy, J Health Edu Res Dev 2015, S1:001
DOI: 10.4172/2380-5439.S1-001

Commentary Open Access

A Transcending Insight into Disease Etiology and Life Sciences-Enhancement of Oxygenation for Reestablishing Homeostasis

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Rec date: Jun 03, 2015; **Acc date:** Jun 25, 2015; **Pub date:** Jun 27, 2015

Abstract

Oxygen is the fundamental electron transport mechanism in the universe. Its the way through which the universe is monitoring, recording, maintaining internal stability, obtaining coordinated responses and is managing the ecology of life. All processes of integration and coordination of function in the ecology of life, whether mediated by nervous and hormonal systems comes under homeostatic regulation. The primary target and aim of every disease and disorder in the ecology of life is to impair oxygenation the outcome of which is the disruption of homeostatic regulation.

An illness or disease thrives only in an oxygen deficient environment. The homeostatic regulation in the ecology of life is mediated through oxygen. Universe is an unquestionable natural truth that identifies itself and us as 'unity'. In all of the mechanisms in the ecology of life, has only one object of maintaining constant conditions in the internal environment. A perfect homeostasis is the one and only requirement for healing of any disease or disorder in the ecology of life.

Keywords: Homeostatic regulation; Neurodegeneration; Bipolar spectrum disorders; Schizophrenia; Diabetes; Morbid obesity

Abbreviations

HPA axis-Hypothalamic–Pituitary–Adrenal axis; HPG axis-Hypothalamic–Pituitary–Gonadal axis; CNS-Central Nervous System

Introduction

The term homeostatic regulation subsumes diverse physiological processes which is what results in the biological regulation of life. These include processes of regulation such as cardiovascular regulation, gastrointestinal regulation, respiratory regulation, urogenital regulation, neuroendocrine regulation, HPA and HPG axis regulation, regulation of biological rhythms, thermoregulation, pH balance, regulation of metabolism. All forms of integration and coordination of functions whether mediated by nervous and hormonal systems comes under homeostatic regulation. Since oxygen is the mediator of this homeostatic regulation, an impairment in oxygenation implies disruption of homeostatic regulation. The underlying processes which regulates life is highy dynamic in nature and hence it is subject to real time monitoring and regulation. This broad spectrum mechanisms of homeostatc signalling are performed by several underlying processes of intracellular signalling. These signalling mechanisms are dependent of electrical activity, the underlying electron-transport mechanism mediated through oxygen. The entire concept of 'Vata Raktha Chikitsa' mentioned in 'Ashtangahridayasamhitha' – ayurvedic medicinal system is suggestive of this underlying mechanism [1]. Furthermore the rasayana concept of ayurveda aimed in tissue regeneration, cell renewal, improving longevity and vitality has an underlying mechanism of profound enhancement of oxygenation thereby reestablishment of homeostatic regulation.

Major factors that can cause vitiation of blood thereby harmfully impairing or spoiling the oxygenation capacity includes presence of inflammations, sequalae of infections, sequalae of trauma, as a result of substance and drug abuse, sequalae of alcoholism, as a result of tobacco use, sequalae of ionizing radiation, sequalae of diabetes, underlying dyslipidemia, any factors such as environmental pollution, or exposure to toxic chemicals, neurotoxins, dietary intakes intoxicated with pesticides; that will be resulting in disruption of homeostasis governing life.

The disruptions in homeostatic regulation can be corrected by promoting oxygenation that is by modifying the capacity of blood to transport and deliver oxygen; this includes mechanisms of oxygen binding and oxygen metabolism through oxidases, peroxidases, catalases, hydroxylases, and electron transfer-cytochromes. Enhacement of oxygenation activates multiple targeted actions and activation of multiple clearance pathways such as glymphatic clearance pathway, enhancement in circulatory system, lymphatic system, and enhanced immune response. This can further result in prevention and cure for complex disorders. This approach is effective in sustaining natural health also.

Background

Homeostasis refers to stability, balance or equilibrium; it's an attempt to maintain a constant internal environment. Maintaining a stable internal environment requires constant monitoring and adjustments as conditions change. This adjusting of physiological systems within the body is called homeostatic regulation. The mechanism of immunologic response also comes under homeostatic regulation governing life. Clinical features of disruptions in physiologic

homeostasis varies according to disease or condition, also depends on the underlying factors. Previous studies suggested drinking oxygenated water has profound benefits on the immune system, enhanced immune activity, also suggests T-cell activation after mitogen stimulation, the soluble IL-2 receptor, the CD^{4+} and the naive CD4+CD45RA+ cells increased [2]. This is a result of improved homeostatic regulation.

Oxygen is the fundamental electron transport mechanism in the universe. It's the way through which the universe is monitoring, recording, maintaining internal stability, obtaining coordinated responses and is managing the ecology of life. All processes of integration and coordination of function in the ecology of life, whether mediated by nervous and hormonal systems comes under homeostatic regulation. Human consciousness cannot be considered locally stored in nervous system. Universe is an unquestionable natural truth that identifies itself and us as 'unity'. Memory is attributed to strengthened synaptic connections among particular brain neurons, yet synaptic membrane components are transient, whereas memories can endure. This suggests synaptic information is encoded and 'hard-wired' elsewhere [3].

