

## CLINICALLY OBSERVED EFFECTS

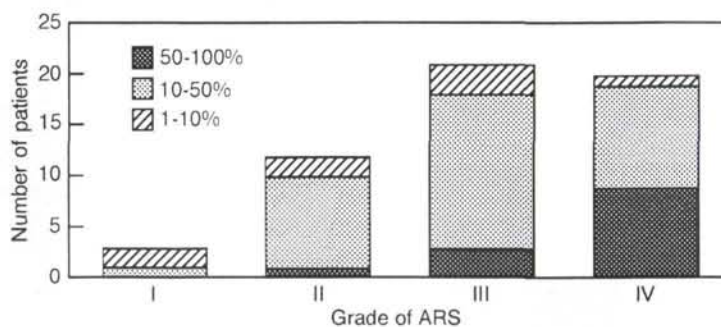
*Report by Gerard Wagemaker, Erasmus University, European Commission, who served as Rapporteur, Topical Session 1: "Clinically observed effects" and by Angelina K. Guskova, Institute of Biophysics, Moscow, Russia, who served as Session Vice-Chairwoman, and Vladimir G. Bebesko, Scientific Center of Radiation Medicine, Kiev, Ukraine; and Nina M. Griffiths, ISPN, Fontenay aux Roses, France, both members of the Session's Expert Committee.\**

When radiation doses to the tissues of a mammalian organism are large enough, there may be a partial or complete loss of function. In extreme cases, there may be complete tissue death. If the tissue is vital, it may result in death. There have been many accidents with radiation sources that have caused serious local injury, sometimes calling for the amputation of limbs.

Among the victims of the Chernobyl accident were people who were accidentally exposed to high doses of radiation. Such high-dose exposures — which acutely and severely affect blood cell production, resistance against infections, and intestinal functions — may result in severe damage to the skin. The complex of disease symptoms from such exposures is known as "acute radiation syndrome", or ARS. Its most common symptoms are initially nausea, vomiting, and diarrhea and, later on, bleeding and generalized infections with high fever, often caused by micro-organisms that are normally not harmful. If untreated, ARS is lethal, even following radiation doses which are not necessarily incompatible with survival of the human organism and are regularly used in clinical medicine to treat some forms of cancer. In an accident situation, the radiation damage is frequently even more complicated by other injury, such as thermal burns.

\*The authors are indebted to material supplied by Alexander A. Baranov, State Research Center, Institute of Biophysics, Moscow, Russia; John W. Hopewell, The Research Institute, Oxford University, United Kingdom; Ralf U. Peter, Department of Dermatology, Ludwig-Maximilians-University, Munich, Germany; and T.M. Fliedner, Department of Clinical Physiology and Occupational Medicine, University of Ulm, Germany. Research has been partly supported by Nuclear Fission Safety contracts of the Commission of the European Communities.

ARS and skin damage in Chernobyl patients



The Chernobyl accident resulted in a total number of 237 individuals who were suspected of suffering from ARS. The diagnosis was confirmed in 134. Of these, 41 had mild (grade I) ARS; all survived; one additional case is still disputed. Fifty patients had grade II ARS, of whom one died. Twenty-two patients had grade III ARS, of whom seven died. Of the 21 patients most severely affected, who suffered from grade IV ARS, all died except one. Among this group, gastrointestinal damage was the most severe problem in patients who received doses greater than 10 Gy and resulted in early and lethal changes in intestinal function. Deaths in 26 patients in the first three months after the exposure were associated with skin lesions involving over 50% of the total body surface area. In general, there appeared to be a relation between ARS and the skin area damaged, indicating that almost all severely affected patients had combined injury. (See graph.)

The Chernobyl nuclear power plant accident led to exposure with high amounts of beta irradiation (both contamination and incorporation), causing a clinical pattern of involvement which

A patient with skin lesions being examined at the Institute of Biophysics in Moscow within the framework of an EU-supported project.  
(Credit: Wagemaker/EC)



was different from the experience at Hiroshima and Nagasaki. From the onset, a striking feature was the large number of patients suffering from radiation-induced damage of the skin and mucous membranes, especially of the upper digestive and respiratory tract, due to contamination by beta and gamma-emitting isotopes, such as caesium-137, caesium-134, and strontium-90. Skin lesions and/or oropharyngeal mucositis were a major contribution to the death of patients who died as an immediate consequence of the accident.

