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No. 101

Medical Management of Radiation Injuries

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MEDICAL MANAGEMENT OF RADIATION INJURIES

The Agency's Statute was approved on 23 October 1956 by the Conference on the Statute of the IAEA held at United Nations Headquarters, New York; it entered into force on 29 July 1957. The Headquarters of the Agency are situated in Vienna. Its principal objective is "to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world".

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FOREWORD

Literature on the medical management of patients involved in radiation emergencies has evolved significantly since the publication of the first IAEA medical publication on emergency preparedness and response. Issued in 1978, Safety Series No. 47, Manual on Early Medical Treatment of Possible Radiation Injury, was the first IAEA publication aimed exclusively at first aid and early medical treatment of workers involved in accidents resulting from external or internal exposure to radiation. In 1988, Safety Series No. 88, Medical Handling of Accidentally Exposed Individuals, established a set of general criteria and recommendations based on lessons learned from recent accidents to aid specialists engaged in the medical handling of overexposed persons. In 1998, Safety Reports Series No. 2, Diagnosis and Treatment of Radiation Injuries, updated the information provided on the early medical management of radiation victims, drawing special attention to localized radiation injuries, which were the most frequently observed direct health effects of ionizing radiation.

In the past two decades, developments in scientific research and diagnostic methods, and new medical techniques and new applications in dose assessment and treatment have significantly changed the means and methods of treating radiation injuries, and new scientific knowledge has been acquired from clinical and preclinical experience. The medical management of individuals (patients) involved in nuclear and radiological emergencies has progressed considerably, and the new medical approaches have incorporated lessons from experience gained from accidents occurring in such diverse settings as industry; medicine; and source control, replacement and disposal.

This Safety Report on the medical management of radiation injuries includes new information on medical preparedness and response to nuclear or radiological emergencies. It is set within the overall framework outlined in IAEA Safety Standards Series No. GSR Part 7, Preparedness and Response for a Nuclear or Radiological Emergency, which, in Requirement 12, addresses the management of the medical response in a nuclear or radiological emergency. This publication supersedes Safety Reports Series No. 2.

The publication is co-sponsored by the International Federation of Red Cross and Red Crescent Societies (IFRC) and the Pan American Health Organization (PAHO); it is endorsed by the American Society for Radiation Oncology (ASTRO), the European Association of Nuclear Medicine (EANM), the European Society for Radiotherapy and Oncology (ESTRO), the International Association of Radiopathology (IAR), the Latin American Association of Societies of Nuclear Medicine and Biology (ALASBIMN) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

The IAEA officer responsible for this publication was E.D. Herrera Reyes of the Incident and Emergency Centre.

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1. INTRODUCTION

1.1. BACKGROUND

According to IAEA Safety Standards Series No. GSR Part 7, Preparedness and Response for a Nuclear or Radiological Emergency [1], an emergency is:

> "A non-routine situation or event that necessitates prompt action, primarily to mitigate a hazard or adverse consequences for human life, health, property or the environment. This includes nuclear and radiological emergencies and conventional emergencies such as fires, releases of hazardous chemicals, storms or earthquakes. This includes situations for which prompt action is warranted to mitigate the effects of a perceived hazard."

Nuclear and radiological emergencies have provided considerable information which has increased the medical knowledge related to the diagnosis, management and treatment of individuals with radiation injuries. For the purposes of this publication, nuclear or radiological emergencies are subsumed under the term 'radiation emergencies'.

The accident at the Chernobyl Nuclear Power Plant on 26 April 1986 resulted in the hospitalization of 237 patients identified as severely overexposed persons [2]. Acute radiation syndrome (ARS) was diagnosed in 134 persons admitted to the specialized hospitals in Moscow and Kyiv. Among them, 28 died within three months of ARS associated with extensive local radiation burns combined with thermal burns [3]. ARS was not confirmed in another 103 hospitalized patients. Nineteen additional patients died in the period 1987–2004 of various causes; however, their deaths were not directly attributable to radiation exposure. Among the general population exposed to the Chernobyl radioactive fallout, however, the radiation doses were relatively low, and ARS and associated fatalities did not occur [4].

In September 1987, two scrap metal dealers removed a shielded radioactive ^{137}Cs source (50.9 TBq) from the protective housing of an abandoned teletherapy machine in Goiânia, Brazil [5]. Subsequently, the source was ruptured. As a result, many people incurred large doses of radiation by both external exposure and internal/external contamination[1]. Four people ultimately died from ARS, while 28 people developed local radiation injuries (LRIs) of different levels of severity, some very severe. In the case of one patient, amputation of the right

[1] For the purposes of this publication, the term 'contamination' will be used to denote 'radioactive contamination'.

forearm was necessary. A total of 249 cases of contamination were detected. Out of that number, 129 had suffered both internal and external contamination [6]. There was extensive contamination of homes, other buildings and surface soil in the urban area of Goiânia.

In 2000, a severe radiological accident occurred in Samut Prakarn (a suburb of Bangkok), Thailand, when scrap metal dealers removed an abandoned container with a spent ^{60}Co radiotherapy source and sold it at a scrapyard. Ten scrapyard workers were exposed to high radiation doses and developed ARS. Three of them died within three months, and six developed LRIs of different levels of severity. One of the patients was so seriously injured that all fingers of both hands had to be amputated [7].

The IAEA has published detailed reports on radiation safety, medical and emergency management aspects of about two dozen severe radiation accidents.[2]

1.2. OBJECTIVE

The objective of this publication is to provide guidelines to health care professionals in carrying out prompt diagnostic measures and medical management of individuals affected by radiation injuries. Experience has shown that the management of radiation emergencies involves a comprehensive team of health care professionals, including medical doctors, nurses, biologists, radiation protection officers, radiopathologists, and health and medical physicists.

1.3. SCOPE

This publication provides information on the medical management of radiation injuries (diagnosis, assessment, treatment), including LRIs, ARS and contamination (external and internal). It also discusses a multidisciplinary approach to medical preparedness and response to radiation emergencies. Guidance provided here, describing good practices, represents expert opinion but does not constitute recommendations made on the basis of a consensus of Member States.

[2] Accident report publications since 1987 can be downloaded from the IAEA website www.iaea.org/publications.

1.4. STRUCTURE

The structure of this publication is based on the technical, logistical and operational aspects of the medical management of radiation injuries. Section 2 summarizes the types of radiation emergency, the types and modes of accidental radiation exposure, as well as principles of their medical management, including clinical and radiological triage. The latter measures are important in establishing priorities for medical treatment and hospitalization. Section 3 describes the clinical consequences and the medical management following a local or whole body external exposure, including diagnosis, assessment, treatment, rehabilitation and medical follow-up of both ARS and LRI patients, with case studies for practical illustration. Section 4 provides information on the medical management of individuals externally and internally contaminated with radioactive materials; the Goiânia radiological accident is revisited as a case study of autopsies in bodies contaminated with radioactive material. Section 5 deals with specific aspects of combined radiation injuries. Section 6 includes information on risk communication and psychosocial aspects in radiation emergencies. Section 7 deals with all relevant information to be collected for the care of patients and subsequent dosimetric evaluations and medical follow-up, as well as for medico-legal considerations.

The two appendices include further information on important aspects of the medical management of radiation injuries: Appendix I provides information on preparedness for radiation emergencies, while Appendix II contains basic aspects of radiobiology for the general practitioner from a medical perspective.

2. GENERAL CONCEPTS OF RADIATION EMERGENCIES AND MEDICAL MANAGEMENT

2.1. TYPES OF RADIATION EMERGENCY

A nuclear or radiological emergency is defined in GSR Part 7 [1] as:

"An emergency in which there is, or is perceived to be, a hazard due to:

(a) The energy resulting from a nuclear chain reaction or from the decay of the products of a chain reaction;
(b) Radiation exposure."

The hazard involves a sealed or unsealed radioactive source and may lead to an uncontrolled release of ionizing radiation or radioactive material into the environment or to individuals. Such radioactive sources include sealed sources of radioactive isotopes such as ^{60}Co, ^{137}Cs, or ^{192}Ir irradiators, used mostly in medicine and industry, and unsealed sources used in nuclear medicine and scientific research. Less frequently, X ray equipment, linear particle accelerators and other equipment have also been involved in the uncontrolled exposure of people.

In terms of the IAEA safety requirements, assessed hazards are grouped in accordance with the five emergency preparedness categories shown in Table 1 (reproduced from GSR Part 7 [1]).

TABLE 1. EMERGENCY PREPAREDNESS CATEGORIES

Category	Description
I	Facilities, such as nuclear power plants, for which on-site events[a, b] (including those not considered in the design[c]) are postulated that could give rise to severe deterministic effects[d] off the site that would warrant precautionary urgent protective actions, urgent protective actions or early protective actions, and other response actions to achieve the goals of emergency response in accordance with international standards[e], or for which such events have occurred in similar facilities.
II	Facilities, such as some types of research reactor and nuclear reactors used to provide power for the propulsion of vessels (e.g. ships and submarines), for which on-site events[a, b] are postulated that could give rise to doses to people off the site that would warrant urgent protective actions or early protective actions and other response actions to achieve the goals of emergency response in accordance with international standards[e], or for which such events have occurred in similar facilities. Category II (as opposed to category I) does not include facilities for which on-site events (including those not considered in the design) are postulated that could give rise to severe deterministic effects off the site, or for which such events have occurred in similar facilities.
III	Facilities, such as industrial irradiation facilities or some hospitals, for which on-site events[b] are postulated that could warrant protective actions and other response actions on the site to achieve the goals of emergency response in accordance with international standards[e], or for which such events have occurred in similar facilities. Category III (as opposed to category II) does not include facilities for which events are postulated that could warrant urgent protective actions or early protective actions off the site, or for which such events have occurred in similar facilities.

TABLE 1. EMERGENCY PREPAREDNESS CATEGORIES (cont.)

Category	Description
IV	Activities and acts that could give rise to a nuclear or radiological emergency that could warrant protective actions and other response actions to achieve the goals of emergency response in accordance with international standards[e] in an unforeseen location. These activities and acts include: (a) transport of nuclear or radioactive material and other authorized activities involving mobile dangerous sources such as industrial radiography sources, nuclear powered satellites or radioisotope thermoelectric generators; and (b) theft of a dangerous source and use of a radiological dispersal device or radiological exposure device[f]. This category also includes: (i) detection of elevated radiation levels of unknown origin or of commodities with contamination; (ii) identification of clinical symptoms due to exposure to radiation; and (iii) a transnational emergency that is not in category V arising from a nuclear or radiological emergency in another State. Category IV represents a level of hazard that applies for all States and jurisdictions.
V	Areas within emergency planning zones and emergency planning distances[g] in a State for a facility in category I or II located in another State.

[a] That is, on-site events involving an atmospheric or aquatic release of radioactive material, or external exposure (due, for example, to a loss of shielding or a criticality event), that originates from a location on the site.

[b] Such events include nuclear security events.

[c] This includes events that are beyond the design basis accidents and, as appropriate, conditions that are beyond design extension conditions.

[d] See 'deterministic effect' under definitions in GSR Part 7 [1].

[e] See the goals of emergency response in para. 3.2 and the generic criteria in appendix II of GSR Part 7 [1].

[f] A radiological dispersal device is a device to spread radioactive material using conventional explosives or other means. A radiation exposure device is a device with radioactive material designed to intentionally expose members of the public to radiation. They could be fabricated, modified or improvised devices.

[g] See para. 5.38 of GSR Part 7 [1].

As explained in para. 5.14 of GSR Part 7 [1]:

"The operating organization of a facility or activity in category I, II, III or IV shall make arrangements for promptly classifying, on the basis of the hazard assessment, a nuclear or radiological emergency warranting protective actions and other response actions to protect workers, emergency workers, members of the public and, as relevant, patients and helpers in an emergency, in accordance with the protection strategy."

2.2. MODES OF EXPOSURE TO RADIATION AND RADIOACTIVE SOURCES

A review of past accidents involving radioactive sources identified the following three generic exposure scenarios involving radiation injury to an individual as being typical of many situations. These generic scenarios may be used to estimate potential radiation exposures which may occur if control of sources is lost [8, 9]:

— *External exposure to an individual from a source in very close proximity.* A radioactive source may be lost or stolen. A scenario that has occurred several times is an individual putting an unshielded radiation source into a pocket (e.g. accidents related to industrial radiography with gamma sources). The individual may do this for a number of reasons, including theft, interest in an unknown object, or ease of transfer to another location. The person involved may be a worker at the facility or a member of the public, resulting in significant doses to one or several persons.
— *External exposure from an unshielded source (involving several individuals).* It is possible that once control of a source has been lost, it may irradiate workers or members of the public without the knowledge of those involved. Again, gamma radiography provides an example: after making an exposure, the source may become jammed and the operator(s) and other persons may be unintentionally exposed, resulting in significant doses to several persons. Accidents involving exposure of multiple individuals from an unshielded source have occurred in: Mexico (1962); Algeria (1978); Estonia (1994) [10]; China (1996); Turkey (1998) [11]; Egypt (2000); and Thailand (2000) [7].
— *Exposure following rupture of source casing.* If a source which is not controlled becomes ruptured, the radioactive material may be dispersed, resulting in contamination of equipment or individuals; exposures from inhalation of radioactive material, inadvertent ingestion of radioactive material, and contamination of the skin; and external exposure from the spillage. Exposure following the rupture of a source occurred in Juarez, Mexico, in 1983, and in Goiânia, Brazil [5], in 1987.

Among factors to be considered in planning the medical response, the number of individuals involved, possible radiological and other health consequences, the presence of contamination with radioactive material, or the association or combination of radiation exposure with thermal or chemical exposure or trauma, are essential components for any medical plan.

The kind of radiation injury eventually presented by an exposed individual is dependent on several factors. The characteristics of the nuclear or radiological facility in which the emergency occurred, and the types of radioactive source and their activities are useful pieces of information for the proper medical management of patients involved in accidents.