There are several pathological processes that tend eventually to become malignant. Carcinogens refer to the substances that increase the risk of neoplasms in humans or animals which include genotoxic chemicals which affect DNA directly, and nongenotoxic chemicals. But as a matter of fact, the prime cause of cancer is the replacement of the respiration of oxygen in normal body cells by fermentation. All normal body cells meet their energy needs by respiration of oxygen, whereas cancer cells meet their energy needs by fermentation. Neoplasm cannot develop in a well oxygenated alkaline environment. Impairment or spoiling of the oxygenation capacity of blood is the prime cause for carcinogenesis, which develops only in a disrupted homeostasis. This disruption in homeostatic regulation brought by impaired oxygenation which upset the normal balance between cell proliferation and cell death. Anaplasia is the condition whereby cells lose the morphological charateristics of mature cells and their orientation which implies the loss of structural differentiation. This condition includes an increased capacity for multiplication. Lack of differentiation means loss of structural and functional differentiation of normal cells. This is directly related to aggressive malignancies. This lack of differentiation suggests a disruption in the homeostatic regulation. Also the transcription factors in the class of Hypoxia Inducible Factors, respond to changes in oxygen availability in the cellular environment specifically to hypoxia. HIF-1, when stabilized by hypoxic conditions up regulates several genes to promote survival in low-oxygen conditions. These include glycolysis enzymes which allow ATP synthesis in an oxygen-independent manner, and vascular endothelial growth factor which promotes angiogenesis [4] Carcinogenesis generally undergoes a sequence of steps which may occur quickly or over a period of years. Cancer cells can spread to other parts of the body through the blood and lymph systems. Neoplasm invasiveness refers to the ability of neoplasms to infiltrate and actively destroy surrounding tissue. This includes metastasis which refers to the transfer of a neoplasm from one organ or part of the body to another remote from the primary site. Also recurrence of a neoplasm following treatments is an unavoidable possibility. It arises from microscopic cells of the original neoplasm that have escaped therapeutic intervention and later become clinically visible at the original site. German biochemist Dr. Otto Heinrich Warburg is world renowned for his research into cellular respiration, showing that cancer thrives in anaerobic or acidic conditions [5] and hence the disruption in homeostatic regulation resulting from impaired oxygenation is the prime underlying factor in carcinogenesis. Reestablishing homeostatic regulation by enhancing oxygenation can provide a better immune response and resistance to carcinogenesis. The anti-cancer activity exhibited by Withania Somnifera [6,7] which was found useful in the management of malignancy by targeting at multiple pathways has a profound underlying mechanism of enhancing oxygenation.

The etiology of disorders of psychological development, mental retardation, pervasive developmental disorders, autistic disorder, down syndrome shares a common factor of impaired oxygenation with respect to the development and activity of CNS either while developing in the uterus or during or after development leading into disruption of homeostatic mechanisms regulating synaptic and neuronal plasticity and multiple abnormalities. The etiology of Bipolar Spectrum disorders and Schizophrenia holds only one plausible explanation of impaired oxygenation due to presence of inflammatory factors and resulting ventricular enlargement. This further causes disruptions in homeostatic mechanisms regulating neuronal plasticity. The same is with the case of Major Depressive disorder, Obsessive Compulsive disorder, Attention Deficit Hyperactivity disorder. Mounting evidence suggests region-specific changes to synaptic form and function occur as a result of chronic stress and in depression [8].

Homeostatic regulation of neuronal excitability refers to the collective phenomena by which neurons alter their intrinsic or synaptic properties to maintain a target level of electrical activity. Dysfunction of these fundamental processes could thereby contribute to the pathophysiology of neuropsychiatric presentations [9]. The term neuroplasticity relates to diverse processes of vital importance by which the brain perceives, adapts and responds to a variety of internal and external stimuli. The manifestations of neuroplasticity in the adult CNS have been characterized as including alterations of dendritic function, synaptic remodeling, long-term potentiation (LTP), axonal sprouting, neurite extension, synaptogenesis, and even neurogenesis [10,11]. Clinical presentations of disruptions in homeostatic mechanisms regulating neuronal plasticity accompanies mood destabilization, suicidal ideation, visual and auditory hallucinations, psychosis, delusions and other neuropsychiatric presentations. Consider the case of 'rabies' which is a viral disease that causes acute inflammations in brain, which directly impairs the oxygenation capacity of blood. This further disrupts the homeostatic mechanisms regulating neuronal plasticity. The clinical presentations of which includes violent movements, uncontrolled excitement, fear of water, inability to move parts of body, confusions, loss of consciousness.

