

Combined Radiation Injury Impacts Development of Radiation Countermeasures and Biodosimetry

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Large-scale radiation exposure events in history have shown that irradiated victims are also often subjected to other trauma such as wounds, burns, hemorrhage, or infection. Preparedness for medical responses to major radiation accidents and increasing threat of nuclear warfare worldwide necessitates an understanding of the complexity of combined radiation injury (CI) and identifying drugs to treat CI. Biomarkers that remain the same changes between CI and radiation alone are inevitably critical for biodosimetry and triage. CI synergistically reduces body weight, delays wound healing, depletes blood cells, impairs organ recovery (bone marrow, GI, Brain, spleen) and worsens survival compared to irradiation only, due to amplification of the microRNA-34a pathway, NF- κ B-iNOS signaling, Cytokine elevations, C3 high productions, the AKT-MAPK cross talk, and TLR/MMP increases. At present, no FDA-approved drugs to protect, mitigate, or treat CI are available. We have reported that Gentamicin, Silvadene, WR-151337, Alxn4100TPO, Ghrelin, Ciprofloxacin, mesenchymal stem cells or bone marrow transplantation effectively mitigate CI. Because of the worsened acute hematopoietic and gastrointestinal radiation syndrome resulting from CI, diagnostic triage can be problematic. However, CI with irradiation followed by wound trauma or hemorrhage or radiation only result in similar changes in circulating Flt-3 ligand and microRNA-34a. Most importantly, data from our laboratory and others suggest that sex disparity to radiation sensitivity is present. Females are found to be more resistant to radiation than males. Additionally, other confounding factors including ages, hypertension, diabetes, high cholesterol should be addressed. However, to explore whether the sex disparity is also present to efficacy of radiation medical countermeasures for RI or CI is imminent. In summary, the effects of CI represent significant confounders in understanding the resultant organ impair and survival as well as delayed outcomes, and the development of preparation for medical response both in the assessment and medical management of injuries. (Supported by SAPO: G17070 of NIH CMCRC U19AI067773-18, AFR-B2-12812, and RAB33336. Views do not reflect the position and policies of NIH, DOD, USU, or AFRRRI. No conflict of interests.)