Examples of the potential exposure of individuals involved in radiation emergencies are given in Table 2. These examples are classified by source, possible exposure and type of facility [8].

In the event of a radiation emergency occurring in group 1, such as power reactors, or industrial and research facilities, there is a potential risk of external and internal exposure for individuals involved in the emergency.

In group 2, the role of medical interventions has significantly increased the cases of overexposure of individuals (external exposure) [12]. This is due to the wide use of X rays in interventional cardiology and radiology, especially since 1990.

Group 3 includes sealed sources, which are widely used in industry and medicine. The most common radiation accidents involve sealed sources, such as those used for radiotherapy. A study reported that 60% of radiation accidents and overexposures of persons in the period 1980–2013 were related to medical exposures [12].

Group 4 consists of the largest number of facilities and devices with unsealed sources of low activity and, as a consequence, with a low potential for severe accidents. These include the use of radionuclides with short half-lives (in nuclear medicine). A small number of people have been involved in accidents in these latter categories. However, only a few cases were severe enough to cause deaths.

Although the potential for accidents in transport and radioactive waste management (groups 5 and 6) is high, individuals have rarely been severely exposed to radiation in these accidents. Table 3 provides information on different areas of the use of radioactive sources, as well as the potential exposure of individuals involved in radiation emergencies and some examples from past accidents [8].

2.3. CLINICAL AND RADIOLOGICAL TRIAGE

Triage is the sorting of patients into priority groups according to their need and the resources available [16]. Triage in radiation emergencies will be initially based on the severity of medical conditions using conventional triage systems and not on radioactive exposure or contamination. Primary attention will always be aimed at life threatening conditions.

TABLE 2. FACILITIES, SOURCES AND POSSIBLE EXPOSURE MODES IN A RADIATION EMERGENCY

Group	Facility/source	Potential external exposure	Potential contamination (internal/external)	Both conditions (external exposure and contamination)
1	Critical assembly	Yes	Yes	Yes
	Reactor	Yes	Yes	Yes
	Fuel element manufacture	Yes	Yes	Yes
	Radiopharmaceutical manufacture	Yes	Yes	Yes
	Fuel reprocessing plants	Yes	Yes	Yes
2	Radiation devices:			
	Particle accelerator	Yes	[a]	[a]
	X ray generator	Yes	No	No
3	Sealed source (e.g. industrial radiography)	Yes	No	No
	Unsealed source (airborne, volatile liquid or powder)	Yes	Yes	Yes
4	Nuclear medicine department	Yes	Yes	Yes
	In vitro assay laboratory	Yes	Yes	Yes
5	Source transport	Yes	Yes[b]	Yes[b]
6	Radioactive waste	Yes	Yes	Yes

[a] In cases where neutrons are captured by atomic nuclei, radioactivity may be induced depending on the chemical element involved. In the case of neutrons, induction of radioactivity by exposure to neutrons in the body may produce radionuclides such as Na-24 and K-42 in the body.

[b] No significant contamination with radioactive material has been reported during a transport accident.

The second step is to identify those individuals possibly exposed or contaminated [17]. The severity of radiation injuries depends on the radiation dose incurred, the dose rate, the radiosensitivity of affected tissues and organs, and the area and extent to which the body has been exposed. For the same

TABLE 3. AREAS OF USE, RADIOACTIVE SOURCES, POTENTIAL EXPOSURE AND EXAMPLES OF ACCIDENTS

Areas of use	Source, radionuclide	Potential exposure during a radiation accident	Example
Industry:			
Sterilization	Co-60; Cs-137	WBE[a] or LE[b]	Nesvizh, Belarus (1991) [13]
Radiography	Ir-192; Cs-137	WBE[a] or LE[b]	Yanango, Peru (1999) [14]
Medicine:			
Diagnostics	X ray generators	LE[b]	Los Angeles, USA (2008–2009)
Therapy	Co-60; Cs-137 and accelerators	WBE[a] or LE[b]	San Jose, Costa Rica (1996) [15]
Research	Broad spectrum of sources, including reactors	WBE[a] or LE[b]	Sarov, Russian Federation (1997)
Orphan sources	Co-60; Cs-137 and others	WBE[a] or LE[b], internal and external contamination (if unsealed)	Goiânia, Brazil (1987) [5]
Nuclear reactors	Cs-137; Sr-90; I-131	WBE[a]; internal and external contamination	Chernobyl (1986) [2–4]

[a] WBE: whole body exposure.
[b] LE: local exposure.

absorbed dose, the health consequences of a partial body exposure are less severe than those of a whole body exposure.

A single absorbed dose of about 3.5 Gy to the whole body is generally expected to result in the death of 50% of the exposed population group within two months if there is no medical treatment (LD50/60, meaning a lethal dose for 50% of the population in 60 days). The LD50/60 can be increased to about

5.0–6.0 Gy with advanced mitigative treatment (e.g. bone marrow transplants, haematopoietic growth factors) or supportive treatment, as well as when the exposure is prolonged or fractionated. The survival probability of patients exposed to significantly higher doses is very limited. These patients require standard supportive care.

Radiation accidents involving radiation exposure can be combined with trauma, thermal, chemical or other exposures [18, 19]. A combination of radiation injury with trauma, or thermal or chemical burn makes the prognosis poorer for the patient. The decision on hospitalization, in cases of whole body exposure or local exposure depends in some cases on the presence of early clinical signs, as set forth in Table 4 [20]. However, hospitalization might be necessary depending on the condition of the patient, the medical diagnosis and the estimated dose. An alternative treatment is to monitor the appearance of skin lesions and analyse the patient's laboratory tests during the first 48 hours (i.e. through a haemogram) [8].

2.4. PRINCIPLES OF MEDICAL MANAGEMENT

The goals of the medical response to a nuclear or radiological emergency are as follows [21]:

— To save lives and perform required emergency medical procedures;
— To treat radiation injuries and injuries resulting from an emergency situation;
— To perform required public health actions, including providing public advice and counselling, and long term medical follow-up of exposed persons.

Some considerations in the medical management of patients include the following:

— The medical triage of patients will be determined primarily by their clinical status and their conventional injuries (such as trauma, wounds and burns).
— The need for treatment of radiation injuries/internal and external contamination does not constitute per se a medical emergency, although some early essential actions must be taken (such as blood sampling for assessing the radiation dose to the patient, or removing clothes when external contamination is suspected).

After assisting persons with life threatening conditions and conventional injuries, eventual prodromal manifestations serve to sort persons externally exposed to radiation and decide upon proper medical care at an individual level. Important early clinical symptoms are: nausea, vomiting (emesis), diarrhoea,

TABLE 4. INITIAL DECISION MAKING FOR MANAGING RADIATION INJURIES BASED ON VOMITING AND ERYTHEMA

(modified from Refs [8, 20])

Clinical manifestations		Estimated dose		Initial decision
WBE[a]	LE[b]	WBE[a]	LE[b]	
No vomiting	No erythema	<1 Gy	<3 Gy	Outpatient with five week surveillance (blood, skin).
Vomiting 2–3 h after exposure	Primary erythema[c] 12–24 h after exposure	1–2 Gy	>3~8 Gy	Monitoring in a general hospital.
Vomiting 1–2 h after exposure	Primary erythema 8–15 h after exposure	2–4 Gy	>15 Gy <25 Gy	Hospitalization in haematological or surgical (burn) department or specialized surgical department (ideally in a room with laminar air flow and air filtering, and with a plastic surgery team trained in radiation injuries).
Vomiting earlier than 1 h after exposure	Primary erythema within 3–6 h (or less) associated with itching, oedema and pain	>4 Gy	>25 Gy	Hospitalization in a haematological or specialized surgical department (ideally in a room with laminar air flow and air filtering, and with a plastic surgery team trained in radiation injuries). Specialized counselling is necessary.

[a] WBE: whole body exposure.

[b] LE: local exposure.

[c] Primary erythema is a deterministic manifestation referring to a transient erythema appearing at an early stage after the exposure; also called early erythema.

and skin and mucosa erythema. They may develop in hours or in a few days, depending on the characteristics of the irradiation.

It is important to emphasize that patients only exposed to external radiation present no radiation hazard to the emergency medical personnel. In cases of external or internal contamination with radioactive material (usually airborne or liquid), patients' clothes and uncovered parts of the body (primarily hair, hands and face) may represent a source causing a very low level of radiation exposure to the assisting team [18, 19, 21].

Even in the most severe nuclear and radiological accidents (Chernobyl and Goiânia), the medical personnel directly in contact with the patients, treating and decontaminating them, received just a few mSv of radiation exposure, comparable to the average radiation exposure received annually by any member of the public due to natural radiation sources [22]. Note that use of the universal precautions for the management of patients will provide adequate protection to avoid contamination of the health care staff caring for the patient.

Table 5 [23] presents the main methods for early diagnosis of whole body or partial body irradiation, including the procedures, manifestations, expected time of onset and minimum doses necessary for the appearance of the early symptoms and signs of radiation exposure (threshold). These estimated doses can be influenced by the individual radiosensitivity, as well as genetic and other factors [8].

The severity of the exposure will usually be assessed in an iterative manner. A very early evaluation — as outlined in Tables 4 and 5 — will be based on clinical manifestations and on haematological findings. These manifestations, as well as the time of their appearance, and their frequency and severity, need to be carefully recorded. This will allow the classification of patients into distinct categories corresponding to their estimated absorbed doses.

Further assessment of exposed patients will be performed, based on the evolution of clinical, biological and laboratory parameters. Depending on the type of exposure (whole body exposure or local exposure), haematological evolution and other procedures, such as cytogenetic and physical dosimetry (electron spin resonance (ESR), also known as electron paramagnetic resonance) are vital [23].

However, as the requisite medical expertise and the required supporting capabilities for the evaluation and management of these patients are not available in all countries, two conventions were developed after the Chernobyl accident that provided the basis for the international collaborative framework between countries and organizations during radiation emergencies. One is the Convention on Early Notification of a Nuclear Accident and the other is the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency [24].[3]

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[3] The Convention on Early Notification of a Nuclear Accident entered into force on 27 October 1986. The Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency entered into force on 26 September 1986.

TABLE 5. METHODS FOR THE EARLY DIAGNOSIS OF RADIATION INJURIES

Procedure	Manifestation	Time of onset[a]	Minimum exposure (Gy)
Clinical observations	Nausea, vomiting	Within 48 h	~1
	Erythema	Within hours to days	~3
	Epilation	Within 2–3 weeks	~3
Laboratory examinations:			
Blood cell count	Absolute lymphocyte count $<1 \times 10^9$ L[b]	Within 2–72 h	~0.5
Cytogenetics[c]	Dicentrics/rings, micronuclei, translocations	Within hours	~0.1 (detection level)

[a] The latency time is inversely dependent on radiation dose.

[b] The lymphocyte count may decrease within hours. Experts recommend that a baseline count be obtained as soon as possible and the counting be repeated every 4 h on the first day and then daily.

[c] Results can be available in three to five days depending on the technique used [23].

Arrangements for response to any nuclear or radiological emergency and the measures for developing, maintaining, exercising and improving these arrangements for all participating international organizations are described in the Joint Radiation Emergency Management Plan of the International Organizations [25].

3. EXTERNAL EXPOSURE

Exposure is the act or condition of being subjected to irradiation. Persons are externally ‘exposed’ to ionizing radiation in much the same way persons are ‘exposed’ to light when someone shines a flashlight on them. In the case of external exposure (irradiation) there is no radioactive material transferred, and the source is outside the body [26]. This means that persons externally exposed to

radiation have no radioactive material on or inside them and pose no radiological hazard to the treatment team or to any other individual [27].

For individuals externally exposed, the consequences, prognosis and treatment depend on whether exposure affected the whole body, affected a significant part of the body or was limited to a small area or volume. It is very important for prognosis and choice of treatment to know the distribution of absorbed dose within the body.

A source external to the body can cause local, partial or whole body exposure. The farther away the source and the more the person moves, the higher the probability of a more uniform body dose distribution. The medical consequences will depend on the dose received by different tissues and organs and also on the volume of the body irradiated.

Other physical variables, such as the source activity, energy of the radiation emitted, duration of the exposure, and dose rate, will provide valuable information for the dose assessment, and consequently will contribute to guiding the treatment and establishing the medical prognosis.

If a radioactive source is located relatively close to an individual and part of the body is shielded, a partial or local exposure would be expected. The dose rate is also important. If the same dose is delivered within a shorter time (higher dose rate), a more severe radiation effect would be observed [8].

After an external exposure to ionizing radiation, two different conditions may manifest within a variable latency time (hours, days, weeks): LRI and ARS.

Detailed descriptions of the molecular and cellular changes following radiation exposure, detailed pathophysiology, laboratory assessment and the scientific fundamentals of therapeutic aspects of LRI and ARS are out of the scope of this report and can be found in other publications [28–31].

3.1. LOCAL RADIATION INJURY

3.1.1. Diagnosis, medical assessment and dose estimation

When external exposure is restricted to a limited area of the body, an LRI may develop depending on the absorbed doses delivered to the skin and deeper tissues, with possible severe medical consequences to the affected tissues. In this case, ARS will not be expected unless a significant volume of the body has been exposed.

Extensive skin involvement may be part of a complex pathology that may jeopardize life after whole body exposure to high radiation doses, frequently

called cutaneous radiation syndrome[4] (CRS) [13]. This condition has to be differentiated from an LRI.

Local external exposure to gamma radiation is of major concern because of its frequency in cases of accidental overexposure to ionizing radiation and the possibilities of damage to deeper skin and other body structures developing severe injuries. The term 'beta burns' is widely used for shallow skin injuries caused by external exposure to beta radiation. The same condition can also occur in rarer instances, as shown in the Goiânia accident [5], following unremoved deposition of beta emitters on the skin. In this case, beta radiation injuries are characterized by a non-homogeneous distribution, with isolated areas of healthy skin, particularly in areas that were protected by clothes. In such instances, radiation doses are a function of the time taken for the removal of the beta emitting radionuclide after its contact with the clothes or the skin.

