

Is Humanity Passing Up The Greatest “Life Force” Ever Discovered?

by Bill Sardi

May the force be with you.” - Star Wars

Strange as it may seem, largely because of difficulties in figuring out how to commercialize on what it promises, both alternative and conventional medicine fail to put into practice a compelling discovery that promotes health and longevity in an unmatched fashion.

It’s not a high-tech invention. It is not a patentable process. It is not a machine or a drug. Nor is it new. It has been recognized in the medical literature for decades now.

It is an adaptive internal response to mild biological threats that trigger incomparable defenses in the human body.

Despite considerable personal investigation into this topic, even the most avid health nut or PhD pursuer of longevity is likely to have missed the greatest mechanism to promote the human healthspan and lifespan ever discovered because it is not found in our external world but is rather a built-in adaptive response within the human body that has many triggers.

Historically this life force dates back to reports published in the 1940s, but it still has not hit the public’s radar of awareness. A few reports of people [bathing in radium hot springs](#) or spending time at the [bottom of old mine shafts](#), to be exposed to sub-lethal amounts of radon gas, have been published. These practices are examples of mild biological stressors that tap into this life force, but the power of this

mechanism and its numerous environmental triggers goes largely unrecognized and untapped.

This “*life force*” promises to make super humans who can think faster and more cogently, who are resistant to pain via production of endorphins, and who are resistant against disease in a manner that would antiquate most prescription drugs in use today.

Pray tell, what is it? And why hasn’t the public been alerted to it sooner?

This “*life force*” is called [hormesis](#), which is defined as exposure to a low level toxin that triggers biological defenses.

The historical father of hormesis is Swiss-born Phillipus Aureolus, who used the pseudonym “*Theophrastus Bombastus von Hohenheim*” and later went by the pen name Paracelsus (1493-1541 AD), was among the first to utilize chemicals as medicines and became famous for saying “*All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy.*” His statement has been shortened to say “*the dose makes the poison.*”

The absence of a hormetic agent will obviously produce no biological response, while a low dose produces a profoundly measurable protective effect and a stronger dose is toxic and even deadly.

The [dose response of hormesis is visualized in the so-called U-shaped or J-shaped risk curve](#) where maximum biological survival is produced at a low dose and with increased dosage the protective effect vanishes and toxicity becomes worse than if the living organism were not exposed to it at all.

In an antioxidant world ushered in by researcher Denham Harman in the 1950s, when [antioxidants were first posed as antidotes to all disease](#) given that about 5% of the oxygen humans breathe becomes unstable oxygen that can damage living tissues, stronger antioxidants were often posed as superior.

But there is a growing body of scientific evidence to show that the competitive commercial war to produce products that offer stronger and stronger antioxidant protection in various health food supplements may be counterproductive. There is a body of evidence showing certain natural plant extracts, particularly polyphenols found in grapes, berries and spices, are antioxidants at low dose and promote oxidation (pro-oxidant) at high doses.

Only recently has it been recognized that [dietary antioxidants may exert the majority of their protective properties via activation of hormesis](#).

The first time the word hormesis is used is in 1943 when researchers were studying an antibiotic substance extract-

ed from Western Red Cedar which stimulated rather than killed off certain organisms at certain concentrations. The next year other researchers reported the [bacteria count of a refrigerated sample containing red blood cells was much higher when exposed to higher rather than lower doses of penicillin](#).

As [researchers explain](#), “novel types of innovative, mild, repeated stress or stimulation that challenge a biological system in a dose-response manner are likely to have an effect that, properly harnessed, can be used to delay, prevent, or reverse age-related changes in humans.”

Toxicologists have now identified a number of environmental triggers of hormesis which includes exposure to low amounts of:

- ✓ [Radon gas](#) or other forms of [gamma or x-ray radiation](#).
- ✓ [Low-oxygen environments](#), such as at high altitudes.
- ✓ [Heat](#), such as in [sauna baths](#).
- ✓ [Near starvation or so-called calorie restriction](#), practiced regularly in some human cultures as fasting.
- ✓ [Molecular mimics of hormesis](#), that is, molecules that trigger the same defensive genes. These are small molecules found in the diet that can get into genetic machinery within living cells, molecules from grapes, spices and other botanicals.

