A PERSPECTIVE ON IONIZING RADIATION EXPOSURE AFTER THE JAPANESE WAKE-UP CALL – PART VI – PROTECTION FROM RADIOACTIVITY – ANTIOXIDANTS

INTRODUCTION

In the last installment of this series I began a discussion on the use of supplemental antioxidants as protective agents against the damaging effects of ionizing radiation, focusing on melatonin. Given that we tend not to think of melatonin as an antioxidant that counteracts the effects of ionizing radiation, I hope you are like me in regarding this news as a pleasant departure from the usual gloom and doom reports we tend to see in the media when the issue of radiation exposure is considered. Even more fortunate, though, is the fact that, as you are about to see, melatonin is not the only radioprotective antioxidant that has been reported upon in the medical literature. In the review that follows, published papers have indeed pointed out several other antioxidants that appear to have radioprotective properties.

While the bulk of what I am going to present comes from papers that are reviews of the literature, I would like to begin with two small, somewhat obscure studies that I feel deserve our attention. Why? Most of the research I will be discussing is either animal research or research performed on patients undergoing radiation therapy. In contrast, the studies I am about to review considered individuals actually involved in the only other major nuclear power plant disaster before Fukushima: Chernobyl.

USE OF VITAMIN E AND LIPIOIC ACID WITH CHILDREN LIVING IN AN AREA CONTAMINATED BY THE CHERNOBYL DISASTER

In the study “Antioxidant therapy in children affected by irradiation from the Chernobyl nuclear accident” by Korkina et al (1), the authors begin their paper by pointing out that vitamins, because of their antioxidant properties, have treatment potential for individuals suffering from radiation exposure:

“Natural non-toxic vitamins that possess antioxidant and chelating properties offer excellent possibilities for treatment of diseases that involve free radical events in their pathogenesis.”

The experiment conducted by Korkina et al (1) involved use of two of these nutrients — vitamin E and α-lipoic acid:

“This paper reports the results of administration during 28 days of two antioxidants, vitamin E and α-lipoic acid, separately and together to children living in an area contaminated with 15-40 Ci/km². The children were healthy but all showed an elevated level of spontaneous chemiluminescence (CL) in their leukocytes which was interpreted as an indication of enhanced oxygen radical activity.”

The specifics of the experiment were as follows:

“56 children, age 11.4±21 years (22 males, 34 females), who were invited to a holiday-house near Moscow, were divided randomly into four groups and given the following treatments with the informed consent of their parents:

Group A: 16 children given 400 mg α-lipoic acid daily;
Group B: 14 children given 400 mg α-lipoic acid daily + 200 mg RRR-α-tocopherol daily;
Group C: 14 children given 200 mg RRR-α-tocopherol daily;
Group D: 12 children given no treatment.”

(200 mg of α-tocopherol is roughly equal to 200 IU.)

As was mentioned above, other than the abnormal CL findings, the children appeared to be in good physical health:
“The children were without measurable biochemical or haematological abnormalities and were examined by paediatricians and deemed to be normal.”

What were the findings of this study? The authors point out:

“The initial spontaneous CL in leucocytes of the children was elevated to about double the level in normal children, and \(\alpha\)-lipoic acid and the combination of \(\alpha\)-lipoic acid and \(\alpha\)-tocopherol lowered this level to near to or below, the ‘normal’ level; \(\alpha\)-tocopherol alone was without effect. Erythrocyte GSH levels were not raised significantly in the irradiated children but \(\alpha\)-lipoic acid caused a fall in the level to about half its original value. In combination with \(\alpha\)-tocopherol this effect was not found. Urinary excretion of radioactive isotopes was significantly lowered by \(\alpha\)-lipoic acid and the presence of \(\alpha\)-tocopherol did not enhance this effect suggesting that the effect of \(\alpha\)-lipoic acid was in this instance to act as a chelating agent.”