An LRI may occur after a localized radiation exposure in different situations. According to past experience, the affected individuals can include radiation workers, the general public and patients. The possible scenarios are also variable. Some examples are:

— Radiotherapy and interventional radiology accidents (overdose to a patient) [32, 33];
— Industrial radiography accidents (mainly gammagraphy) [14, 34, 35];
— Accidents with irradiators [36];
— Accidents at nuclear power plants [2, 4];
— Criminal or terrorist acts involving radioactive material.

An LRI is a deterministic effect, also called a 'tissue effect', from a radiation exposure. Therefore, its severity follows a dose dependent pattern. The main feature of an LRI is its dynamic process (inflammatory waves), which develops in time, sometimes in an unpredictable way [17].

The pathophysiology of an LRI is complex, and many aspects of it are not fully understood. It combines cytokine mediated antiproliferative and local/systemic inflammatory reactions, and microcirculation damage, all in a temporal and superimposed pattern [37, 38].

The earliest responses to skin irradiation are transient manifestations, namely a primary erythema. A primary erythema may appear within a few hours after high dose acute exposure as a result of capillary dilation. The time of appearance of a primary erythema has a prognostic value because an earlier

[4] In some countries the term 'cutaneous radiation syndrome' is used instead of LRI to express the manifestations of local radiation exposure. These are two different entities that also can overlap; therefore, it is necessary to use the appropriate respective medical terminology.

manifestation after the exposure to radiation will imply a higher dose absorbed by the tissues (skin). Correspondingly, its severity serves as a dose indicator [39]. A primary erythema may be unnoticed, especially in individuals with dark skin. The primary erythema disappears spontaneously and is followed by a secondary erythema and by dry desquamation at about one to five weeks (latent period) on a dose dependent time relation (the shorter the latent period, the higher the dose). This phenomenon is attributable to the release of proteolytic enzymes from damaged epithelial cells [40]. The next stage is the manifestation phase if the dose is high enough to induce an LRI.

A late erythema may also occur in cases of high dose LRI between 6 and 18 months post-irradiation. It precedes and follows vasculitis crises.

In high dose exposures, an initial erythema may be accompanied by a phlogistic and painful oedema with paraesthesia on the erythema area. The earlier an oedema appears, the higher the dose. This also applies regarding its severity.

Besides dry desquamation, the manifestation phase may evolve to moist desquamation, blistering, ulcers, and even deep radiation necrosis (radionecrosis) for doses greater than 25 Gy [17].

Pain as a result of deep ulceration and necrosis is a major symptom in LRIs that evolve. In general, the treatment and management of the pain is extremely difficult. The severity of the pain is also an indicator of future recurrences over the long term and is thus another prognostic indicator of the evolution of the LRI [17].

For acute exposures, approximate dose thresholds for clinical manifestations are given in Table 6. These values are influenced greatly by the irradiation field and the radiation quality, as well as individual biology, radiosensitivity, genetics and other factors.

Skin appendages and hair follicles are of particular interest by virtue of their radiosensitivity. A dose of 2 Gy can cause follicular dysplasia, while 3 Gy can cause temporary epilation between the second and fourth week after exposure. For doses higher than 7 Gy, epilation is definitive. The hair follicle reaction to radiation represents a retrospective dose indicator. It should be noted that a biopsy in a zone of LRI is dangerous; this can induce the formation of an ulcer in the tissues that have been made fragile by the radiation damage.

The irradiation of sweat and sebaceous glands can lead to functional and structural alterations, with pronounced cellular depletion.

Late effects of local radiation exposure are not within the scope of this publication. Briefly, telangiectasia, angioma formation, nail and nail bed changes, dermal erythematous reactions, atrophy, induration, fibrosis and non-melanoma skin cancer (basal cell and squamous cell carcinomas) are well documented possible local late effects. Radiation can lead to hyperpigmentation through the activation of melanogenesis. After high doses, hypopigmentation or

TABLE 6. THRESHOLD DOSES AND TIME OF ONSET FOR DIFFERENT MANIFESTATIONS OF LOCAL RADIATION INJURIES

Manifestation	Threshold dose (Gy)	Time of onset[a] (d)
Second phase erythema[b]	3	14–21
Temporary epilation	3	14–18
Definitive epilation	7	25–30
Dry desquamation (dry epithelitis)	10	20–28
Moist desquamation (exudative epithelitis)	15	15–25
Necrosis	25	>21

[a] Time of onset is a reference; it is influenced by factors such as the dose rate, duration of the exposure and individual radiosensitivity.

[b] Second phase erythema is a deterministic effect referring to an erythema that develops during the manifestation phase of a local radiation injury.

depigmentation (dyschromia) can result owing to the death of a great number of melanocytes.

Muscular damage may be observed after high dose irradiation to human skeletal muscle (observed in some of the radiological accidents, such as those at Lilo [41] and Dakar [42]). The microscopic analysis of a muscle biopsy obtained from a patient in the 2006 radiological accident in Dakar is presented in Fig. 1(a) [42]. The pathological characteristics of the muscle fibre were associated with a severe reduction of the fibre diameter and area, as shown in Fig. 1(c). In addition, the degree of fibrosis was very abundant in the irradiated muscular region in Figs 1(a) and 2(a). A significant loss of cytoplasm in the myofibres was also observed; the nuclei appeared very close to each other. Finally, some inflammatory infiltrates were evident in the irradiated muscle tissue after detecting macrophages and T lymphocytes (Fig. 2(b)) by immunostaining. In the irradiated tissue, the microvascular circulation was disrupted and the number of microvessels reduced, which has been considered one of the most important effects of radiation on normal tissue (Fig. 1(b)) [19].

As illustrated in Fig. 3, irradiated bone biopsies from patients were analysed in 3-D microtomography and showed that the trabecular bone volume was greater in irradiated bone tissue compared with the non-irradiated area,

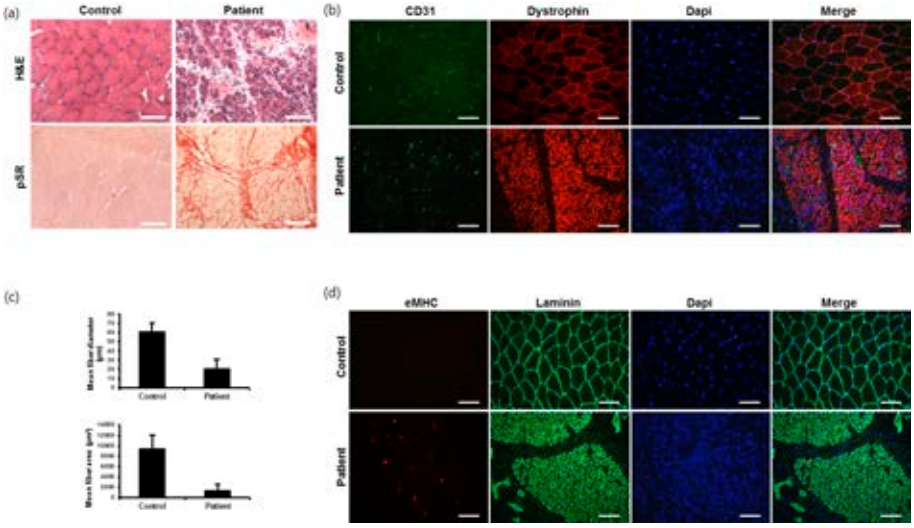


FIG. 1. Muscular damage in a patient exposed in an industrial radiography accident at Dakar in 2006. (a) Haematoxylin and eosin (H&E) and picro-Sirius red (pSR) colorations on muscle cross-sections from a healthy donor (control) and the patient. (b) Immuno-histochemical analysis for CD31 and dystrophin, using transversal sections of control and patient muscles, showing radiation induced vascular abnormalities. (c) Fibre diameter and fibre area quantification (N = 411–590 myofibres, P < 0.005). (d) Analysis of muscle regeneration on cryosections of the control and patient stained with eMHC and laminin. (Courtesy of the Institute for Radiological Protection and Nuclear Safety.)

indicating morphological changes occurring in a time and dose dependent manner. The medical management of the bone tissue necrosis is based on a surgical approach that could lead to amputation. This has been also described as a serious complication from radiotherapy (i.e. patients with osteonecrosis of the mandible treated for head/neck tumours [43]). Radio-osteonecrosis has been described months or years after local irradiation at high dose (Fig. 4).

The clinical recognition of radiation induced skin lesions by non-specialized health personnel has been deficient in the history of medical management of LRIs. Acute manifestations of radiation skin damage have been taken as insect bites, skin allergies, thermal or chemical burns, and even very distinct pathologies such as pemphigus foliaceus [4, 8]. The clinical features of LRIs are non-specific, and unless there is an evident history of accidental exposure to ionizing radiation and an elevated level of suspicion on the part of the attending physician or any other health personnel, the condition will probably be misdiagnosed. A ‘burn’ without a history of exposure to heat or chemicals provides striking evidence for the early diagnosis of LRI.

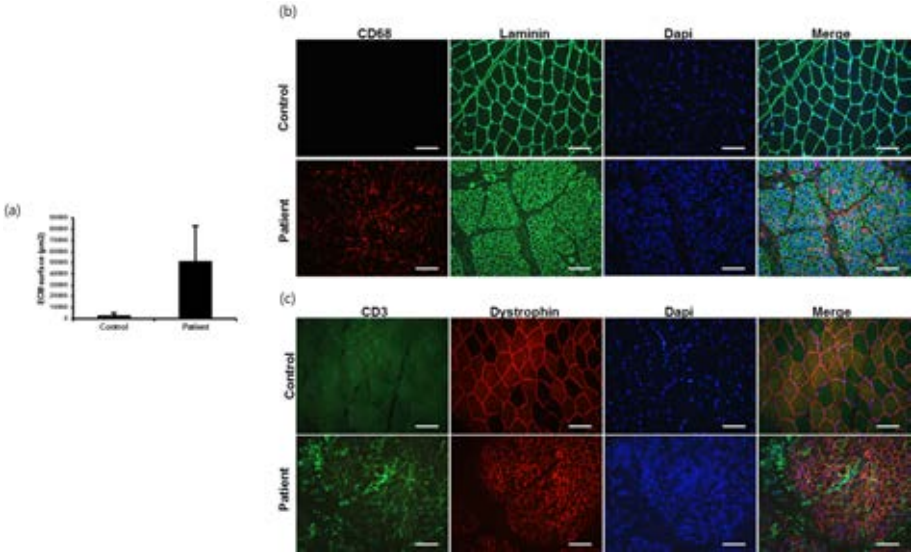


FIG. 2. Muscular damage due to irradiation: human muscle. (a) Connective tissue quantification in the control and irradiated muscle ($P < 0.005$). (b) Inflammatory infiltrate detection by immunostaining for CD68 and laminin on transversal sections of the control and patient biopsies. (c) Similar detection by immunostaining for CD3 and dystrophin. (Courtesy of the Institute for Radiological Protection and Nuclear Safety.)

In all instances of LRI, it is good practice to have an initial complete blood count (CBC), another CBC after 6–8 h, and then one after every 24 h, with

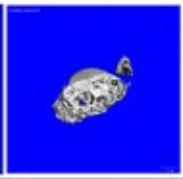
	Non Irradiated (Finger bone)	Irradiated (Finger bone)	Irradiated (Toe bone)
			
BV/TV (%)	**12.35**	**21.13**	**26.37**
Dose received (Gy)	-	**10**	**28**
Time after IR (Years)	-	**6**	**2**

FIG. 3. Three-dimensional microtomography analysis of bone microarchitecture from human bone samples. BV/TV: bone volume/tissue volume (bone volume in percentage of total tissue volume); IR: irradiation. (Courtesy of the Institute for Radiological Protection and Nuclear Safety.)

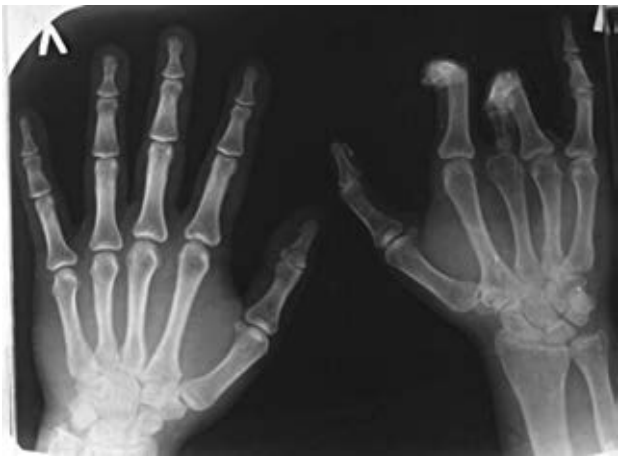


FIG. 4. Osteoporosis of the right hand bones. (Photograph courtesy of I.A. Galstyan.)

special attention paid to lymphocyte kinetics, to evaluate the possibility of whole body exposure and the possible development of ARS.

Severe cases of LRI, as well as those with the possibility of becoming severe, demand a comprehensive assessment by means of complementary diagnostic procedures. The assessment protocol will depend on clinical judgement, and on the available diagnostic resources.

A number of procedures are useful for the medical evaluation of LRIs, such as:

— Serial high quality and standardized colour photography for documentation and evolution analysis (date and time must be carefully recorded);
— Ultrasonography with high resolution equipment;
— Computed tomography and magnetic resonance imaging;
— Blood flow evaluation (scintigraphy, Doppler ultrasound);
— Thermography;[5]
— Early physical dose reconstruction (Monte Carlo simulation).

[5] Thermography is a non-invasive imaging technique that involves infrared scanning. It is intended to measure the temperature distribution of various organs and tissues. The visual display of this temperature information is known as a thermogram. It has been used for the evaluation of skin lesions such as diabetic ulcers or of the potential for ulcer formation. It has also been used to detect breast cancer through increased skin heat generation related to an intramammary tumour and its increased metabolism and blood supply. Thermography may be an auxiliary method to establish the severity and extent of an LRI. In contrast, a significantly lower skin surface temperature will be observed in patients with necrosis [17]. Two techniques are available: telethermography and contact thermography.

