



Role of Damage to the Cutaneous System in Radiation-Induced Multi-Organ Failure

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Radiation damage to the skin is a key diagnostic and prognostic parameter for patients who accidentally have been exposed to radiation. The skin, moreover, is one of the key organs in radiation-induced multi-organ involvement and failure.

For systematic as well as for practical reasons, different radiation-exposure situations have to be distinguished. When discussing clinical aspects of the cutaneous radiation syndrome (CRS), these different scenarios have always to be taken into consideration. First of all, there is a need to differentiate between an acute and chronic radiation syndrome of the skin. The determinants in this case are time after radiation exposure as well as radiation quality and dose. From a biological and clinical point of view, damage to the skin organ and potentially other organs involved in the radiation field, including distant effects, is the important endpoint. Moreover, it must be differentiated between localized radiation injuries (e.g., one to several radiation ulcers) and the situation of whole or at least significant partial body exposures. These totally different situations may not only show up with different clinical courses (including varying patterns of biological indicators) but, furthermore, significant different requirements for therapeutic strategies. The existence of radiation-induced multi-organ interactions is a fact that must be faced nearly in all radiation exposure situations. The progression of these radiation-induced organ interactions, a so to say cascade-like process into a radiation-induced multi-organ failure, depends not only on the amount of damage to single organs but rather on interactions between more- and less-affected organs (and even not irradiated organs) and, thus, has a potentiating or self-augmenting effect. The crucial point of radiation response in organs and tissues is the individual capacity of these organs and organ systems to cope with radiation damage in a way other than the development of multi-organ failure.

To illustrate a model of radiation-induced multi-organ failure, the skin is an ideal candidate. A study based on the databank system SEARCH (System for Evaluation and Archiving of Radiation Accidents based on Case Histories) focused on the investigation of the timely course of radiation-induced skin reactions, the percentage of affected skin surface and the severity of affection. The percentage of affected skin surface turned out to be very important criteria for prognostic estimation of the clinical course of the acute radiation syndrome beneath the well-known categories regarding the haematopoietic system. This study underlined the importance of the CRS as a diagnostic parameter and triage pattern. It also revealed the skin as a crucial organ system for the prognosis of radiation victims, both independent of radiation-damage to other organ systems but also in a potentiating way.

The special so-called combined injury situation proved to worsen prognosis of radiation victims a long time ago. In the case of combined injuries, the important role of the skin was shown in several studies on



animal models. Radiation exposure was combined with burns and open skin wounds, which became entrance ports for bacteria and could cause septicaemia leading to increased lethality. This fact, therefore, also must be taken into consideration when discussing contingency planning for radiological emergencies.

To a great extent, the pathophysiological background of radiation-induced multi-organ failure remains unclear. The recent pathophysiological understanding considers the endothelium as one connecting factor. Exposing the organism to a significant radiation dose causes an immediate response of the capillary bed both by direct and indirect action, resulting in an increased permeability (oedema) and fragility (petechial bleeding) and resembling inflammatory reactions. Changes and interactions on the level of cytokines and other proteins also are intensively discussed. Therefore, future research on biomarkers of radiation exposure might also help to understand the pathophysiology of cellular and organ damage caused by ionizing radiation.

Due to the complexity of radiation exposure situations and the subsequent clinical pictures, one fact already is clear. Estimating radiation damage in a serious way can only be done by integrating biological and clinical data. There will be no single parameter allowing a reliable diagnosis of radiation injury or, moreover, clinical therapeutic decision-making.

This fact must be taken into account for future clinical research and, in particular, medical management of radiation-exposed patients.