**USE OF BETA CAROTENE WITH CHILDREN LIVING IN AN AREA CONTAMINATED BY THE CHERNOBYL DISASTER**

The next study I would like to discuss is “Effect of natural beta-carotene supplementation in children exposed to radiation from the Chernobyl accident” by Ben-Amotz et al (2). This study involved 709 children (324 boys and 385 girls) who had been exposed to radiation for the Chernobyl accident but had moved to Israel between 1990 and 1994. They were divided into three groups based on how far they lived from the reactor and the level of radiation exposure (No radiation, <5Ci/m², and 5 Ci/m²). Blood serum analyses of the children demonstrated increased levels of conjugated dienes, “…indicating increased levels of oxidation of in vivo blood lipids in children from the contaminated areas.” Levels tended to be higher in girls than in boys. The following treatment protocol was instituted:

“…57 boys and 42 girls were given a basal diet with a diurnal supplementation of 40 mg natural 9-cis and all-trans equal isomer mixture beta-carotene in a capulated powder from of the alga Dunaliella bardawil, for a period of 3 months. Blood serum analyses were regularly conducted before supplementation to determine the baseline effect of radiation exposure to the children, after 1 and 3 months of natural beta-carotene supplementation.”

The authors noted the following results from this experiment:

“After supplementation, the levels of the oxidized conjugated dienes decreased in the children’s sera without any significant changes in the level of total carotenoids, retinol or alpha-tocopherol. Other common blood biochemicals were within the normal range for all tests and no statistical differences before or after supplementation of beta-carotene were noted. High pressure liquid chromatography (HPLC) analyses for carotenoids in the blood detected mainly oxycarotenoids, and to a lesser extent, all-trans beta-carotene, alpha-carotene, but not 9-cis beta-carotene.”

Based on the above findings, the authors concluded the following:

“The results suggest that irradiation increases the susceptibility of lipids to oxidation in the Chernobyl children and that natural beta-carotene may act as an in vivo lipophilic antioxidant or radioprotector.”

While I realize that the small scope of these studies suggest that we extrapolate to the population at large with caution, I feel that they are a powerful demonstration that clinical nutrition, beyond the use of potassium iodide, can play a vital role in helping us deal with the aftermath of any future Fukushima/Chernobyl-like disasters.

**MORE EVIDENCE CONCERNING THE RADIOPROTECTIVE EFFECTS OF ANTIOXIDANTS**

The next paper I would like to discuss is a review paper by Prasad entitled “Rationale for using multiple antioxidants in protecting humans against low doses of ionizing radiation” (3). The first quote I would like to present from this paper reinforces the statements I have previously made about the limits of potassium iodide in protecting from radiation-induced sickness:

“…potassium iodide remains a valuable strategy for protecting the thyroid gland against damage produced by radioactive iodine. However, this agent does not protect any other radiosensitive organ against \(\gamma\)-radiation that is produced by radioactive iodine. In addition, potassium iodide does not protect against damage produced by other radioactive isotopes or...”
other radiation sources such as X-irradiation or γ-irradiation. Therefore, additional non-toxic agents must be identified to protect humans against radiation damage produced by sources other than radioactive iodine.”

Fortunately, according to Prasad (3), dietary antioxidants can fill this void:

“Based on published data on antioxidants and radiation protection, it is possible to develop a non-toxic, cost-effective mixture of antioxidants (dietary and glutathione-elevating agents) that can provide biological protection against radiation damage in humans.”

Next, Prasad (4) presents an overview of animal research on antioxidants as radioprotective agents:

“Alpha-lipoic acid, a glutathione-elevating agent, increases LD_{50} in mice with a dose reduction factor (DRF) of 1.26. Vitamin E, vitamin C and β-carotene protected rodents against the acute effects of irradiation. Vitamin A and β-carotene protected normal tissue during radiation therapy of cancer in an animal model. A combination of vitamin A, C and E protected against radiation-induced myelosuppression during radiation therapy of cancer in an animal model. It has been reported that L-selenomethionine and several different types of antioxidants (vitamin C, vitamin E, glutathione, N-acetylcysteine (NAC), lipoic acid, and co-enzyme Q10 and soy bean-derived Bowman-Birk inhibitor) protected human cells in culture and rats in vivo against oxidative stress produced by photons, protons and 1 GeV iron ions.”