In the event of a possible high dose accidental local overexposure, it is essential to perform dose reconstruction at different levels in skin and other structures. Some of the tools to evaluate the isodose curves are similar to those used in radiotherapy. The dose reconstruction provides doses as a function of tissue depth. Depth dose distribution depends upon many factors, such as radiation energy, activity of the source, source geometry, duration of the exposure, extent and anatomical and tissular characteristics of the irradiated area, and existence of attenuating conditions (shielding).

A high quality computed tomography scan of the exposed area is obtained and a number of slices are used with specialized software to generate a personalized numerical voxel phantom representative of the patient with external contours and bone structures. Using this voxel phantom, the accidental exposure to the skin is repeated (same type of source, distance from the skin, time of exposure, etc.). Then a map of the dose distribution is obtained with numerical simulations associating a Monte Carlo code and the personalized voxel phantom [44].

Dose reconstruction provides valuable information for determining the prognosis and the best treatment strategy. Whenever surgery is contemplated for the management of LRIs, it is essential to have a well established evaluation of depth doses (see description of dosimetry guided surgery in Section 3.1.2).

3.1.2. Treatment

The medical management of severe cases of LRI (i.e. radionecrosis) demands hospitalization in specialized plastic and reconstructive surgery or burn departments with experience in this kind of injury.

The medical management of pain with conventional analgesics, non-steroidal anti-inflammatory drugs, central action analgesics and sedatives is indicated for the partial relief of most of the painful episodes during the initial phases of the injuries. As the severity of pain increases, more potent analgesics (e.g. tramadol, trometamol, meperidine) may be needed either alone or in combination with antihistamine drugs (promethazine) and neuroleptics (chlorpromazine). Anxiolytics, hypnotics and antidepressants have an accessory role in pain management.

Secondary infections may be a complication and local antibiotics are indicated in such instances. In severe or complicated cases, systemic antibiotics might be needed and must be administered in accordance with the results of cultures and antibiograms.

The following therapies have been used mainly at the chronic stages of LRI:

— Pentoxifylline, a methylxanthine, reduces blood viscosity and improves perfusion at the microcirculation level. It has been used in some patients with local injuries. A good hydroelectrolytic balance is essential to avoid haemoconcentration [45, 46].
— By virtue of the role of oxidative stress phenomena in the pathophysiology of LRI, both in the early and late stages, local treatment with antioxidants, such as superoxide dismutase, has been proposed for chronic lesions [47].

Hyperbaric oxygen therapy has been used for the management of some cases of LRI with apparent good results [48], but the lack of controlled trials does not allow a clear indication of this kind of treatment for LRIs.

The medical management of deep ulceration and radionecrosis demands surgery. The surgical approach has evolved as the clinical experience with accidental exposures has increased. In the past, management of LRIs was based on a conservative approach: 'wait and see, then intervene'. This kind of approach has shown poor results in cases of severe LRIs, with serious consequences for the quality of life of these patients [48]. Conventional surgical techniques have been used in LRI cases, including ulcerectomy and necrectomy with wound closure by rotation flap, amputation, and a combination of these [30, 41]. In the eventuality of superficial lesions, experts recommend a conservative approach. Surgery is required in cases of deep ulcer and necrosis.

A significant problem with respect to surgery in cases of deep ulcer and profound and large radionecrosis is that the intervention stimulates new waves of inflammation. To overcome this drawback, a new surgical approach has been used since 2006 in cases of severe LRI with good results and significantly less morbidity. This new approach, known as dosimetry guided surgery, combines local dose assessment of the exposed area with early conventional surgery guided by dosimetry [30, 49, 50].

Experts recommend dosimetry guided surgery as an early procedure in cases of severe local radiation exposure when deep ulceration or necrosis can be expected (for example, when erythema, blistering and oedema develop within a short period after irradiation). Isodoses are calculated using a 'dosimetric map', which informs surgeons of soft tissue areas of high dose (>25 Gy) where necrosis is likely to occur. This information guides the surgical decision with the aim of performing a preventive surgical excision of the area that will possibly develop necrosis. If parts of bones need to be excised during surgery, an ESR from a sample of bone may provide important information about radiation dose in this area.

Mesenchymal stem cells (MSCs) are characteristically multipotent cells obtainable from the bone marrow and, alternatively, from other tissues, such as umbilical cord and adipose tissue. The main effect of MSCs is to deliver paracrine factors such as anti-inflammatory cytokines, growth factors and microvesicles that promote the healing of the injured tissues. In dosimetry guided surgery, MSCs are injected during surgery in different parts of the surgical area, and again in a number of sessions following surgery [51]. MSCs can be used for the treatment of late radiation ulcers with a surface area <20 cm^2 [52].

Although in a different context from acute LRI, autologous adipose derived regenerative cells, obtained from suctioned adipose tissue, have also been used along with minimally invasive surgical procedures in the treatment of local injuries from radiotherapy with reported success [53].

Specialized physiotherapy plays a pivotal role for rehabilitation after surgery in LRI. Among other objectives, it aims to maintain or recover as much joint functionality and strength as possible and to prevent excessive scarring.

3.1.3. Medical follow-up

Any patient who manifested severe lesions from the spectrum of LRIs needs to be carefully followed up, emphasizing the following:

— Offer the patient counselling on how to avoid behaviour that could facilitate the recurrence of lesions, including unprotected exposure of the affected area to extremes of temperatures, irritating chemicals and trauma. The patient will be also advised to maintain proper personal hygiene to minimize infectious complications in the irradiated area.
— Identify and address possible LRI recurrences and surgery complications.
— Provide general counselling on a healthy lifestyle aimed at preventing diseases and conditions and ensuring a better prognosis by identifying them before clinical manifestations occur or their complications are observed. This will also improve adherence to the medical follow-up. Special attention will be given to situations that could cause ischaemia to the affected area, such as smoking, diabetes and arterial diseases.
— Promptly identify possible malignant development in the exposed area.
— Help in validating any novel modalities of treatment adopted.
— Facilitate early detection of stochastic effects.

In principle, follow-up is to be established on a lifelong basis. The medical protocol to be used is dependent on the type of LRI, the therapy that was used, individual characteristics of the patient, such as gender and age at exposure,

comorbidities, and the extent of the accidental radiation exposure (i.e. concomitant irradiation of eyes, thyroid, significant bone marrow tissue, etc.).

3.1.4. Case study: The radiological accident in Nueva Aldea

An accident occurred on 14 December 2005 at a cellulose plant under construction in Nueva Aldea, Concepción, Chile [34, 35]. Industrial radiography operators were performing a non-destructive test with equipment containing an ^{192}Ir source with an activity of 3.3 TBq. As a result of a failure in the equipment, and unknown to the operators, the source (pigtail) became detached.

Although the gamma radiography company had procedures in place and had identified the responsibilities of individuals, they were not strictly followed, their implementation was not supervised and a safety culture was absent. Moreover, the failure to monitor dose rates during the radiography operations contributed decisively to the accident's consequences. In addition, there was no evidence that the radiography company had a preventive maintenance programme in place for the radiography equipment.

The following day (15 December 2005), 27 year old scaffolding worker A found the source and, not recognizing it as such, picked it up with his bare hands (at about 11:20, according to his account). He held it in his hands for 10–15 min, shifting it from his left to his right hand and turning it upside down. After he put it into his left back trousers pocket, for about 10 min, the worker felt a local increase of temperature on his skin. He then took it out of his back pocket and put it into the left outside pocket of his jacket for a short period (about 1 min) until scaffolding worker B arrived at the platform (about 11:40).

When the radiation source was discovered, worker A was instructed to put the source in a "container". He put the source into a metal pipe that was lying on the ground near the office facility, from where it was safely recovered later. Although individuals other than worker A (hereinafter referred to as 'the patient') were exposed to radiation and three of them also developed mild to minor LRI, only worker A turned out to be severely injured (Fig. 5).

The patient developed an erythema of about 4 cm in diameter on the left buttock five hours after exposure. This fact, on clinical grounds alone, is indicative of a very high local dose. Following the request of the Chilean authorities through the IAEA, the patient was hospitalized at the Burn Treatment Centre of Percy Military Hospital, in Paris, France, on 29 December 2005. The buttock skin lesion evolved into moist epidermitis (moist desquamation 4–5 cm in diameter), then quickly worsened and progressed to ulceration. In the weeks following exposure, the left hand exhibited erythematous lesions with swollen fingers. These radiation skin lesions were accompanied by intense pain, which was only partially alleviated by morphine. The early development of the buttock

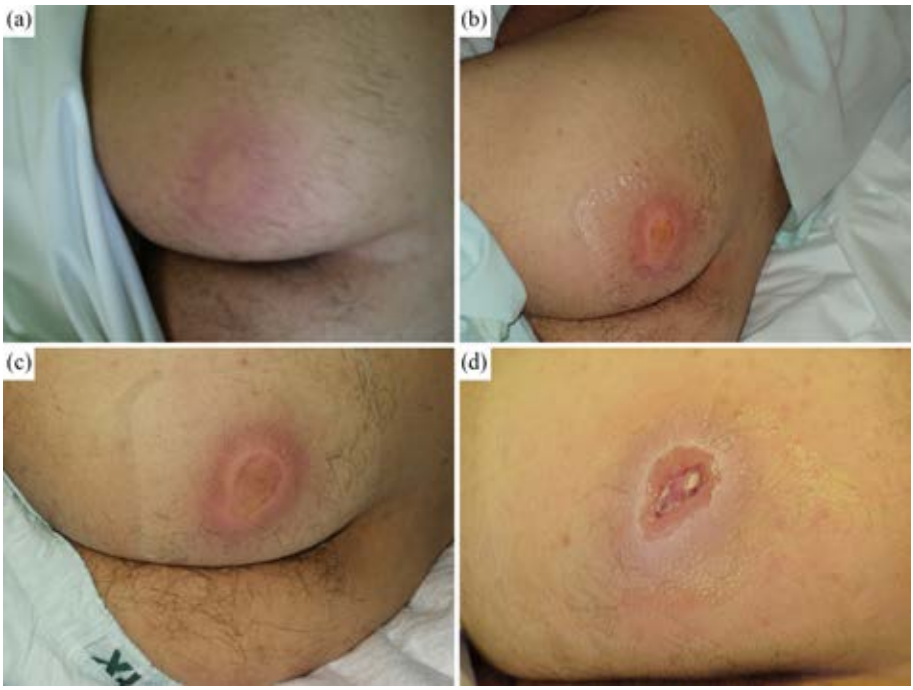


FIG. 5. Images of the local radiation injury in the left gluteus of the patient, and evolution of the lesion over ten days. (a) Image taken two days after exposure (16 December 2005). (b) Image taken five days after the exposure (19 December 2005). (c) Image taken six days after the exposure (20 December 2005). (d) Image taken 12 days after the exposure (26 December 2005).

lesion without any latency phase, its rapid evolution towards ulceration and the uncontrolled pain were characteristic of a very severe radiation burn with poor prognosis [17, 30].

A dose reconstruction of the radiation lesion using a numerical method and taking into account the anatomical characteristics of the patient was performed to improve the accuracy of the surgical excision (Fig. 6). The dose absorbed at the centre of the skin lesion was very high (almost 2000 Gy), but it dropped rapidly owing to the combined effect of distance and tissue attenuation. Thus, the 20 Gy and 5 Gy isodoses were situated at 5 cm and 10 cm, respectively, from the centre of the lesion.

Based on dose reconstruction mapping, a wide resection in apparently healthy tissues was performed on day 21 post-exposure. All tissues exposed to a dose over 20 Gy (those situated between the centre of the lesion and the 20 Gy isodose curve) were excised in a hemisphere 10 cm in diameter and then covered with a cryopreserved allograft.

Following surgery, no infection or subsequent radiation inflammatory wave was observed for one month. Owing to this apparent normal evolution, a skin autograft was performed on day 49 post-irradiation. Rapid lysis of the skin graft occurred with the development of a painful infected radiation ulceration (Fig. 7).

The information received as of the date of this publication indicates that the patient is doing well, with normal social and work activities. Since the accident, patient follow-up indicated two recurrences of ulcers on the hands. There were no new recurrences on the buttocks. He is in good medical condition, with preserved function of the lower extremity [17, 30, 34, 43].

3.2. ACUTE RADIATION SYNDROME

ARS is the acute illness caused by exposure to a high dose of ionizing radiation to the body. ARS is a deterministic effect of radiation exposure to the whole body or to a significant volume of the body (partial body irradiation) above

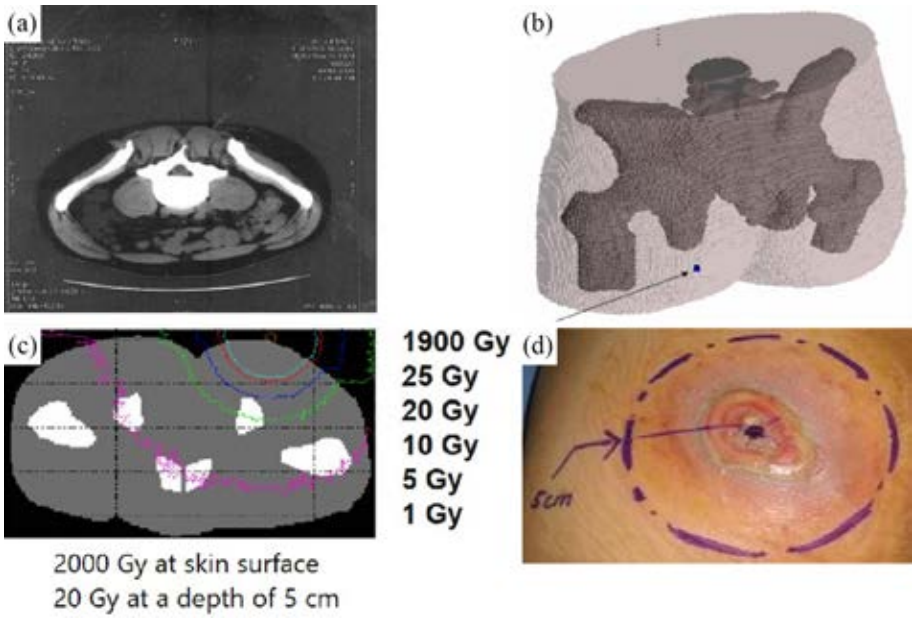


FIG. 6. Dose reconstruction mapping to improve the accuracy of the surgical excision. (a) computed tomography scan of the patient. (b) Phantom voxelization. (c) Dosimetric map. (d) First excision (day 21 after the exposure). (Courtesy of the Institute for Radiological Protection and Nuclear Safety, Percy Military Hospital.)