Patients surviving ARS have all been subjected to a traumatic experience with extensive physical injury and long convalescence periods. Some will bear the marks of their trauma for the rest of their lives, both in the psychological and somatic sense, just as victims of other severe accidents have done. Although the extreme bone marrow suppression may have been resolved in a couple of months, full reconstitution of immune functions may take at least half a year and may well not normalize within years after exposure. This does not necessarily mean that these patients have a functionally impaired immune system.

In patients with severe skin injury complicated by surgery and ill-healing wounds, the long recovery period may cause chronic stress. It may also be expected that biochemical stress indices in these patients score high. In males, reproductive recovery may be very slow and in the higher dose ranges, impaired fertility may be a lasting effect. Several components of the eye are rather sensitive to radiation, and patients in particular may develop cataracts, starting years after exposure. Following high radiation doses, cardiovascular and late gastrointestinal problems may cause considerable discomfort.

After the accident's acute phase, 14 of the 237 patients have died over the last decade. Their deaths do not relate to the original severity of ARS and are, in most cases, probably not directly attributable to the radiation exposure,

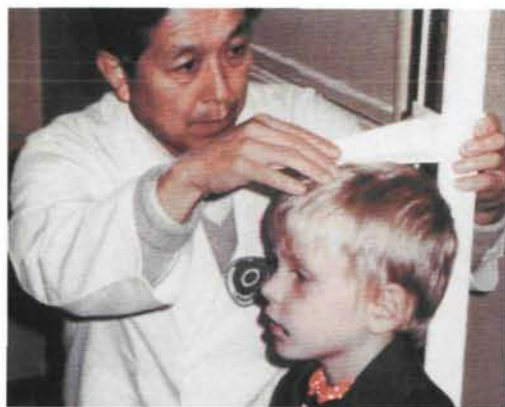
although it is difficult to exclude an impact from the accident. In fact, five of these 14 patients did not suffer from ARS in the first place and may have received only very low doses of radiation.

The remaining patients who have suffered ARS are in general in an acceptable health condition and are being monitored regularly. There is good evidence that the quality of life of the surviving patients may be amenable to improvement. At least the more severely affected patients suffer presently from multiple diseases and are in need of up-to-date treatment and secondary prevention; also their mental health might be suboptimal. Therefore, more has to be done in the future to distinguish in the encountered disease patterns those that are attributable to the radiation exposure and those that are due to confounding factors intrinsic to the population. The follow-up of these patients needs to be assured for the forthcoming two to three decades, preferably co-ordinated by a single center of high clinical and research competence.

The Chernobyl cases have taught us that much needed (and still needs) to be improved in the clinical management of ARS in accident situations generally complicated by radiation injury to the skin and injuries that are not radiation related. There is little doubt that ARS patients, and those with severe skin injury, have received the best possible treatment in line with the state of knowledge at the time in the most experienced center available.

The therapy of bone marrow transplantation recommended at the time was of little benefit for the most severely affected patients. From today's knowledge this is understandable. In any future accident, it is inconceivable that bone marrow transplantation as applied in the most severe cases of the Chernobyl accident will be used. New agents have become available, in particular a group of cytokines collectively known as hemopoietic growth factors, which have the capacity to stimulate recovery of the blood and immune system.

Bone marrow damage can in future cases best be managed by rapid administration of hemopoietic growth factors, even though the most optimal combination and dose scheduling still needs to be worked out. However, advances in the transplantation of blood stem cells and tissue typing make it very likely that transplantation will still be considered as a life-saving supportive measure, especially in cases where bone marrow damage is too severe to expect an effective response to the newer therapeutics. Also for other radiation damage, new diagnostic tools may contribute to a more accurate prognosis and more tailored treatment. □



A physician from Japan examines a child in a village near the Chernobyl plant during the 1990 International Chernobyl Project.  
(Credit: Mettler/USA)