The next quote I would like to feature highlights a practical approach to supplementing individuals who are undergoing radiation-based diagnostic procedures or might be at risk for higher levels of exposure to background radiation:

“It is suggested that patients receiving diagnostic radiation doses take orally an appropriately prepared multiple antioxidant pill once 30 to 60 min before the radiation procedure. Radiation workers are advised to keep the body level of antioxidants high at all times by taking the appropriate multiple vitamins with antioxidants, B-vitamins and appropriate minerals, but no iron, copper or manganese. They may take a booster dose antioxidant pill 30 min to 60 min before exposure when higher radiation doses are anticipated. Frequent-flyers may also follow the same dose and dose schedule as radiation workers. The proposed strategy of increasing antioxidant levels in the body can also be implemented in populations living in regions with high background radiation that show increased levels of intermediate risk markers such as increased chromosomal damage or evidence of increased oxidative damage such as lipid peroxidation.”

Of course, all of the above would be used in addition to potassium iodide with a nuclear accident:

“The proposed antioxidant strategy, in addition to potassium iodide, should be adopted in the event of nuclear accident or explosion of a ‘dirty bomb’.”

Prasad (4) concludes his paper by pointing out that adding antioxidant supplementation to other accepted approaches to radiation protection has the potential for benefit no matter what the level of radiation exposure may be:

“In summary, following the physical principles of radiation protection and the guidelines of as low as reasonably achievable combined with the biological protection provided by multiple antioxidants, may further reduce the health risks of low doses of radiation no matter how small that risk might be.”

Before continuing, I would like to offer some “big picture” thoughts on the significance of the information provided by Prasad (4). Most importantly, Prasad (4) points out that radioprotection does not necessarily need to involve heroic, sometimes risky, limited impact preventive measures such as ingestion of large doses of potassium iodide. What do I mean by limited impact? As I hope I have made clear, potassium iodide can only protect the thyroid gland from damaging effects of I-131. However, as I hope I also made clear, health risks from radiation involve other isotopes and present risks to many other organ systems besides the thyroid. In contrast, it appears that antioxidant supplementation is much more versatile in terms of radioprotection and far less risky in terms of adverse impacts related to excessive intake. Finally, I feel we need to educate the public that, during the days immediately following the Fukushima disaster when fear and panic was driving people to obtain any potassium iodide that was available for radioprotective purposes, effective radioprotection was occurring already each time
they ingested their daily multivitamin/mineral supplement.

**MORE ON RADIOPROTECTION FROM ANTIOXIDANTS FOUND IN NATURAL SUBSTANCES**

The next paper I would like to review not only considers antioxidant-based radioprotection from micronutrients but from many other natural substances in addition. The first quote I would like to feature from “Some novel approaches for radioprotection and the beneficial effect of natural products” by Maurya et al (5) points out that radioprotective mechanisms involve more than just quenching or suppressing the formation of free radicals:

“The radioprotectors can elicit their action by various mechanisms such as: (1) suppressing the formation of free radicals, (2) detoxifying the radiation induced reactive species, (3) inducing the cellular radioprotectors such as superoxide dismutase (SOD), glutathione, prostaglandins and interleukin-1, (4) enhancing the DNA repair pathways, and (5) delaying cell division and inducing hypoxia in the tissues.”

Because radioprotection can occur in so many different ways, there are many natural substances that can fulfill these various roles. The authors state:

“Many natural antioxidants, whether consumed before or after radiation exposure, are able to confer some level of radioprotection. In addition to achieving beneficial effects from established antioxidants such as vitamins E and C and folic acid, some protection is conferred by several novel molecules, such as flavonoids, eipgallocatechin, and other polyphenols. Immune system was protected against radiation by the following natural compounds: polyphenols, vitamin C, glutamine and arginine, palm carotene, fatty acids, ubiquinone and hydroquinone. Similarly central nervous system was protected by the following components: aged garlic extract and polyphenols. Eye was protected against radiation by vitamin C, fruits and vegetables as well as by aged garlic extract. Radiation induced carcinogenesis can be reduced by the following components: zinc, vitamins C and E, selenite, polyphenols, thiols, fatty acids, yellow-green vegetables/fruits, curcumin, niacin and nicotinamide adenine dinucleotide.”

