

OXIDATIVE STRESS COUNTERMEASURES:
FROM THE SPACE PROGRAM TO YOUR MEDICINE CABINET

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Since 2005 when NASA executed a Space Act Agreement with us, AmeriSciences has been intrinsically involved in the research, development, and testing of the viability of nutritional supplements to be incorporated as part of the daily nutritional routine of astronauts. Throughout the past six years, however, mounting evidence has forced a shift in focus from mere ancillary “supplements” to the astronaut diet into functional countermeasures to the many physiological factors that affect the human body during space travel. Today, AmeriSciences’ partnership with NASA has produced a wealth of scientific data, with potentially ground-breaking applications.

Indeed, while many people associate the challenges of space travel with the engineering marvels of the Apollo and Shuttle-era spacecrafts, the reality remains that it is the human physiological and health-related challenges that present the biggest threat to spaceflight. With everything from microgravity, to decreased metabolic function, to radiation exposure, a multi-year mission to Mars and near-earth bodies poses a huge problem for astronauts and flight surgeons alike. Currently, the potential for oxidative stress-related health conditions is one of the principal concerns of the medical operations board at NASA. The causes for such oxidative stress and the health conditions that it can lead to (cataracts, cancer, cognitive impairment, etc) are many, but it is known that the primary potential source comes in the form of ionizing radiation. Without the protection afforded by the Earth’s geo-magnetosphere, spacecraft are exposed to the grave dangers of solar particle events, coronal mass ejections, deep-space gamma rays, and other forms of radiation which may lead to radiation sickness and death.

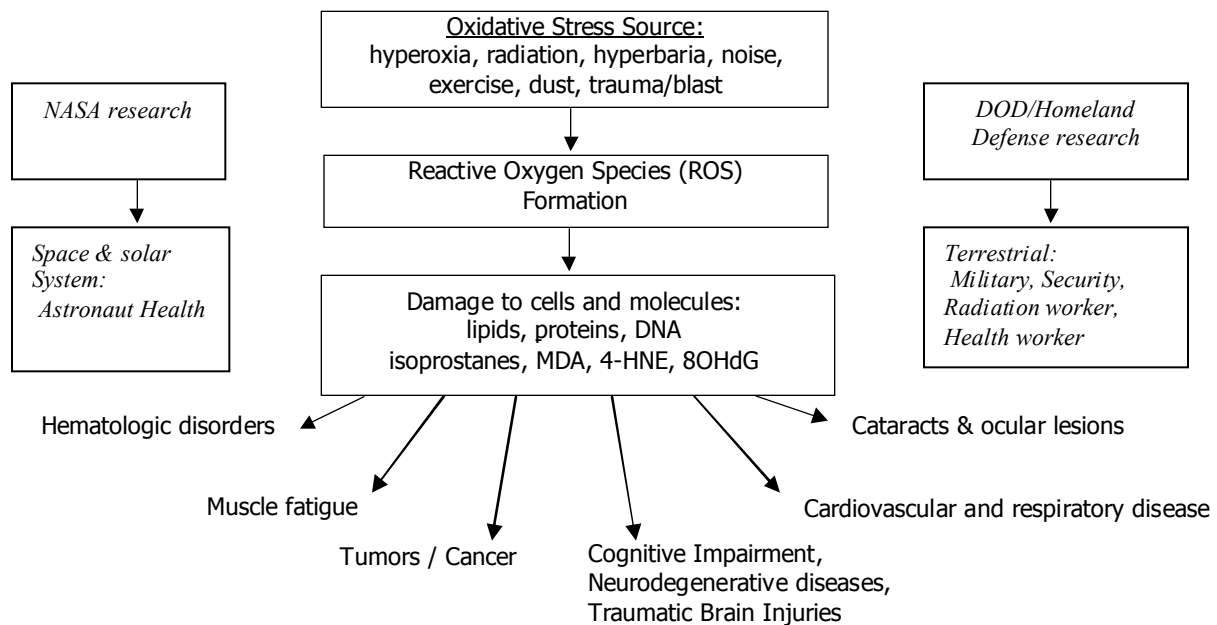


Figure 1- Sources of oxidative stress and physiological consequences of the exposure; synergistic needs and pathways for research amongst governmental agencies and scientific communities.