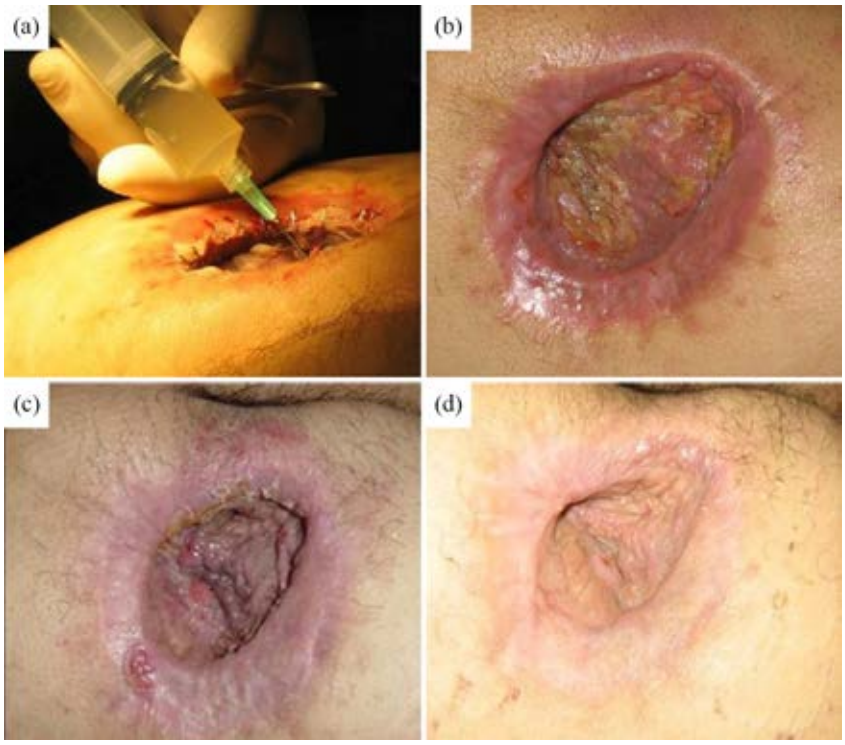


FIG. 7. Evolution of the lesion (located in the gluteus) after surgery and mesenchymal stem cell (MSC) injections. (a) The second excision, on 15 March 2006, was an autograft with MSC grafting and first injection of approximately 168 million MSC. (b) Image taken 109 days after exposure. (c) Image taken 162 days after exposure. (d) Image taken 204 days after exposure. (Courtesy of the Institute for Radiological Protection and Nuclear Safety, Percy Military Hospital.)

a dose threshold of about 1 Gy. This deterministic effect induces a set of clinical and biological manifestations in the organs and tissues affected.

To facilitate the understanding of clinical manifestations and how they overlap, ARS has typically been subdivided into three groups depending on the absorbed dose and the organs primarily involved (haematopoietic, gastrointestinal and neurovascular types). However, the overlapping of these clinical manifestations reflects the expression of an inflammatory body response affecting all the organs and tissues, which in severe cases may lead to multiple organ failure.

The last two reported examples of large field, high dose accidental irradiation, in Nesvizh [13] and Tokaimura [54], showed that after extensive, highly specialized, multidisciplinary treatment, it would be possible to 'bridge'

the acute phase of radiation induced haematopoietic and gastrointestinal damage, although multiple organ failure developed with fatal outcomes [55]. The hypothesis is that the organ system involvement is due not only to the radiation induced depletion of proliferating cells of rapid turnover tissues, but also to radiation induced changes in the vascular system, and specifically in the endothelial cells and the immune system, leading to the development of an uncontrolled systemic inflammatory response.

For instance, it appears that cytokines play a central role in mediating central nervous system response following irradiation. It has been shown that the radiation response of the central nervous system is characterized by local production of pro-inflammatory cytokines in different brain structures, causing a stimulation of inflammatory cascade, interaction with other inflammatory mediators and up-regulation of the inflammatory process that leads to neurotoxicity [56]. In the same way, radiation induced endothelial dysfunction can cause increased permeability, endothelial cell apoptosis, coagulation disorders, the expression of adhesion molecules, production of inflammatory cytokines and chemokines with transmigration of leukocytes and the release of proteases and reactive oxygen species that can contribute to tissue injury [57]. These alterations in endothelial cell integrity and function could play a critical role in mediating organ dysfunction after acute radiation exposure.

3.2.1. Diagnosis and classification

If whole body exposure to penetrating ionizing radiation is suspected, the development of ARS may be a concern. The medical consequences in most of the cases will depend mainly on the radiation dose (a function of the activity of the source, dose rate and duration of the exposure), the radiation quality and the dose distribution in the body (homogeneous/heterogeneous). ARS is a set of clinical and biological manifestations occurring after acute whole body or significant partial body irradiation with absorbed doses greater than 1 Gy (dose threshold). ARS includes the haematopoietic, gastrointestinal and neurovascular types [8, 58].

ARS is usually associated with a single acute exposure. Nevertheless, the manifestations of ARS may be expressed differently over time, whether caused by an acute (up to hours) or a protracted exposure (days) [59].

The prodromal phase of ARS develops within the first hours after exposure and is characterized by different unspecific symptoms and clinical signs, including nausea, vomiting and diarrhoea. The prodromal phase usually occurs in the first 48 hours [58]. These manifestations last for a variable period of time, depending on the dose, but usually disappear spontaneously, giving way to the so called latent phase which lasts from two to three days to three weeks, the

duration of which is inversely dependent on the dose incurred. The latent phase is followed by the critical phase (manifestation of the illness), which is in turn followed by recovery or death. When a severe exposure occurs, the latent period might be absent. The development of diarrhoea in the short period after radiation exposure indicates a grave prognosis.

The haematopoietic type of ARS (HT-ARS) is characterized by haematological alterations (leukopenia, thrombocytopenia, reticulocytopenia and, finally, erythropenia, completing pancytopenia in three to four weeks, which is characteristic for whole body exposure). The HT-ARS originates primarily from the irradiation of stem cells and progenitor cells in the bone marrow and, to some extent, from the irradiation of circulating cells, mainly lymphocytes. In the following weeks, the consequent bone marrow aplasia or hypoplasia predisposes the individual to infection, bleeding and poor wound healing.

The gastrointestinal type of ARS (GIT-ARS) is caused mainly by injuries to the stem cells of the crypts of the intestinal epithelium, causing a fall in mitotic activity, mucosa denuding, and water and mineral imbalance. Additionally, the action of bile acids on the injured intestinal mucosa aggravates the loss of fluids and electrolytes. The loss of the epithelium becomes more and more severe as a function of increasing dose. The symptoms and clinical signs are anorexia, severe nausea, vomiting, cramps and diarrhoea. Patients with severe cases of this syndrome usually die within two weeks. The cause of death is usually infection, dehydration and electrolyte imbalance as a result of destructive changes in the gastrointestinal tract and bone marrow. With doses of 6–10 Gy, septicaemia (rather than dehydration) is likely to cause death between two and three weeks after exposure. With doses of 10–15 Gy, the denuding of the small intestine mucosa exacerbates water and mineral imbalance. With doses at 12 Gy, death occurs around the tenth day post-exposure as a result of dehydration and water and mineral imbalance. The consequent clinical picture is of abdominal colic pain, severe bloody diarrhoea, bacteraemia, sepsis, hypovolemic shock and death [60].

The neurovascular type of ARS (NVT-ARS), also called cerebrovascular, occurs after irradiation at very high doses in the range of 20–30 Gy. Prodromal manifestations (nausea and vomiting) are almost immediate, followed soon by neurological and vascular manifestations that lead to death a few days after exposure. Most of the individuals suffering such lethal exposure present fever, hypotension, rapidly progressive severe oedema and major impairment of cognitive function [61]. Histological evidence of microvascular and cerebral oedema indicates that the manifestations of the NVT-ARS result from intracranial hypertension. A massive vascular leakage leading to irreversible vasoplegic shock is also an important component of the pathophysiology of this condition.

While the precise aetiology of radiation induced vomiting remains unknown, the time of onset of this manifestation and its severity after radiation exposure has been considered to be of interest as a clinical dose indicator and of importance as a triage tool in mass casualty events [62]. Nevertheless, more reliable methods for after the fact assessment of radiation dose are needed to complement the use of time to emesis for triage purposes [63].

Though most patients who have been exposed to acute whole body (or large body volume) doses of penetrating photon radiation of about 1.0 Gy will experience radiation induced nausea/vomiting, the onset and severity of this symptom is dose and dose rate dependent. Vomiting is a complex, multifaceted event that requires the coordinated response of neural, respiratory and gastrointestinal centres. Vomiting is not specific for radiation exposure. It may occur with many clinical disorders in mass casualty events involving physical trauma, psychological stress, and biological and chemical threats [63]. While time to vomiting is a rapid and inexpensive method for estimating the radiation dose, caution is necessary because it is imprecise and may lead to a very high false positive rate. Therefore, other methods for the assessment of radiation dose also need to be used. These include lymphocyte and neutrophil kinetics in peripheral blood, experimental dose reconstruction, numerical dose reconstruction, ESR, cytogenetic dosimetry, biochemical markers, and clinical evolution [21, 23, 64]. The existing limitations for dose estimations based on time to vomiting after radiation exposure notwithstanding, this parameter may play an important role, especially in mass casualty events for triage and management decisions. Table 7 presents the relationship between time to vomiting and dose estimation.

3.2.2. Medical assessment and dose estimation

A complete emergency history must be carefully obtained from the patient or, if that is not possible, from other individuals involved (first responders, relatives, witnesses, etc.) to determine the possibility of exposure to radiation from external sources. If the history is incomplete, radiation induced manifestations need to be determined by observation of clinical manifestations. The anamnesis to be obtained will be as extensive and detailed as possible. The information needs to contain the past medical history, previous diseases and treatments (e.g. recent nuclear medicine tests), medications, allergies, personal habits (smoking and drinking to be quantified), and occupational exposure to radiation and other agents (e.g. chemicals). The patient's level of anxiety is an important factor when the history is obtained. Experience has shown that patients under stress tend to modify the history owing to multiple factors (fear of legal consequences, omission of safety procedures, economic or other consequences). It is best practice to perform the anamnesis following the usual ethical guidelines.

TABLE 7. DOSE RANGE ESTIMATION FOR WHOLE BODY EXPOSURES IN MASS CASUALTY EVENTS BASED ON TIME TO VOMITING

(adapted from Ref. [8])

Time of vomiting after exposure	Dose range estimation (Gy)	Estimated incidence of vomiting in exposed individuals (%)	Severity of ARS
No vomiting	<1	n.a.[a]	n.a.[a]
≥2 h	1–2	10–50	Mild
1–2 h	2–4	70–90	Moderate
<1 h	4–6	100	Severe
<30 min	6–8	100	Very severe
<10 min	>8	100	Lethal

[a] n.a.: not applicable.

Although some patients may need urgent treatment because of their poor general condition or owing to severe conventional trauma, whenever patient condition allows, a comprehensive physical examination is advisable as soon as possible. A chronological register of signs and symptoms needs to be compiled, as well as the photographic documentation of the probable irradiated body regions. Attention should be paid to the following clinical manifestations:

— Vital signs (fever, hypotension, tachycardia, tachypnea);
— Neurological manifestations (impaired cognitive function, level of consciousness, ataxia, papillary oedema, motor/sensory deficits, presence or absence of reflexes);
— Hydration condition, mucosae examination (conjunctivae, oropharynx);
— Skin, nails and hair (skin lesions, erythema, bullae, ulcers, nail alterations, epilation, bruising, ecchymosis);
— Other manifestations, such as abdominal tenderness.

The frequency of the clinical evaluation needs to be established taking into account the patient's medical condition, and needs to be done daily at the very least.

It is advisable that pregnant women, or women suspected to be pregnant, as well as children, receive a faster initial dose assessment by a health/medical physicist considering that embryos, fetuses and children are at highest risk of eventually developing radiation effects. Table 8 summarizes the basic laboratory tests when whole body exposure is suspected and provides a brief description of the rationale for those tests. Correlation with the threshold doses can be found in Tables 6 and 7.

Of the pathological changes that may follow after whole body radiation exposure, none is more striking than the rapid fall in the number of circulating lymphocytes. This effect is manifested within a few hours of a single short exposure.

The absolute lymphocyte count is of special importance (especially in mass casualty events for individuals with nausea and vomiting) and needs to be obtained ideally every 6–8 h for at least 2 d and then every 12 h for an additional 5 d. The absolute lymphocyte count could be used as an effective criterion for survival prognosis (see Table 9).

The reduction in the absolute lymphocyte count is dose dependent and may be used for evaluating exposed individuals; however, other blood cells also present changes in their normal values. The neutrophil/lymphocyte ratio increases over the first few days post-exposure. Both are sensitive indicators of radiation dose [21].

One of the main causes of death after whole body radiation exposure is neutropenia related infection. The granulocyte levels reach a nadir 5–10 d post-irradiation, and the level of depression corresponds to the radiation dose received. The length of time before recovery is also dose dependent [65, 66].

