Evaluation of the combined effects of gamma radiation and high dietary iron on peripheral leukocyte distribution and function

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**Background:** NASA is concerned with the health risks to astronauts, particularly those risks related to radiation exposure. Both radiation and increased iron stores can independently increase oxidative damage, resulting in protein, lipid and DNA oxidation. Oxidative stress increases the risk of many health problems including cancer, cataracts, and heart disease. This study, a subset of a larger interdisciplinary investigation of the combined effect of iron overload on sensitivity to radiation injury, monitored immune parameters in the peripheral blood of rats subjected to gamma radiation, high dietary iron or both. Specific immune measures consisted of (A) peripheral leukocyte distribution; (B) plasma cytokine levels; (C) cytokine production profiles following whole blood stimulation of either T cells or monocytes.

**Results:** Both radiation exposure and the high iron diet resulted in an altered leukocyte distribution. Iron alone resulted in a significantly elevated WBC, which appeared to be via a lymphocytosis. While radiation did not significantly alter the total WBC, it induced a significant increase in the granulocyte percentage and a reduced CD4:CD8 T cell ratio. Iron treatment alone did not have an effect these cell subsets. Radiation treatment had a significant effect on cytokine production following T cell stimulation. Production of IFNγ, IL-10, IL-4 and TNFα were significantly elevated following radiation treatment, however for all cytokines measured the high iron diet inhibited the radiation effect. Following monocyte stimulation, radiation treatment resulted in elevated IL-4 and decreased IL-6 production, with both effects abrogated by the high iron diet. Interestingly, the high iron diet, radiation treatment, or both resulted in a significant decrease in monocyte IL-10 production. No significant differences were observed in plasma cytokine levels for either treatment.

**Conclusion:** Gamma-radiation treatment resulted in demonstrable alterations in peripheral leukocyte distribution and leukocyte cytokine production following mitogenic stimulation. The high iron diet abrogated the functional alterations but not the phenotypic alterations. The high iron diet alone resulted in an elevated WBC but with a normal subset distribution. In most cases, the high iron diet reduced mean cytokine production levels but these changes were not significant. Thus, a high iron diet appears to inhibit both constitutive immune functional responses and the elevated functional responses observed following radiation treatment.