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Linking the Human Response to Unplanned Radiation and Treatment to the Nonhuman Primate Response to Controlled Radiation and Treatment: A New Approach to Compare Human and Animal Data

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A new project funded by the U.S.National Institute of Allergy and Infectious Diseases, Radiation Nuclear Countermeasure program has been launched to link human data from radiation accidents to animal data resulting from controlled radiation studies in nonhuman primate (NHP) models. The aim of this project is to gain more insight into similarities and disparities concerning the pathophysiology of the acute radiation syndrome (ARS). A key objective is to determine whether the developmental sequence of the early signs and symptoms of ARS runs parallel in both systems. Other issues will focus on the similar consequences of acute and delayed radiation effects. Radiation-induced multi-organ failure as described in humans will be compared with that observed in the NHP models. We have initiated a comparison of radiation exposure dose versus signs, symptoms and consequent organ injury as a function of time in both humans and NHP.
Materials& Methods: The human data derive from the Ulm SEARCH database (System for Evaluation and Archiving of Radiation Accidents based on Case Histories) which contains more than 800 case histories of radiation victims since 1945. The animal data are being provided by the NIAID-sponsored Preclinical Radiobiology lab at the University of Maryland. It is planned to build an"Interspecies Bridge". Exposed individuals and NHP will be assigned to comparable categories for clinical severity and response categories (RCs) according to the METREPOL concept, where applicable. This will be done in an adapted mode for the animal model. A second step will focus on a comparative analysis of signs and symptoms within the RCs.
Results: The method for"bridging"human and NHP data proved to be successful. The initial results of this interspecies comparison and dose shift modeling are presented.
Discussion: A validated interspecies comparison of relevant radiation dose effects and clinical data will be a sound approach to approve the use of radiation countermeasures in humans on the basis of relevant and controlled animal data.This interspecies approach should be expanded to include other animal species and models currently in use by the scientific radiation research community.

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