Figure 8 shows postulated neutrophil behaviour in circulating blood after homogeneous whole body radiation exposures (<1, 1–2 and >5–6 Gy) [67]. The kinetics of neutrophils and platelets in circulating blood are extremely important not only for prognosis but to indicate the need for specific medical interventions, as listed in the second row of Table 8.

Red blood cells have an estimated mean life span of 120 d. They are radioresistant, but circulating reticulocytes are sensitive to radiation exposure. Moreover, radiation induced micronucleated reticulocytes represent radiation genotoxic effects on the bone marrow progenitor and precursor cells for erythropoiesis.

Platelets have a life span of 9–12 d. The platelet levels fall after whole body irradiation. The decrease in platelet count is also dose dependent and

TABLE 8. BASIC INITIAL EVALUATION IN CASES OF POSSIBLE WHOLE BODY EXPOSURE TO RADIATION

Laboratory tests	Rationale
Haemogram/CBC[a] and analysis of reticulocytes	To estimate the exposure dose range; initial counts establish a baseline; subsequent counts reflect the degree of injury.
CBC[a] and differential with absolute lymphocyte counts every 6 h for 48 h when the history indicates possibility of whole body irradiation	The kinetics of neutrophils and platelets in circulating blood are extremely important for prognosis and also to indicate the need for specific medical interventions, such as the administration of cytokines (e.g. G-CSF[b] or GM-CSF[c]), platelet transfusions and the use of antibiotics.
Serum amylase	Irradiation of the salivary glands produces a rapid increase of salivary amylase in serum, released by the highly radiation sensitive serous cells of the glands. Serial assays may serve as an indicator of the upper neck region dose and indirectly of the whole body dose [63].
C-reactive protein	Inflammation marker, associated with the severity of the exposure.
Biological dosimetry (chromosomal aberration analysis from cultured circulating lymphocytes, mainly to estimate the frequency of dicentric chromosomes)	To provide timely assessments of radiation exposure, particularly when physical dosimetry is unavailable or unreliable. For mass casualty events involving public exposure to ionizing radiation, it is relevant to rapidly provide dose estimates to support the medical management of casualties. Different strategies have been proposed to provide faster counting of metaphases; this will depend on each laboratory.

[a] CBC: complete blood count.
[b] G-CSF: granulocyte colony stimulating factor.
[c] GM-CSF: granulocyte macrophage colony stimulating factor.

their dynamics must be carefully observed for the appropriate management of radiation induced thrombocytopenia.

The irradiation of the salivary glands produces a rapid increase of salivary amylase in serum, released by the highly radiation sensitive serous cells of the glands. However, an increase in amylase concentration is expected after 24 h in

TABLE 9. ABSOLUTE LYMPHOCYTE COUNT 48 h AFTER WHOLE BODY EXPOSURE AND SURVIVAL PROGNOSIS

Absolute lymphocyte count per μL	Severity grade of ARS	Survival prognosis
700–1000	Mild	Good
400–700	Moderate	Probable
100–400	Severe	Possible at a highly specialized treatment centre
<100	Very severe	Poor

case of significant radiation exposure (above 2 Gy) to the whole body or upper part of the body including the neck area [67–70].

Plasma Flt-3 ligand concentration has been proposed as a biological marker of bone marrow damage [69]. The Flt-3 ligand is a cytokine that acts mainly on haematopoietic and lymphoid stem and progenitor cell proliferation and differentiation. Dose effect, time effect, volume effect and high correlation of this parameter to the intensity of bone marrow damage, as observed in different animal models, make the plasma Flt-3 ligand a potentially useful physiological marker for radioinduced bone marrow damage monitored during the medical management of the irradiated patient [71, 72]. C-reactive protein and serum amyloid A have also been demonstrated to be possible early phase and prognostic indicators in preclinical studies [73].

Plasma citrulline, a nitrogen end product of glutamine metabolism in small bowel enterocytes, has been suggested as a marker of radiation induced small bowel epithelial cell loss in mice after single dose whole body irradiation. Indeed, during fractionated radiotherapy for abdominal or pelvic cancer, the citrulline concentration decreased significantly as a function of the radiation dose and the volume of small bowel treated. Plasma citrulline may be a simple objective marker for monitoring epithelial cell loss, a major event in GIT-ARS [74].

Other tests that can be performed for baseline information and future evaluation of possible late radiation related effects are: sperm count (hypospermia or azoospermia), eye examination (lens opacities/cataracts) and thyroid function tests (hypothyroidism).

Dose estimation by means of 'biological dosimetry' (biodosimetry) is a method to estimate absorbed dose of radiation for an individual using biological markers induced by radiation, such as chromosome aberrations in the lymphocytes of peripheral blood. Dicentric chromosome and ring assay is based on the analysis of solid stained dicentric chromosomes and has been used since the mid-1960s. The intervening years have seen great improvements, bringing the technique to a point where dicentric analysis has become a routine component of the evaluation of persons accidentally exposed to whole body radiation. Among the assays for biological dosimetry, chromosomal aberration analysis (dicentric scoring) from cultured circulating lymphocytes is the most widely accepted and reliable. The dose–response relationships are well established in many laboratories around the world. The lower limit of dose detection by dicentric assay for lower linear energy transfer radiation is 0.1–0.2 Gy, and the upper limit is about 5 Gy [23].

There are limitations for using this technique in cases of partial body irradiation. The presence of chromosomal aberrations might indicate a radiation injury, but does not allow a precise dose assessment. In addition, doses from internal radiation sources cannot always be assessed, owing to the varying distributions of different radionuclides [8].

While dicentric scoring continues to be the gold standard for biological dosimetry, other biological dose reconstruction techniques (assays) can be used under special circumstances [23].

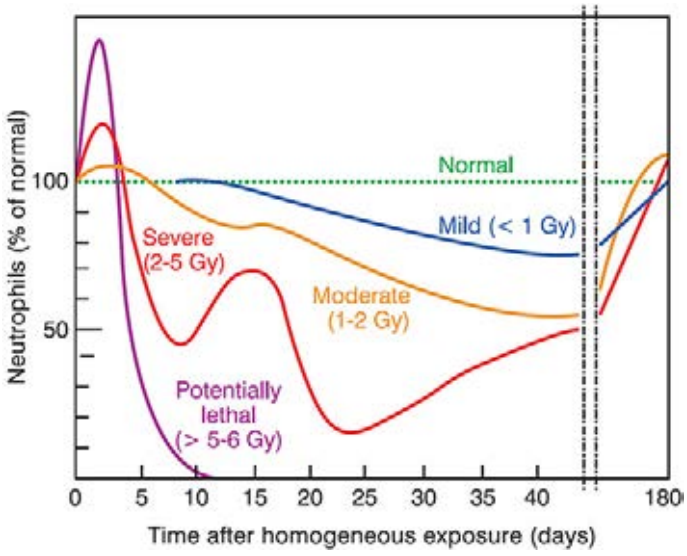


FIG. 8. Postulated neutrophil behaviour in circulating blood after homogeneous whole body radiation exposure [67].

Ionizing radiation induces the formation of acentric chromosome fragments and, to a small extent, non-segregation of whole chromosomes. Acentric chromosome fragments and whole chromosomes that are unable to interact with the spindle lag behind at anaphase and, as a result, they are not included in the main daughter nuclei. A lagging chromosome fragment or whole chromosome forms into a small separate nucleus; hence the term micronucleus [22]. Micronucleus assay is less specific for radiation exposure than dicentric analysis. There is also a high inter-individual variability in the spontaneous frequency of micronuclei (influence of factors related to age and lifestyle), and its sensitivity in the low dose region is poor. In any case, micronucleus assay could be used in the dose range of 0.3–5 Gy, and it has the potential for a high level of automation.

Premature chromosome condensation (PCC) techniques can induce a condensation of the chromosomes in quiescent and cycling cells, either by fusion with mitotic cells or by chemical treatment. In quiescent cells, the number of excess PCC fragments (>46 chromosomes for humans) is scored. In cycling cells, it is also possible to score ring chromosomes, dicentrics and translocations if the PCC assay is combined with fluorescent in situ hybridization, chromosome painting or c-banding. PCC has been reported to be most useful for assessing high dose acute exposures to low linear energy transfer radiation. Dose response data from 0.2 to 20 Gy have been acquired using the PCC fragment assay, whereas with the PCC ring method, the sensitivity ranges from 1 to >20 Gy [23].

Ionizing radiation generates large numbers of unpaired electron species. While most of these react immediately and disappear, in some materials in which diffusion is limited, the unpaired electrons can persist for long periods. This is the basis for ESR. Teeth are especially attractive as a sample for the method because the signal intensity is stronger in them and because of the higher amount of crystalline matrix in enamel [75]. Fingernails, clothes buttons and other materials could also be used as alternative samples for ESR if teeth are not feasible or available [76, 77]. ESR has also been considered as a possible triage method in case of a radiation mass casualty event [78], but ESR laboratories are generally limited to specialized centres, and are not usually found in hospitals. Therefore, arrangements need to be made beforehand between the hospital and other institutions if the use of this technique is also considered for dosimetry following an emergency.

Whole body dose assessment may be a challenge, especially in cases of possible multiple casualties. Whenever possible, biological, mathematical and physical reconstruction methods will provide more precise dose estimations. In this respect, international assistance and cooperation may provide resources and support to the affected Member State, as demonstrated in several radiological accidents [32–36].

It is important to mention that all methods of dose assessment are important for medical management, providing complementary and relevant information which will influence the treatment and therefore the prognosis of these patients. A brief summary of dose assessment methods is given in Table 10.

3.2.3. Treatment

In general terms, persons exposed to whole body radiation with an absorbed dose lower than 1 Gy can be followed up as outpatients. For this decision to be taken, it is essential to consider the kinetics of blood cells, especially the variability in the blood curves of lymphocyte counts, the most useful single parameter to rule out severe bone marrow radiation injury within the first 48 h after exposure. Additionally, the clinical decision whether to admit the patient is based on his/her medical status, as the existence of comorbidities and their respective severity may influence the health status of the patient. Also, if the

TABLE 10. SUMMARY OF DOSE ASSESSMENT METHODS FOR PATIENTS POTENTIALLY EXPOSED TO RADIATION

Dose assessment method	Example	Applicable
Clinical	Evaluation of clinical manifestations (vomiting, nauseas, erythema, fever, etc.)	At the scene and at the hospital
Biological	Laboratory (CBC[a], reticulocytes, amylase, C-reactive protein, etc.)	At the hospital
	Chromosomal analysis (dicentric, micronucleus assay, PCC[b], etc.)	In a specialized centre
Physical	External dosimetry (if dosimeters are available) ESR[c] (not suitable for mass casualties, evaluation case by case) Monte Carlo reconstruction Internal dosimetry methods (urine, faeces samples, etc.) when suspecting internal contamination	In a specialized centre

[a] CBC: complete blood count.
[b] PCC: premature chromosome condensation.
[c] ESR: electron spin resonance.

number of patients is significant, it may be necessary to use more flexible criteria for indicating hospitalization. Complex cases of ARS will demand in-hospital handling in specialized referral centres, as specified in Table 11.

Management of ARS at the prodromal phase is based on the symptoms exhibited. For patients suffering from persistent vomiting, the prescription of ondansetron (or another compound from the same 5-HT_3 antagonist family) and dopamine-D_2 antagonists is usually very efficient.

The latent phase of ARS is relatively asymptomatic, except for cases involving high whole body doses (>6 Gy). A medical challenge in the latent phase is identifying accidental radiation exposure, and deciding whether any measure will be adopted to reduce the severity and the duration of the high risk aplastic period that follows [79].

TABLE 11. FACILITIES FOR IN-HOSPITAL MANAGEMENT OF SEVERE CASES OF ACUTE RADIATION SYNDROME

Localization	Facilities
At the hospital	Specialized care unit for immunosuppressed patients with laminar flow and absolute HEPA[a] filtering system Intensive care unit Haematology and haemotherapy (leukoreduced and irradiated blood products, including availability for platelet infusions) HSCT[b] centre Specialized departments (e.g. gastroenterology, infectious diseases, paediatrics, mental health and neurology) Medical imaging technologies (magnetic resonance imaging, thermography, nuclear medicine tests) Other laboratory technologies, which could include HLA[c] typing and other specific tests
Not necessarily at the hospital	Bioassay laboratory Biological dosimetry laboratory ESR[d] laboratory External dose assessment laboratory

[a] HEPA: high efficiency particulate air.
[b] HSCT: haematopoietic stem cell transplantation.
[c] HLA: human leucocyte antigen.
[d] ESR: electron spin resonance.

3.2.3.1. Haematopoietic type acute radiation syndrome

The treatment of HT-ARS is focused on supporting the spontaneous (autologous) or stimulated recovery of the hypoplastic bone marrow, and on preventing or treating infectious/haemorrhagic complications from this condition.

General supportive care includes admission at a specialized care unit for immunosuppressed patients with laminar flow and absolute high efficiency particulate air (HEPA) filtering systems. The conventional care protocols for immunosuppressed patients will be applied as long as necessary and determined on an individual basis by the medical team. The prevention and treatment of infections during the neutropenic period is a fundamental therapy principle that is based on protocols very similar to those used for the management of neutropenia of other aetiology.

Neutropenia in adults is usually defined as a count of ≤1700 neutrophils/μL of blood. The cell count indicating neutropenia in children varies with age. 'Severe' neutropenia is defined as an absolute neutrophil count of <500 cells/μL. The term 'profound' is sometimes used to describe neutropenia in which this count is <100 cells/μL.

Routine intestinal sterilization is not universally recommended, but if a decision is made for this procedure, quinolone is the drug of choice if no contraindication exists for its use. In one study, the use of fluconazole (or other alternative antifungal agents) caused the colonization of non-*Candida albicans* species [80].