The same is with the case of diabetes and other disorders of metabolism and major cardiovascular conditions. Whatever be the disease the primary target and aim of every disease and disorder in the ecology of life is to impair oxygenation the outcome of which is the disruption of homeostatic regulation. An illness or disease thrives only in an oxygen deficient environment. Improving the oxygen transport by blood will lead to enhanced insulin secretion without the risk of hypoglycemia and increased insulin sensitivity without body weight gain. Also improvement in dyslipidemia that coexists with diabetes and preservation of pancreatic beta cell action and delayed beta cell failure. Further benefits includes delayed development of diabetes related complications, namely, retinopathy, nephropathy, neuropathy, and cardiomyopathy. Enhancing oxygenation using novel therapeutic approaches also seems to be promising in morbid obesity. Also applicable for disorders of circulatory systems, lymphatic system.

When we look into the pathogenesis of neurodegeneration, it can be seen that a wide array of neurodegenerative conditions are caused by

intraneuronal accumulations of intracellular or extracellular protein aggregates [12]. This inturn is due to disruption of homeostatic regulation. Alzheimers disease, Parkinsonism, ALS, Dementia with LB inclusions suggests a related Pathophysiology. Neurodegenerative diseases are caused by breakdown in this homeostatic regulation, which leads to progressive intracellular or extracellular plaque buildup. Moreover the decline in the efficiency of homeostatic regulation due to accumulated dysfunction can persist and become progressive if the homeostatic regulation is not re-established. The effects are accumulative over years unless regeneration occurs by re-establishing the disrupted homeostatic regulation. The involvement of glymphatic system in neurodegenerative conditions is very prominent. Enhancement of oxygenation can activate glymphatic clearance pathways which have promising effects in delaying progression.

The process of respiration is an ATP – generating process in which an inorganic compound such as molecular oxygen serves as the ultimate electron acceptor. The series of energy transformations which is known as the cellular respiration is generally concluded in Oxidative phosphorylation. The final phase of the oxidative phosphorylation is carried out by ATP synthase, which is an ATP synthesizing assembly.

In Ayurvedic Medicinal system, Withania Somifera has been used for centuries for its effects in longevity and vitality. Several research favors its anti-inflammatory, immune-modulating, hematogenic activities. The broad spectrum benefits provided by Withania Somnifera in neoplasms, neurodegeneration, neuropsychiatric disorders, diabetes, disorders of metabolism is confirming its action on enhancing oxygenation and thereby reestablishing homeostatic regulation. Withania Somnifera is known to alter the oxidative stress markers of the body, found to have neuroprotective activity, free radical scavenging activity and has found to significantly reduce the lipid peroxidation and increase the superoxide dismutase (SOD) and catalase activities. It is proved to have hepatoprotective effect against radiation induced and iron induced toxicity [13,15]. It's by the underlying mechanism of enhanced oxygenation thereby reestablishing homeostatic regulation targeting multiple pathways Withania Somnifera demonstrates its effects. The benefits associated with an organic diet and intermittent fasting is also suggesting a similar mechanism.

Conclusion

The process of healing or cure can be termed as the reestablishment of homeostatic regulation. The homeostatic regulation in the ecology of life is mediated by oxygen. In all of the mechanisms in the ecology of life, however varied they may be, have only one object that of preserving constant conditions of life in the internal environment. The internal environment must possess certain conditions within tolerable limits to continue healthy function. A perfect homeostasis is the one and only requirement for healing of any disease or disorder in ecology of life.

Through enhancement of oxygenation capacity of blood, by modifying the capacity of blood to transport and deliver oxygen, enhancing oxygen metabolism the disruptions in homeostatic mechanisms governing life can be re-established which can induce healing and can be used in prevention of diseases. This can be achieved by modifying the quality, concentration, metabolism, storage and oxygen binding capacity of hemoglobin. This includes enhancement of factors associated with oxygen metabolism such as oxidases, peroxidases, catalases, hydroxylases, and electron transfer-cytochromes. With the help of novel nanotherapeutics targeted for enhancing oxygenation this can be achieved and can be effectively used in sustaining natural health, healing of diseases and as a preventive medicinal approach. The branch 'Rasa shastra' of Ayurvedic Medicinal System uses 'Bhasma', some of which are nanomedicinal preparations in traditional manner, some of which have profound hematogenic activity, immune enhancing activity [8] Synergistic medicinal approaches as used in ayurvedic medicinal systems for reducing inflammations, by modulating hematinic , hemopoietic properties, vasodilator activity , immune modulation enhances the oxygenation capacity of blood, furthermore aids in re-establishing the homeostatic regulation. For example 'Withania Somnifera' or Ashwagandha shows a similar therapeutic potential. [1,6,7,16-21]. Also there exists several other potential herbal medicines demonstrating a potential enhancement of oxygenation and thereby an improved homeostatic regulation.

Since the homeostatic regulation in the ecology of life is mediated by oxygen, an enhancement in oxygenation thereby results in reestablishment of homeostatic regulation. This reestablishment of homeostatic regulation can neutralize and negate disorder genesis, and will lead to restoration of health. And reestablishment of homeostatic regulation is the one and only requirement for healing.

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This article was originally published in a special issue, entitled: **"Etiology of Diseases,Nutrition and Human Learning"**, Edited by Dr.Miruka Conrad Ondieki