If humans can activate this adaptive response on a regular basis, keeping themselves in survival mode, they would tap into the most powerful life enhancing mechanism apparently designed into living organisms.

In humans hormesis activates antioxidant mechanisms more powerful than taking a whole bottle of antioxidant vitamin pills. In fact, hormesis may explain why some studies show high-dose antioxidant pills begin to lose their effect compared to low doses.

Hormesis demonstrated

It was Moscow-based biologist Felix Meerson [who first described protective adaptation among animals and humans exposed to high-altitude, low-oxygen environments.](#) Meerson's research led to athletes being coached to “*train high and live low*,” that is, to train in mountainous environments and then return to low-altitudes for everyday living, in order to achieve optimum physical performance.

Exposure to [low amounts of radon gas has been shown to be effective in the treatment of chronic pain](#) and glandular and circulatory diseases. [Whole body exposure to low-dose ionizing radiation \(gamma rays, x-rays\) appears to decrease overall cancer incidence.](#)

Some researchers also believe physical exercise causes inflammation that triggers hormesis.

Mechanism of hormesis

A specific internal mechanism of hormesis is the activation of the Nrf2 protein, or what is known as a transcription factor that binds to DNA and controls the dynamic protein-making property of genes called epigenetics rather than the better known inherited alterations in the sequence of DNA known as mutations.

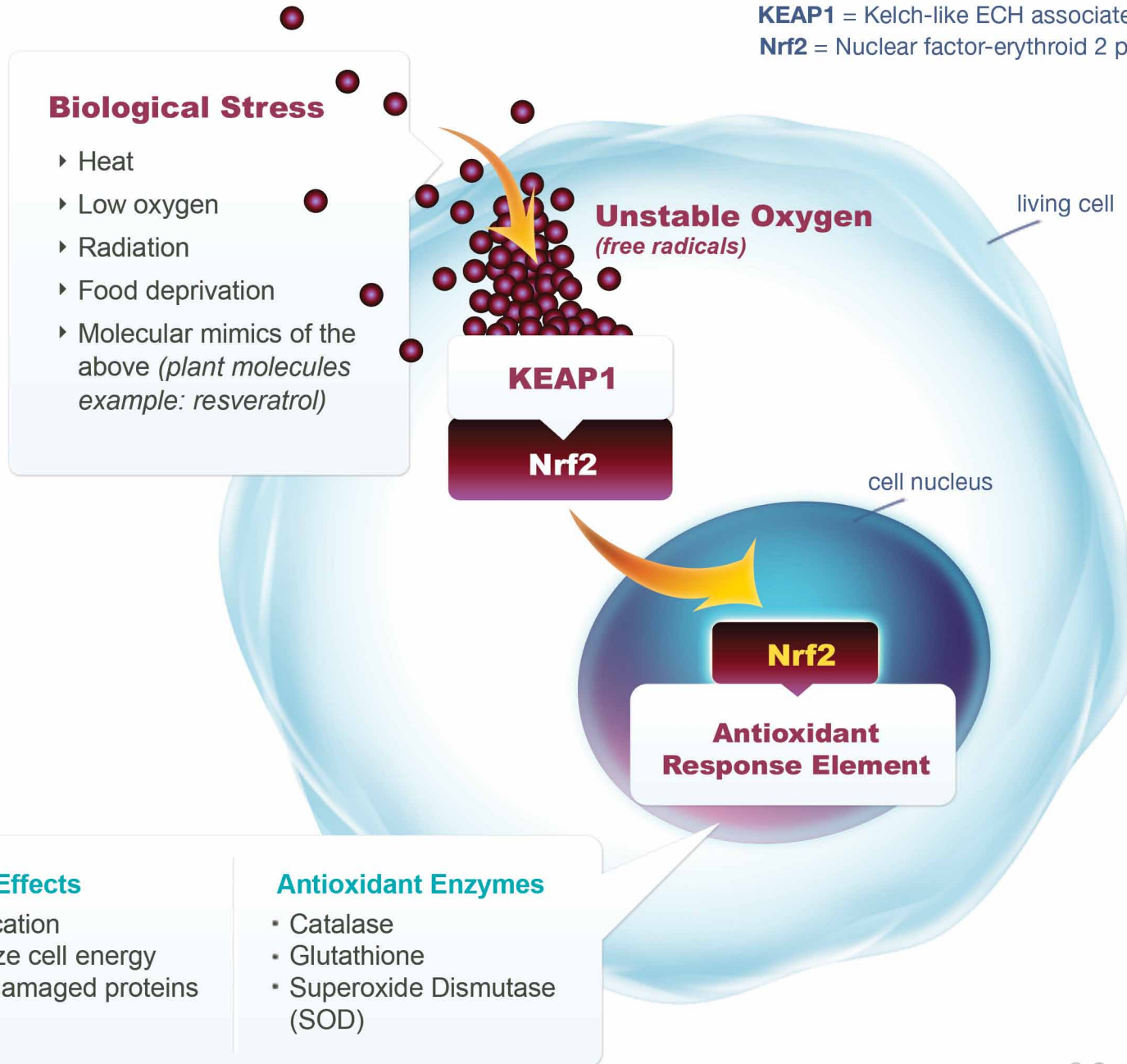
[Nrf2 activates powerful internally-produced enzymatic antioxidants,](#) namely superoxide dismutase (SOD), catalase, glutathione, and heme oxygenase. Transient gases produced in the circulatory system, namely [hydrogen sulfide and nitric oxide are also recognized hormetic triggers.](#)