Studies commissioned by the Johnson Space Center and conducted at NASA sites and academic institutions such as the University of Pittsburgh's Department of Radiation Oncology, have demonstrated the chemopreventative effects of the natural antioxidant cocktail co-developed by AmeriSciences.

An early study assessing the radioprotective effects of this proposed formulation (called the "NASA Diet") along with other potential countermeasures found our formula to be significantly more effective at preventing death upon exposure to lethal levels of radiation (LD_{100/15} radiation). There were no adverse health or weight effects observed in the supplemented NASA diet animal group.

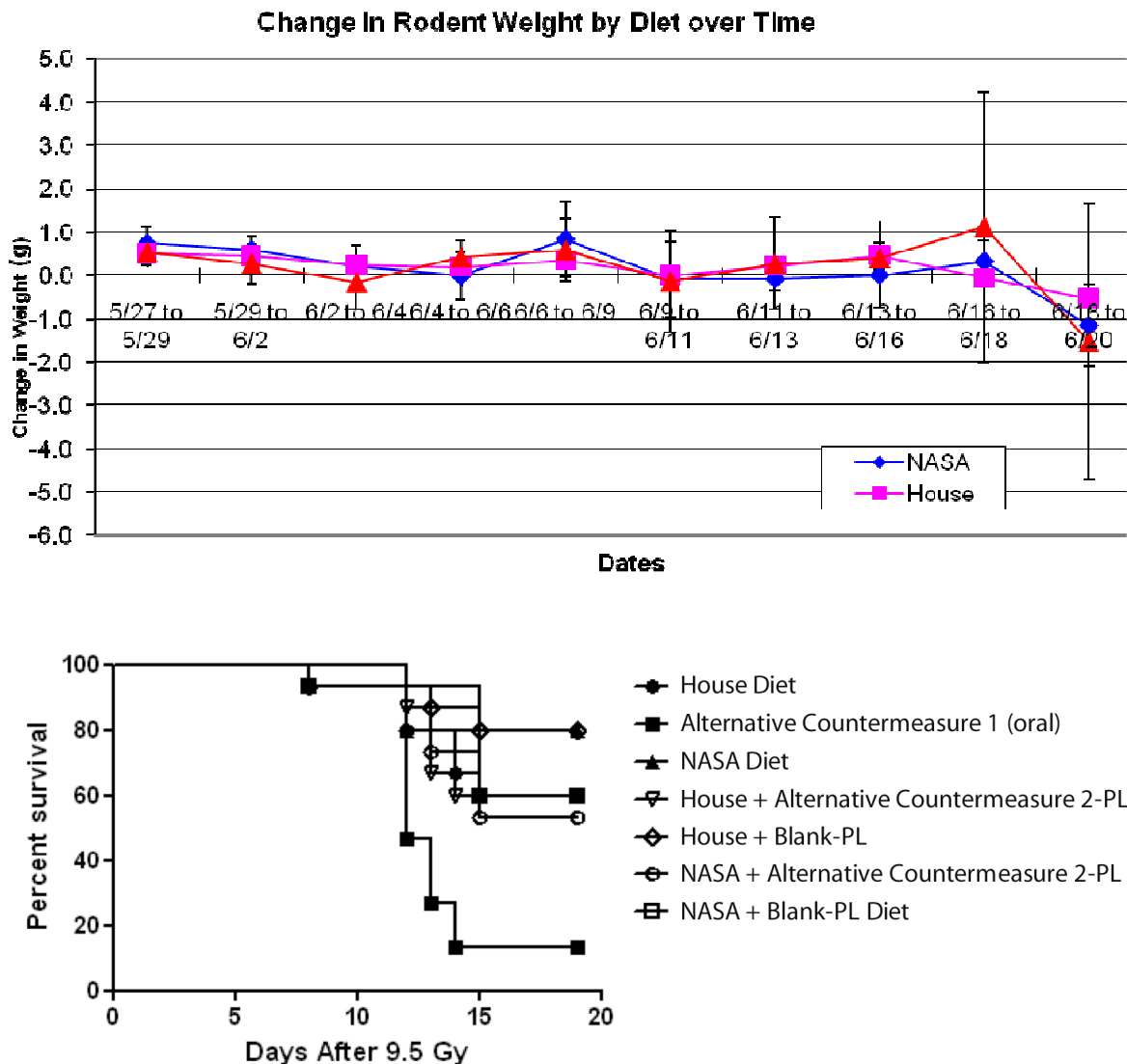


Figure 2- A) Rodent weight tracked over time for 3 diets, with no observed difference between house and supplemented animal weights; B) Rodent survival after 9500 mGy gamma ray exposure, with 80% of rodents surviving 20 days that received the proposed NASA diet supplement, vs. <20% survival for alternative diet

A more recent follow-up study at the same institution further demonstrated the viability of this antioxidant formulation to improve long-term survival, and ameliorate the late effects of radiation. One of the predominant driving forces behind the development of this multi-antioxidant approach has been the need for safety, and a proven track-record of