ARS neutropenic patients with suspected infection (those presenting fever) must undergo an objective clinical and laboratory evaluation to assess their general condition. This will allow classification of the patient as 'low risk' or 'high risk' for infection, and identification of the origin of the process. A recommended approach for the medical management of ARS includes the following [81]:

— Complete blood cell count with differential leukocyte and platelet counts;
— Serum levels of creatinine and blood urea nitrogen;
— Electrolytes;
— Hepatic transaminase (aminotransferase) enzymes and total bilirubin;
— Amylase and C-reactive protein;
— At least two haemocultures, with a set collected simultaneously from each lumen of an existing central venous catheter, if present, and from a peripheral vein site (two haemoculture sets from separate venepunctures to be sent if no central catheter is present);
— Culture specimens from other sites of suspected infection to be obtained as clinically indicated;

— A chest radiograph for patients with respiratory signs or symptoms.

A neutropenic fever is a single oral temperature of 38.3°C or a temperature of greater than 38.0°C sustained for more than 1 h in a patient with neutropenia. The recording of rectal temperature is not advised because of the risk of mucosa damage and bacteraemia.

Patients with febrile neutropenia are classified as 'high risk' if any of the following conditions are met:

— The condition is anticipated to be prolonged (>7 d), or neutropenia is profound (absolute neutrophil count <100 cells/μL).
— The absolute monocyte count is <100 cells/μL.
— Peak temperature is >39.0°C.
— Intravenous catheter site infection exists.
— Significant medical comorbidities, including hypotension, pneumonia, new onset abdominal pain or neurological/mental changes are present.

Those who do not have any of the above conditions are categorized as 'low risk'.

Febrile neutropenia can be one of the complications of HT-ARS, and thus the treatment will follow the established protocols for medical management of this syndrome. There are several published protocols; some of them consider treatment with antibiotics and, depending on the case, with antiviral or antifungal therapy. In any case, owing to the variability among protocols from different hospitals, best practice is for health care professionals to be aware of national guidelines for treatment. A multidisciplinary approach and consultation with an infectious disease specialist should be considered, if available [82].

Another extremely important aspect in the treatment of ARS concerns the bone marrow aplasia itself. Ionizing radiation suppresses mitosis in haematopoietic stem and progenitor cells and their progeny in a dose dependent manner [83]. In this regard, the distribution of the irradiation plays an important role: whole body exposures are never 'uniform' in the sense that all regions of the body absorb the same radiation doses. Residual haematopoiesis is the rationale for cytokine based treatment of radiation induced myelosuppression. Consequently, physical dosimetry is extremely important to help in the identification of areas that were not irradiated, or that were less severely irradiated (exposure heterogeneity).

The administration of cytokines (granulocyte colony stimulating factor (G-CSF) or granulocyte macrophage colony stimulating factor (GM-CSF)) is relevant in the treatment of the irradiated haematopoietic system (bone marrow specifically). It has been indicated when the haematopoietic system is the only organ critically affected in its function after a whole body exposure. Health

care providers need to consider initiating cytokine therapy for exposures of >2 Gy or a significant decrease in the absolute lymphocyte count, or when it is anticipated that neutropenia of <500 cells/μL will persist for >7 d. Experts recommend that cytokine therapy with G-CSF or GM-CSF be initiated within 24 h of exposure [29, 39, 40, 83, 84].

Consensus treatment guidelines have been established which recommend that G-CSF or its pegylated form, pegfilgrastim, be administered soon after exposure (when bone marrow suppression is anticipated), and until granulocyte or platelet recovery occurs [83]. A more individualized approach is to administer G-CSF or GM-CSF when the absolute neutrophil count is <500/μL, with daily administrations until it reaches 1000/μL. The doses of cytokines in adults are presented in Table 12 [27].

Prolonged anaemia, significant decline in haemoglobin concentration or both may be candidates for treatment with erythropoietin. Consideration should be given to the administration of oral iron supplementation in individuals receiving erythropoietin stimulating agents. These agents may be considered in the lowest dosage that induces a sufficiently high haemoglobin level to render blood transfusion unnecessary (weak strength recommendation with a low quality of evidence) [29]. Substitution therapy relates to the use of blood components, especially platelets and red cell concentrate infusions. The criteria for substitution therapy according to the Medical Treatment Protocols for Radiation Accident Victims as a Basis for a Computerized Guidance System (METREPOL) scale are shown in Table 13 [27, 85].

Haematopoietic stem cell transplantation (HSCT) has been used for a long time to treat a variety of haematological and non-haematological disorders. If it turns out that spontaneous (or cytokine assisted) bone marrow recovery after ionizing radiation exposure is impossible, a proper alternative could be HSCT. Its effectiveness and feasibility depend on several factors, including logistical

TABLE 12. USUAL DOSES FOR CYTOKINE ADMINISTRATION IN ADULTS

Cytokine	Dose
Filgrastim (G-CSF)	10 μg · kg^{-1} · d^{-1} subcutaneously
Pegfilgrastim (pegylated G-CSF)	Two doses, 6 mg each, subcutaneously one week apart
Sargramostim (GM-CSF)	5–10 μg · kg^{-1} · d^{-1} subcutaneously or 200–400 μg · m^{-2} · d^{-1}

TABLE 13. CRITERIA FOR SUBSTITUTION THERAPY FOR HAEMATOPOIETIC TYPE ACUTE RADIATION SYNDROME

Patient's individual condition	Threshold value	Substitution therapy
Close monitoring possible, no other complication, no bleeding	Platelets: 10 000/μL	Irradiated and leukoreduced platelet concentrates
Close monitoring not possible, increased risk of manifest bleeding	Platelets: 20 000/μL	Irradiated and leukoreduced platelet concentrates
Additional trauma, surgery, mass transfusion, cerebral oedema	Platelets: 50 000/μL	Irradiated and leukoreduced platelet concentrates
Anaemia	Haemoglobin: 10 g/dL	Irradiated and leukoreduced packed red cells

conditions (availability of a compatible donor) and the patient's individual situation (the existence of comorbidities such as trauma and thermal burns, and the possible association of other radiation induced pathologies such as severe LRI and gastrointestinal injury) [85–87].

Literature reviews show that HSCT in patients exposed to radiation has not been a very effective therapy, mostly because of concomitant severe comorbidity associated with bone marrow aplasia. HSCT could be considered for patients severely affected with ARS (i.e. exposed to 7–10 Gy) who do not show evidence of haematopoietic recovery, are not affected by severe trauma or burns, do not have GIT-ARS and have an appropriate donor [86, 87]. Considering these caveats, there is "a weak recommendation for the administration of allogeneic hematopoietic stem/progenitor cells from the bone marrow, peripheral blood, or cord blood of patients who are unresponsive to cytokine therapy and in whom there is no significant injury to a nonhemopoietic organ system" [29].

When HSCT is considered a therapeutic option, cells will be preferably obtained in the following order of priority: from a human leukocyte antigen (HLA) identical sibling; from another HLA identical member of the family; and from an HLA identical unrelated donor.

3.2.3.2. Gastrointestinal type acute radiation syndrome

After the bone marrow, the gastrointestinal tract ranks as the organ system most sensitive to moderate dose radiation exposure that can cause ARS. In

fact, if part of the bone marrow is shielded, then the gastrointestinal tract can become the critical organ system for survival. Consequently, radiation induced injury of the gastrointestinal tract has been a topic of radiobiological interest for decades [22, 86–88].

The classic GIT-ARS in humans occurs after a whole body radiation dose over 6 Gy. Currently, this condition is not curable and treatment focuses only on the symptoms and is palliative. The effect of total body ionizing radiation on the digestive tract is dose and time dependent. At low doses (1.5 Gy), only a short prodromal phase consisting of nausea, vomiting and gastric suppression can be observed. At doses greater than 6 Gy, the prodromal phase is more marked, and is followed by a 2–5 d remission period characterized by diarrhoea and haematochezia. This gastrointestinal syndrome is superimposed onto radiation induced bone marrow suppression. The combination of GIT-ARS and HT-ARS results in dehydration, anaemia and infection, leading eventually to irreversible shock and death. The treatment of prodromal symptoms is based on the administration of antiemetics and gastrokinetics, although an effective treatment devoid of side effects is not yet available for human therapy. The treatment of GIT-ARS remains difficult and is unsuccessful after exposure to total body doses greater than 8–10 Gy. Supportive therapy to prevent infection and dehydration may be effective if restoration or repopulation of the intestinal and bone marrow stem cells occurs.

The classical ‘target cell’ model of intestinal radiation toxicity attributes radiation injury to the death of clonogenic crypt epithelial stem cells. Other elements within the complex environment of the intestine also contribute to organ dysfunction: the enteric mucosae, immune system, microvasculature and nervous system, as well as the complex community of resident bacteria and fungi [89–92]. A schematic representation is shown in Fig. 9.

Although all cellular compartments may contribute to and modulate organ dysfunction, the key event in the pathophysiology of intestinal radiation toxicity is enterocyte depletion, with possible vascular damage contributing at higher radiation doses [87, 92, 94]. Enterocyte depletion can lead to mucosal barrier breakdown, mucositis and secretory diarrhoea. Indeed, death from pure gastrointestinal radiation toxicity after total abdominal irradiation is the result of massive fluid and electrolyte loss, indicating a primary need for supportive care [89, 95].

Even at radiation doses below the threshold for full blown GIT-ARS, mucosal barrier breakdown allows bacteria to translocate into the circulation, which can cause sepsis and death in the context of concomitant immune suppression [89, 96].

In the long term, the remodelling of tissues after radiation damage alters the structure, motility and absorption of the gut and fibrosis renders it more rigid and

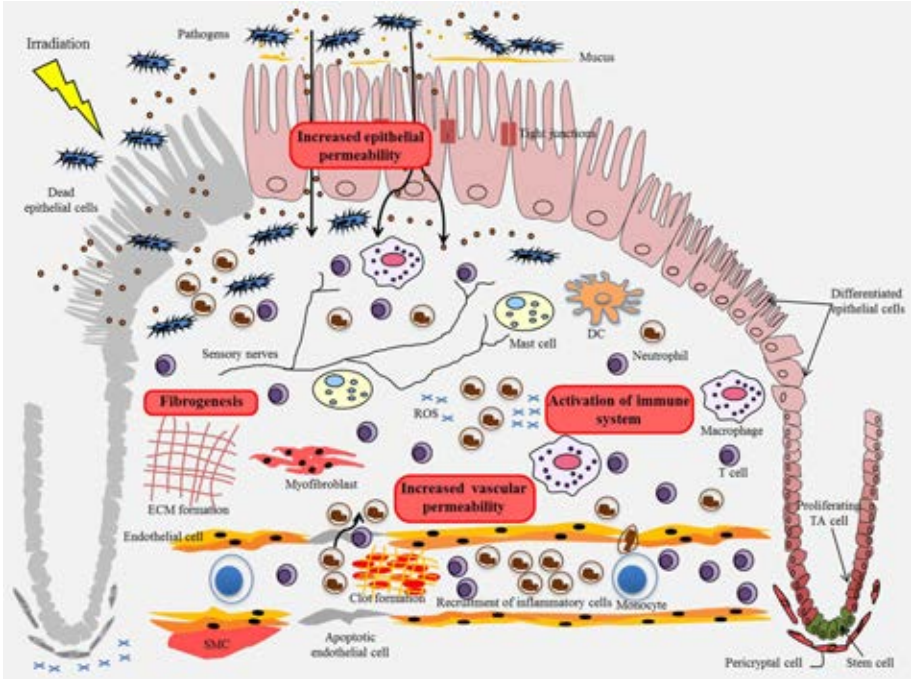


FIG. 9. Pathophysiology of the gastrointestinal type of acute radiation syndrome. The intestinal alterations induced after irradiation are shown in this schematic representation. This view highlights the complexity of radioinduced pathology with the interconnections of events: modification of the epithelial cell compartment; activation of the vascular compartment; and initiation and perpetuation of the inflammatory process, leading ultimately to fibrogenesis. DC — dendritic cell; ECM — extracellular matrix; ROS — reactive oxygen species; SMC — smooth muscle cell; TA — transit amplifying. (Adapted from Ref. [93].)

susceptible to adhesions, stenosis and impaired function [89, 96]. The intestine responds to localized radiation, or to changes in other organs that influence its structure or function; some structural parameters respond differently to different radiation schedules [97].

Systemic effects may include: malnutrition from malabsorption; bowel obstruction from ileus; dehydration, cardiovascular collapse and electrolyte derangements from fluid shifts; anaemia from bone marrow aplasia; damage to the intestinal mucosa; microcirculation disfunction with subsequent gastrointestinal bleeding; and sepsis and acute renal failure.

While progress has been made in the medical management of radiation induced injury to the bone marrow and immune system, advances in treatments for gastrointestinal injury have been far fewer. Long term survival is unlikely in individuals with full fledged GIT-ARS [98].

Supportive measures in the overall management of patients with GIT-ARS include fluid replacement, antibiotic therapy and prophylaxis against ulceration of the gastrointestinal tract. Invasive procedures involving the gastrointestinal tract will be performed judiciously and as an exception or not at all, since the intestinal mucosa is friable and prone to sloughing and bleeding after mechanical manipulation.

The therapeutic arsenal is limited for the management of GIT-ARS and includes stress ulcer prophylaxis (sucralfate, H2 blockers, proton pump inhibitors), enteral or parenteral nutrition, proper handling of vomiting, diarrhoea and motility disturbances, and fluid and electrolyte replacement [98].

Small intestinal epithelial cells have a very high rate of cell turnover, and glutamine, a conditionally essential amino acid, is their preferred energy source. Theoretically, glutamine could decrease intestinal permeability, although this kind of benefit has not been demonstrated in patients with Crohn's disease [97]. The possibility has been raised of indicating glutamine as an intestinal barrier and an agent to improve immunological functions in GIT-ARS [98, 99].

High dose whole body irradiation, as in severe cases of GIT-ARS, causes multiple organ injury that originates in many cases from multiple organ dysfunction syndrome, and consequently multiple organ failure, with an irreversible fatal outcome [100, 101].