[Other biological pathways that trigger hormesis](#) are also described involving the sirtuin/FOXO gene pathway and the NF-kappaB pathway.

This all may sound a bit technical but this simply means that modern biologists have even identified the chief mechanism which activates hormesis. Hormesis is not some spooky unknown biological phenomenon.

Activation Of Cellular Survival Mechanisms Via Nrf2

KEAP1 = Kelch-like ECH associated protein 1
Nrf2 = Nuclear factor-erythroid 2 p45-related factor 2



Hormesis = preconditioning

Another way of describing hormesis is [pre-conditioning, that is, turning on defenses in the body prior to an adverse event such as a heart attack or a stroke](#). It has been known for some time now that if a person experiences a mild circulatory blockage in an artery that supplies the heart with oxygenated blood and then experiences a later full-blown blockage of that artery (a heart attack), the damage to that area of the heart will be minimized because the heart turned on its defenses prior to the event.

[Felix Meerson was the first to describe cardioprotection](#) where the animal or human heart increases protective mechanisms if exposed to brief periods of low oxygen (hypoxia) prior to a full-blown blockage of blood circulation (a heart attack) in a coronary artery that supplies the heart with oxygenated blood.

It has been known for some time now that upon blockage of oxygenated blood to heart muscle (a heart attack) that the heart responds by producing strong antioxidants internally, namely heme oxygenase, adenosine and nitric oxide. Resveratrol, a red wine molecule, does this prior to a heart attack and therefore “*cardio-protects*.” This is described as the best form of prevention for the heart.

Antioxidant theory of aging and disease

A reason why molecules extracted from plants have produced perplexing results is that while they are often widely known as antioxidants they may initially provoke oxidation that triggers hormesis. This runs counter to what Denham Harman, the father of the antioxidant theory of aging proposed, which was a simple straightforward explanation that aging and its accompanying chronic diseases are a consequence of oxidation and are countered by antioxidants. Dietary antioxidants that initially promote an increase in destructive reactive oxygen species known as free radicals within the mitochondria or cellular power plants may actually extend life by switching on internal defenses.

There are a [number of molecules extracted from plants, called phytochemicals, which exhibit a hormetic effect](#). The most studied are curcumin from turmeric spice, resveratrol from red wine grapes, catechins from green tea and sulforaphane from broccoli.

There are [more than 60 molecules that induce the Nrf2 network of antioxidants](#), most of them found in the daily diet. Although known as typical antioxidants, researcher Marc Birringer says a closer look reveals that these molecules initially induce unstable forms of oxygen “*and thereby trigger an adaptive stress response and hormesis*.” This leads

dants, particularly among healthy individuals, may be counterproductive.