Next, Maurya et al discuss several different categories of substances that have radioprotective properties:

**Plant extract based radio-protectors**

(1) Citrus plants (2) Hippophae rhamnoides (Sea buckthorn) (3) Mentha piperita (Peppermint) (4) Ocimum sanctum (Tulsi or Indian holy basil) (5) Podophyllum hexandrum (Himalayan mayapple) (6) Tinospora cordifolia (Guduchi)

**Natural and semi-natural compounds of plant origin as radio-protectors**

(1) Ascorbic acid, (2) Caffeine (3) Chlorophyllin (4) Ferulic acid (5) Glutathione (6) Glycyrrhizic acid (7) Troxerutin (“A derivative of the natural flavonoid rutin extracted from Sophora japonica (Japanese pogoda tree)...” (8) Vanillin (9) Vitamin E and its derivatives (10) Alpha-tocopheryl Succinate (11) Alpha-tocopherol monoglucoside

With all the above options in mind, Maurya et al (5) state the following in the conclusion of their paper:

“From the fore-going review it can be surmised that there are several novel approaches to radioprotection. Many have potential applications. The benefits of using natural products for radioprotection are many. Some of the natural compounds are herbal extracts/preparations that could be effective in mitigating radiation injuries and several radiation related syndromes. The major advantage of using these would be their relative non-toxicity and time tested effectiveness in curing symptoms akin to the pathological situations arising from radiation exposures.”

The next paper I would like to feature, “Opportunities for nutritional amelioration of radiation-induced cellular damage” by Turner et al (6), presents information very similar to that presented in the paper just reviewed by Maurya et al (5). However, the paper does contain two unique perspectives that I would like to share with you. The first involves the value of repleting micronutrient deficiencies as a form of radioprotection:

“Deficiencies of micronutrients (including B12, folic acid, and niacin)...lead to single- and double-strand breaks in DNA and to oxidative lesions, similar to what is seen with ionizing radiation. Therefore, preventing deficiencies in micronutrients should also be protective against oxidative damage and promote repair of strand breakage that occurs in radiation damage."
Folate deficiency alone causes strand breaks in Chinese hamster ovary cells, and when those cells are exposed to $\gamma$-irradiation, the incidence of strand breaks increases.”

The second perspective I would like to feature takes the form of a chart which shows how certain natural substances may preferentially protect certain organ systems or tissues against harmful effects from radiation:

### TABLE II

<table>
<thead>
<tr>
<th>System, tissue, or disease</th>
<th>Food or nutrient</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system</td>
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<td>Vitamin C</td>
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<td>Vitamins</td>
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<td>Glutamine and arginine</td>
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<td>Palm carotene</td>
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<td></td>
<td>Fatty acids</td>
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<td></td>
<td>Restricted intake</td>
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<td></td>
<td>Ubiquinone, hydroquinone</td>
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<td>Central nervous system</td>
<td>Aged garlic extract</td>
<td>106</td>
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<tr>
<td></td>
<td>Polyphenols</td>
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<td>Protein deficiency</td>
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<td>Eye</td>
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<td></td>
<td>Fruits and vegetables</td>
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<td>Aged garlic extracts</td>
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<td>Cancer</td>
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<td>Restricted intake</td>
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<tr>
<td></td>
<td>Niacin/NAD</td>
<td>64</td>
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</tbody>
</table>

NAD, nicotinamide adenine dinucleotide.

What about selenium?

By now many of you may be wondering: Why has selenium not been mentioned in this discussion? In reply to that question I would like to feature two quotes from the paper “Protection against ionizing radiation by antioxidant nutrients and phytochemicals” by Weiss and Landauer (7). First, consider the following:

“A large number of selenium (Se) derivatives have been studied for their radioprotective effects. Se compounds are found in a variety of foods; for example; Se-methylselenocysteine is found in garlic and broccoli. Selenomethionine is a naturally occurring derivative of low toxicity found in soy, grains, legumes, and selenium-enriched yeast.”

While most of the discussion on selenium by Weiss and Landauer (7) involve animal studies, one study mentioned, in particular, was a human study of clinical relevance. Therefore, please consider the authors’ discussion of this study in the following quote:

“Supplementation with 200 $\mu$g/day of sodium selenite, during therapy (surgery and/or radiation) for squamous cell carcinoma of the head and neck, resulted in a significantly enhanced cell-mediated immune responsiveness during and after therapy.”