tolerability. It was postulated that formulating lower levels of each of the most effective chemoprotection molecules would allow for a broad range of cellular protection and bioavailability without the toxicity associated with high-dose single agents, or alternative pharmaceutical approaches.

The results of the study were published by a major peer-reviewed scientific journal (*Radiation Research*, published by the Radiation Research Society – a leading institution in the US). This long-term survival study followed groups of female mice after receiving lethal doses of ionizing radiation (9500 mGy) and quantified their healthy survival. The groups supplemented with our “Antioxidant Diet” (same as “NASA Diet” above) had a very significant improvement in long-term conditional survival, with around 80% healthy living specimens at 250 days post-radiation, vs. 30% for the control group.

B

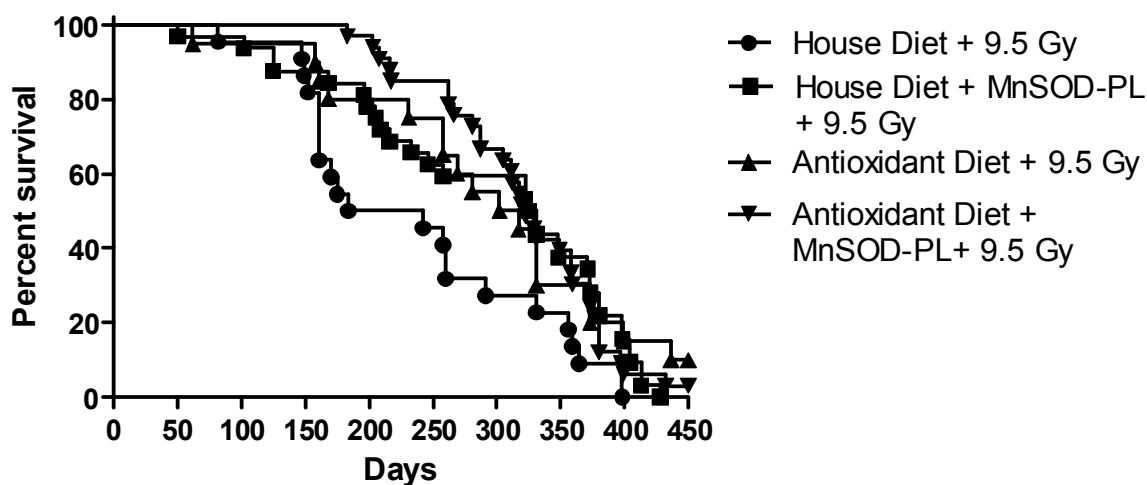


Figure 3: Groups of 40 C57BL/6HNSd female mice per group were divided untreated or were treated with MnSOD-PL (100 μ l/100 μ g plasmid) 24 hours prior to irradiation. All designated for antioxidant diet were fed the antioxidant-chemopreventive diet starting seven days prior to total body irradiation. Mice received 9.5 Gy total body irradiation, and then were followed for survival and maintained on each representative diet. Panel B shows conditional survival.