Pharmaceutical researchers now give nod to the idea of xenohormesis, saying “xenohormetic plant compounds can, when ingested, improve longevity and fitness by activating the animal’s cellular stress response and can be applied in drug discovery, drug production, and nutritional enhancement of diet.”

Hormesis has caught the attention of Big Pharma. Pharmaceutical companies now want to profiteer off of hormesis.

Resveratrol and hormesis

Resveratrol (rez-vair-ah-troll), known as a red wine molecule, is the best studied molecule known to induce hormesis and the only such small molecule where some dosage data is available.

Researchers say “many effects induced by resveratrol are dependent on dose and that opposite effects occur at low and high doses, being indicative of a hormetic dose response.”

Then disappointment came in 2008 when researchers reported that resveratrol did not extend lifespan in laboratory mice on a normal calorie diet. Yet these same researchers

were also talking about resveratrol as a xenohormesis agent (plant-based hormetic agent).

It is as if researchers intentionally over-dosed the lab animals to produce a pro-oxidant rather than antioxidant effect. Resveratrol is an antioxidant at low dose and pro-oxidant at high dose, exhibiting a toxic but cancer killing/germ killing effect. The demonstration of the pro-oxidant effect of resveratrol in lab dishes may not be relevant under physiological conditions where other antioxidants exist to counter any pro-oxidant action.

However, some plant-based antioxidants may, when provided in high-dose concentration, induce destructive oxidation that is capable of killing cancer cells. However, there may be trade offs in that the favorable generation of free radicals to kill cancer cells produced by high-dose resveratrol may also result in a much greater concentration of resveratrol in the kidneys where it is rapidly shuttled for excretion, potentially resulting in kidney failure. While resveratrol has generally been demonstrated to protect the kidneys in animal experiments, mega-dose resveratrol (5000 mg) caused rapid kidney failure among patients with bone marrow cancer (multiple myeloma) that resulted in immediate cessation of the study.

Whether mega-dose concentration of resveratrol has a future in cancer therapy is unknown at the present time. However, there may be a way to use high-dose resveratrol

to cause cancer cells to die off without toxic cell killing action (see below).

Among healthy individuals it appears a [lower dose more favorably mimics the desirable effects of a calorie restricted diet.](#)

Resveratrol, a grape skin and red wine-derived polyphenolic phytoalexin, exhibits hormetic action delivering numerous health benefits at lower doses while being detrimental at higher doses. Some [researchers recognize that human clinical trials need to be based on the clear understanding of hormetic health benefits of resveratrol.](#)

The most exacting research involving resveratrol has been conducted in the animal lab by Dipak Das and colleagues at the University of Connecticut. Higher than dietary doses, but lower than mega-doses, produce a protective effect in the rodent heart. Low doses, equivalent to 175 to 350 mg for a 160-pound human, reduced the size (area of scarring) of a heart attack whereas [a dose ten-times that \(1750 mg\) increases the area of heart muscle damaged by an intentionally induced heart attack.](#)

Of considerable interest is a unique commercial brand of resveratrol (Longevinex®) that protects the heart at an even lower dose (100 mg resveratrol) and continues to protect the heart even at high doses that typically kills 100% of hearts tested with plain resveratrol. In other words, there is

no toxicity at very high dose. [This is the first time in biology an L-shaped toxicity curve has been exhibited.](#) The same results were produced in long and short-term studies on two different species of animals.

Outside of resveratrol there is little instruction as to dosage required to product hormesis with other molecules. However, red wine is a concentrated source of polyphenolic antioxidants via grape fermentation which can serve as a model for dosing. There are many antioxidant molecules in wine which can trigger the Nrf2-controlled survival response (resveratrol, quercetin, catechin, ferulic acid, gallic acid, malvidin, kaempferol, others).

The [optimal beneficial effect of red wine is produced within a dosage range of 3-5 five-ounce glasses.](#) Aged [red wine provides around 60 milligrams of antioxidant molecules per glass, or 180-300 milligrams total in 3-5 glasses.](#) This appears to be a safe and potentially effective range for aggregate dietary and dietary supplement intake of plant molecules that trigger hormesis in healthy individuals.