Before leaving the paper, though, I would like to highlight another quote that I feel contains some clinically relevant information in relation to diet, natural substances, and radioprotection:

“Gingko biloba extract and plant phenols were among the antioxidants shown by Emerit et al. to suppress clastogenic factors in the plasma of Chernobyl accident recovery workers. There was a negative association between clastogenic factor scores and frequency of consumption of fresh vegetables and fruit among children who had immigrated to Israel from regions contaminated by the Chernobyl accident. A prospective study of diet and bladder cancer incidence in a cohort of atomic-bomb survivors in Japan suggested that high consumption of green-yellow vegetables and fruit, but not green tea, were protective against bladder cancer.”

MORE INFORMATION ON THE RELATIONSHIP BETWEEN NUTRITIONAL DEFICIENCY AND RADIOPROTECTION

Most of the research I have reviewed in relation to nutrition and radioprotection considered nutrients such as potassium iodide, melatonin, and antioxidants as “nutraceuticals” where sometimes large doses of nutrients were being used in a pharmaceutical-like manner to create a radioprotective effect. In contrast, the paper I just reviewed by Turner et al (6) pointed out that micronutrient deficiency and the repletion of those deficiencies can also have a profound impact on radioprotection. In the paper “Free radicals, antioxidants, and nutrition” by Fang et al (8) macronutrient and magnesium deficiencies are discussed in relationship to radiation. First, consider the issue of protein as it relates to radiation induced by space flight:

“The net loss of body protein, in particular skeletal muscle protein, is likely a major
factor responsible for protein malnutrition and possibly deficiencies of some amino acids (e.g., glutamine, arginine, and cysteine) during space flight. Interestingly, radiation directly contributes to the increased muscle proteolysis and muscle atrophy under space flight conditions. Amino acids are building blocks for the synthesis of proteins, including antioxidant enzymes. Some amino acids (e.g., arginine, citrulline, glycine, taurine, and histidine), small peptides (e.g., GSH and carnosine), and nitrogenous metabolites (e.g., creatine and uric acid) directly scavenge oxygen free radicals.”

With the above in mind, the authors point out:

“Thus, a dietary deficiency of protein not only impairs the synthesis of antioxidant enzymes but also reduces tissue concentrations of antioxidants, thereby resulting in a compromised antioxidant status.”

Next, consider magnesium deficiency and radiation:

“The role of minerals in enzyme functions has been studied extensively in nutrition and biochemistry. For example, magnesium is a cofactor for glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase, two pentose-cycle enzymes catalyzing the production of HADPH from NADP⁺. Thus, a deficiency of dietary magnesium reduces glutathione reductase activity and results in radical-induced protein oxidation (indicated by the generation of protein carbonyls) and marked lesions in tissues (e.g., skeletal muscle, brain, and kidney).”

**SOME FINAL THOUGHTS**

Since the end of World War II the fear of nuclear radiation is probably, for very good reasons, one of the most deep-seated fears seen with most Americans. While I do not want to minimize the risks to human health inherent with any type of nuclear catastrophe, whether it is the “unthinkable” atomic bomb explosion or a nuclear power plant disaster, I would like to suggest that at least some of the fear we have comes from a sense of helplessness and lack of control. Of course, we cannot control the external circumstances that lead to these disasters. However, I hope I have demonstrated that we can have some control over the impact these disasters have from a metabolic and physiologic standpoint. In turn, it is very conceivable that, with this increased control over the metabolic impact of exposure, a significant difference can be made on quality of life when radiation exposure occurs.

Finally, as suggested in many of the studies, applicability of the information I have presented is not limited to nuclear disasters. Rather, this information can be used today with chances of great benefit for the many patients undergoing diagnostic or therapeutic radiation. Granted, in the case of therapeutic radiation, the use of the nutritional measures I have described has to be considered carefully in terms of dose and timing. Nevertheless, even in this situation, when used in a discerning manner, it appears that radioprotective natural substances can demonstrate great benefit.

In the final installment of this series, I will present a review of what are probably the most controversial papers in the realm of radiation and human health. Could it be that the predominant claim that any level of radiation exposure is too high and damaging to health is incorrect? Could the hormetic principles I have described in previous newsletters and presentations also apply to radiation in that a certain level of radiation exposure is not only lacking harmful outcomes but actually promotes health? Next time I will explore literature that maintains that the answer to these questions is in the affirmative.

**REFERENCES**