This study further validates the relevance of the developed AmeriSciences/NASA formulation, and its potential impact in human life. Moreover, it has led to a flurry of interest in the scientific and news media communities; particularly in light of recent events that directly link concerns about health and radiation exposure: for instance, the nuclear disaster in Fukushima, Japan, and a May 31st announcement by the World Health Organization that radiation from cellular telephone usage can possibly cause cancer. AmeriSciences, NASA, and their contributors have been the subject of a number of interviews and

features in various media outlets nationwide as a result of these groundbreaking discoveries and the above-referenced events.

Currently, a manuscript detailing a comprehensive review of the entire countermeasure research effort by NASA and its Russian counterpart, spanning areas ranging from nutrition to vaccines, is being submitted for publication. Below is an excerpt of the abstract:

Space Radiation Hazards and Strategies for Astronaut/Cosmonaut Protection

Aims: *To discuss the sources of oxidative stress and define the exposure environment of astronauts and cosmonauts working in space and on future exploration-class missions, and review the development of countermeasures for oxidative stress and radiation exposure for workers in extreme environments.*

Methods: *Multiple placebo-controlled, randomized prospective studies have been conducted which have studied the effect of various oral, parenteral and combination countermeasures on the biological effects and survival of acute radiation exposure.*

Results/Discussion: *Employing oral chemoprevention formulas, parenterally administered MnSOD-plasmid liposomes, and hyperimmune serum and vaccines directed on radiation-induced toxins, have resulted in reduced lipid peroxidation and DNA damage, as well as increased survival in cell cultures and whole animals receiving acute high-dose radiation exposures. Each of these strategies, alone and in combination, deserve further investigation in the pursuit of effective countermeasures and treatment for occupational exposures which induce oxidative damage.*

This paper makes it clear that the stated *oral chemoprevention formula* (elsewhere referred to as “NASA Diet,” “AmeriSciences Diet,” or “AS/NASA Diet”) is the alternative of choice for addressing two of the three main areas of radiation concern: late effects reduction to promote a normal life after exposure, and oxidative stress modulation / prevention (caused by radiation and other oxidative factors). The third area of concern (e.g. acute effects mitigation) can be best addressed by a parenteral agent, but its effects can be augmented by this formula.

The significance of these data cannot be overemphasized. While our primary focus is clearly radiation exposure, several other studies not cited here have been conducted to demonstrate the ability of these nutritional countermeasures to serve purposes beyond those originally intended, including exercise; hyperoxic and hyperbaric conditions (recreational divers, airplane pilots, hospitalized patients, COPD sufferers, etc); dust inhalation (coal miners), traumatic brain injuries (football players, soldiers, car accidents); and many others. Oxidative damage produces downstream effects in multiple types of tissues, and since the sources are so widespread, research on oxidative damage and protection overlaps several governmental agencies and scientific groups, as can be seen in Figure 1 above. Countermeasures for space radiation protection could also be applied for nuclear power plant worker as well as civil populations near such sites and in cases of radio-terrorism, athletes, emphysema patients, car accident victims, football/rugby/hockey players, frequent flyers, industrial and construction workers, healthcare/radiology workers, sun-tanning salons, etc.

Lastly, taking into account the viability of all of the currently studied countermeasures (oral antioxidant cocktail, parenteral pharmacotherapy, vaccine), it is proposed that the broader population – as well as the



astronaut and cosmonaut corps – will express preference for the oral supplement co-developed by AmeriSciences, rather than the injectable or pharmaceutical alternatives, given the convenience and dosage advantages, leading to higher compliance and user satisfaction levels.

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Other unpublished works.