While there are numerous hormetic molecules in the human diet it is unlikely that most people will consume enough of them to produce a hormetic effect as they are generally provided in microgram (1/1000th of a milligram) doses. It is in fermented products such as wine from red grapes or hot water extracts in teas that milligram-strength doses are achieved and unusual health benefits are noted. The most

reliable way to achieve hormesis on a regular basis is the wise selection of a properly-dosed dietary supplement designed and tested to produce hormesis.

Homeopathy

A naïve and mistaken thought is that evidence for hormesis validates homeopathy. While some aspects of hormesis apply to homeopathy, [they should not be confused](#). Basically homeopathy asserts that dilutions of a molecule exert a biological effect while hormesis is confirmed with dose-response curves. [There are five cardinal differences between homeopathy and hormesis](#):

- (1) Hormesis is a universal phenomenon, while homeopathy is highly specific;
- (2) Hormesis uses only measurable quantities of compounds, as opposed to homeopathy, where medicines are employed at dilutions far beyond the measurable range;
- (3) Preparation of hormetic solutions follows standard laboratory procedure, while homeopathy requires a sequential series of dilutions, each followed by vigorous shaking (called ‘*succussion*’);
- (4) The effects of hormesis are moderate and temporary, while homeopathy claims curative and permanent responses and

- (5) Hormesis is a lab phenomenon observed primarily in healthy organisms, whereas homeopathy is a mode of treatment administered primarily to ailing individuals.

Transhumanism

Strangely, transhumanists have not widely embraced hormesis.

Transhumanism is a loosely defined effort to understand opportunities to advance the human organism via technology to create super-intelligent, disease-resistant, long-living humans, or so-called “*posthumans*” with vastly greater capacities than present human beings.

As [Nick Bostrom explains](#), transhumanists believe humanity is “*not at the end of evolution.*” Rather than searching for God as a way out of the human dilemma of suffering and death, all mortality would be seen as premature by transhumanists that could be delayed indefinitely by technological advances.

Transhumanism is not elitist, not driven to create a small group that rises above the human condition, but rather values the idea that everybody should have opportunity to become posthuman. As such, any technology that accomplishes this would have to be an economical cure given the estimated high cost of creating 7 billion posthumans.

Transhumanists appear to be more interested in the pursuit than the attainment of their goal. Transhumanists are searching for a technological breakthrough rather than an existing natural phenomenon like hormesis. Maybe standing in a deep mine shaft to soak up radium is just not the type of technology transhumanists envision.

Final comments

The take home lesson here is not to over-do consumption of dietary or supplemental antioxidants.

Modern humans won't be the first to benefit from hormesis. Those who practice fasting or regularly take baths in hot saunas or radium springs would have already put hormesis into practice. Looking back historically, Moses may have activated hormetic triggers by fasting and climbing a mountain where there was less oxygen. Jesus not only fasted and climbed mountains but drank unfiltered wine, a molecular activator of hormesis.

Whether humanity makes a course correction to embrace the powerful health and longevity properties of hormesis is to be determined. It has been over 50 years since hormesis was first described in scientific journals. In this modern world there may be a need to commercialize hormesis to build awareness and allow insurance plans to pay for associated costs of delivery. The calorie restriction society with its small membership is the only known group that advocates a particular hormetic activator.

The biologist Felix Meerson once advocated use of hypobaric (low-oxygen) chambers to treat aging and disease as an alternative to drugs. It is not anticipated that the American Medical Association will embrace hormesis anytime soon. Whether individuals learn about hormesis and choose to adopt hormesis as a self-guided strategy to achieve health and longevity is also unknown.

There are doctors who practice psychiatry, and doctors who practice internal medicine, and geriatric physicians who take care of the aged, but we have no category for doctors who practice hormesis. There is the *International Dose Response Society* that talks about hormesis from a scientific standpoint. Maybe if hormesis can be translated into insurance billing codes then it will gain credence within the institution of modern medicine and be put into practice. For now, hormesis is a self-guided pursuit.

In an informal survey, this author has inquired whether people would want to know about a health force such as hormesis that would heighten measurable markers of health and longevity in an incomparable way. The response has been mixed. Most people who are financially challenged felt the idea of hormesis is of little interest to them because their primary focus is on meeting everyday needs. Others who already pursue healthy longevity through various means expressed more interest in learning about hormesis.

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