Patients with high exposure doses facing serious prognoses need to be identified for appropriate management. The possibility of survival after acute irradiation to the whole body with a single dose higher than 10–12 Gy is extremely low. In such cases, it is more appropriate to provide palliative measures, rather than active treatment. Such care includes attention to pain management and general comfort, as well as administration of antiemetic and antidiarrhoeal agents (e.g. loperamide, diphenoxylate). Psychological support and spiritual care, if requested, are essential not only for the patient but also for family and friends who may be experiencing traumatic grief [58].

3.2.3.3. Neurovascular type acute radiation syndrome

As previously stated, NVT-ARS typically occurs at absorbed doses greater than 20–30 Gy. Currently, NVT-ARS is not curable and treatment focuses on symptoms and palliation. It is characterized by the immediate onset of severe prodromal manifestations, such as disorientation, confusion and prostration, and may be accompanied by loss of balance and seizures. A brief latent period lasting several hours is typically followed by severe incapacitation. Within 5–6 h, watery diarrhoea, respiratory distress, hyperpyrexia and vasoplegic shock can occur, leading to severe irreversible oedema (primarily in the brain, but possible anywhere in the body) resulting in death within one to five days.

At present, management of NVT-ARS is limited to supportive care. Depending on the availability of resources, patients may receive palliative care at a routine care unit of the hospital [28].

3.2.4. Medical follow-up

Patients surviving ARS are to be carefully followed up with the main objective of promptly identifying possible malignant development. This may help in validating any novel therapeutic modalities adopted during the treatment.

In principle, follow-up is to be established on a lifelong basis. The medical approach to be used will depend on the clinical case, the therapies used and the individual characteristics of the patient, such as sex, age at the time of exposure, comorbidities and social situation. Any specific situation related to the exposure is considered (i.e. local overexposure to the eyes, thyroid, bone marrow, gonads, etc). In addition, general counselling can be provided on the importance of following a healthy lifestyle, with the focus on preventing diseases and promoting awareness of conditions that have a better prognosis if they are identified before clinical manifestations occur or their complications are observed.

3.2.5. Case study: The accident at Fleurus, Belgium

On 11 March 2006, in a facility used for the sterilization of medical devices in Fleurus, Belgium, an operator entered the irradiation room following an alarm to close a cell door that was open. Unknown to the operator, the ^{60}Co sources (activity: 2.96×10^{16} Bq, dose rate: ~5000 Gy/h) were partly out of the security position at that time [17].

A few hours after the incident, the individual started feeling nauseous and began vomiting. This was suggestive of ARS, but the operator did not make the connection with possible irradiation. Eighteen days after the incident (29 March 2006), the patient consulted a doctor because of persistent nausea, transitory but refractory diarrhoea, persistent headache and hair loss. A possible accidental exposure was suspected and the patient was transferred to the haematology department of the Percy Military Hospital in France on 31 March 2006 [17].

The dose reconstruction (Fig. 10) provided important information, concluding that a whole body irradiation occurred with an exposure time estimated at 22 s, and consequently an absorbed dose in line with the clinical manifestation of an ARS (approximately 4.2–4.8 Gy by biological dosimetry). Physical dosimetry was performed based on both experimental reconstruction and numerical reconstruction by on-site dose evaluation using a dosimetric phantom, recreating the route taken by the operator during the accident [17].

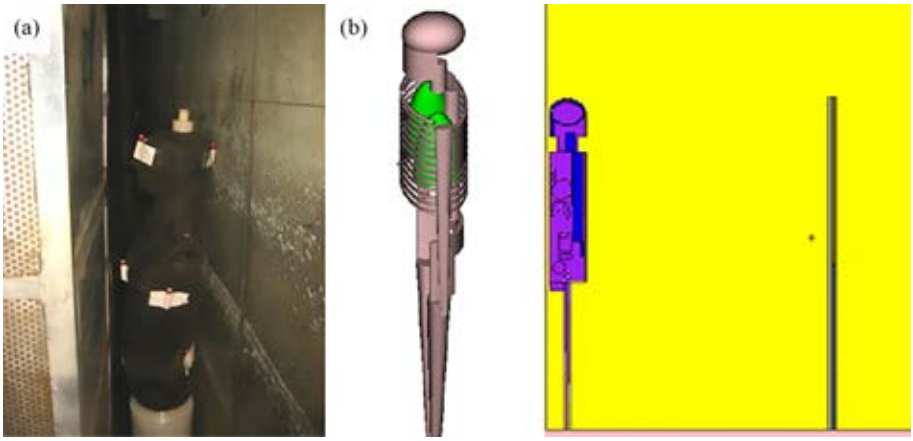


FIG. 10. Dose assessment and reconstruction of the Fleurus accident. (a) Dose evaluation in the reconstruction of the scenario of the accident using a dosimetric phantom (measures were done on the GAMMIR 2 installation). (b) Numerical reconstruction, including the numerical phantom.

Owing to the characteristics of the irradiation, the possibility of an autologous haemopoietic recovery was considered for this patient. Therefore, the heterogeneity of the irradiation needed to be investigated. High exposure heterogeneity was predicted based on the simulation of the dose gradient. Radiation exposure was characterized by a sharp gradient as a function of both ventral/dorsal and vertical axes (Fig. 11). Thus, these data provided important information that helped to determine the medical management of the patient's ARS.

The radiation dose and its distribution in the patient's body supported two main considerations. The first was the possibility that in this case the ARS could be purely of the haematopoietic type. Second, there was a possibility of residual haematopoiesis.

The possibility of multiple organ failure was considered for this patient during the initial hospitalization in Percy Military Hospital, in line with the literature and the considerations included in the European approach for the medical management of mass radiation exposure [65–67]. Fortunately, multiple organ failure was excluded and the patient was diagnosed exclusively with a haematopoietic syndrome. The severity of the syndrome was then evaluated based on the METREPOL scale [85]. Since the patient experienced a 26% drop in haemoglobin level (8.5 g/dL), a platelet low of 2000/mm^3, a leukocyte low of 400/mm^3, and septicaemia 8 d after hospitalization (*Pseudomonas aeruginosa*), severe haematopoietic syndrome (grade 4) was diagnosed [17].

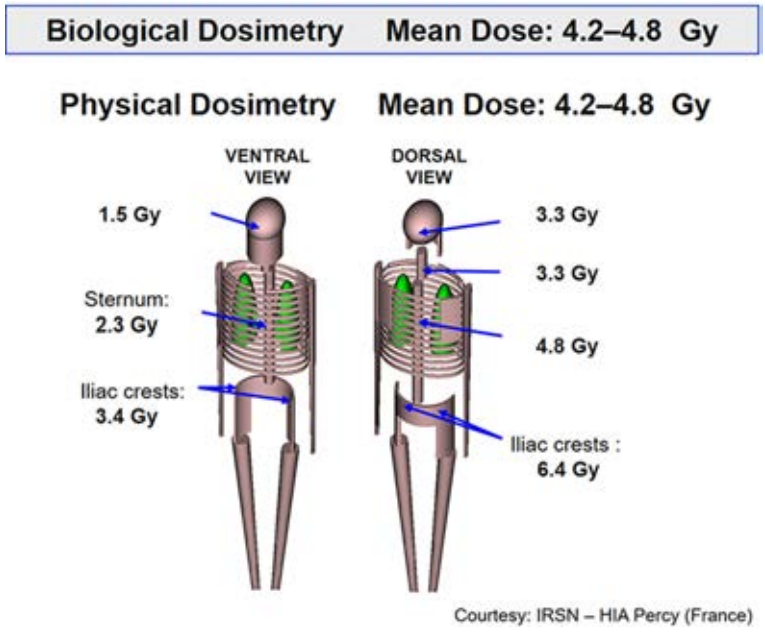


FIG. 11. Dose assessment of the patient involved in the Fleurus accident, highlighting the heterogeneity of this irradiation. Biological and physical dose estimation values are shown [17].

The patient experienced a haematopoietic syndrome. In line with European consensus [67], treatment with pegylated G-CSF (pegfilgrastim) was initiated as soon as possible after diagnosis (day 28 after exposure). Moreover, on days 32 and 33, the patient was injected with pegylated erythropoietin (darbepoetin alfa 500) and recombinant human stem cell factor (ancestim), respectively. Platelet transfusions were initiated on day 21. Since stem cell factor had not yet received marketing authorization, the authorization of a one-off compassionate use of this cytokine for this patient was obtained from the Agence française de sécurité sanitaire des produits de santé, the French regulatory agency. The cytokine treatments had an immediate positive effect and the blood cell counts of the patient recovered rapidly. Complete resolution of the haematopoietic syndrome was observed on day 43.

The heterogeneity of the irradiation and the possibility of autologous haematopoietic recovery must be considered; if severe aplasia persists under cytokines for more than 14–21 days, the possibility of HSCT needs to be considered. HSCT is never an emergency treatment and is not indicated for patients with irreversible multiple organ dysfunction syndrome.

4. CONTAMINATION WITH RADIONUCLIDES

Contamination with radionuclides may be external or internal, or both. Contaminated patients can have radioactive material deposited on skin surfaces, in wounds or internally (ingested, inhaled or absorbed) [21].

4.1. EXTERNAL CONTAMINATION

External contamination occurs when radioactive material from an unsealed or broken source is deposited on skin or clothing. It is assessed by direct monitoring of the skin and clothing. Patients who present external contamination of the skin, clothing or excreta have the potential for spreading the contamination, and special precautions must be implemented to prevent this. Nevertheless, lifesaving actions always need to be performed without delay, even if external contamination is suspected or is present. The risk is limited for the responders when they use universal biosafety precautions.

4.1.1. Management

For persons who require urgent medical attention and subsequent urgent transport to hospitals or other medical centres, priority will be given according to their medical condition, independently from contamination considerations. When health care personnel use standard universal biosafety precautions for handling patients, this will assist in contamination control. Once the medical condition of patients is stabilized, if external contamination is suspected, the possibility of internal contamination also needs to be ruled out.

Personal monitoring will not interfere with medical actions to stabilize an individual's condition or transport patients with life threatening injuries. Radiological surveys at the scene of the emergency can be performed in cooperation with medical personnel only for haemodynamically stable patients, depending on the conditions at the scene.

The clothing of patients who were externally contaminated should be removed promptly, if it was not removed before arrival at the hospital, unless medically contraindicated, taking care to avoid the spread of contaminants embedded in or on the clothing. Place clothing and any accompanying sheets and blankets in sealed plastic bags, label them and store them properly for radiological analysis [21].

External contamination can be reduced by 80–90%, depending on the area of the body covered, when the patient's clothes are cut off the body (see Fig. 12).

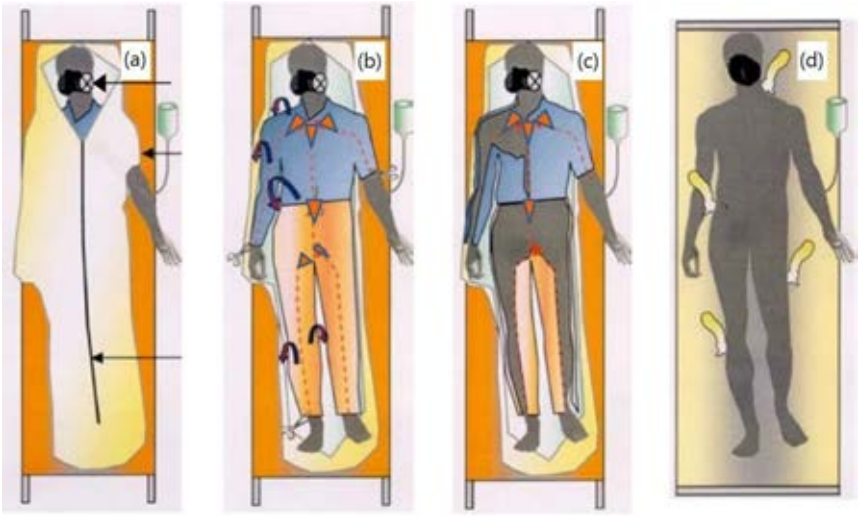


FIG. 12. Procedure for undressing an individual who is lying down [21]. (a) The three arrows identify (from top to bottom): the respiratory protection being used, the covered stretcher, and the blanket or cover of the individual. (b) Cutting clothes off after opening the cover (from the centre to the periphery). The orange arrows show the direction for opening the clothes. (c) Clothes are folded inside out along the patient's body. (d) Transfer of undressed individual to an uncontaminated bed or stretcher. (Modified from Ref. [21].)

This will also reduce the risk of exposure for health care personnel [27]. In addition, clothes can be used in the identification of the contaminant radionuclides.

Where the patient's condition allows, the health/medical physicist or dosimetry team can perform an initial radiological survey of the patient(s) to determine if contamination is present and estimate levels of contamination on specific areas of the body [21].

In cases of external exposure, it is helpful to collect, label and store personal items such as watches, buttons and mobile phones. These can be analysed by dose reconstruction methods (i.e. by neutron activation analysis).

4.1.2. Decontamination of wounds

In a contamination emergency, any wound must be considered contaminated until proven otherwise and has to be decontaminated before the intact skin. When wounds are contaminated, the physician will assume that internal contamination has occurred (uptake) unless the contrary is shown. Therapeutic actions will be based on half-life, solubility, radiotoxicity and the amount of radioactive

material. It is important to initiate measures that prevent or minimize the uptake of the radioactive material into organs or tissues.

Decontamination is achieved by gentle irrigation of the wound with saline solution or water. Several irrigations are usually necessary, with careful monitoring of the wound after every irrigation. Remove embedded pieces of metal or detritus containing radioactive materials, if visible, with forceps and save them for analysis. For accurate results, contaminated materials such as drapes and dressings must be removed before monitoring the wound. The health care staff need to change gloves frequently to minimize the spread of contamination.

Contaminated wounds need to be irrigated repeatedly like other types of wound. If the preceding decontamination procedures are not successful, and the contamination level is still seriously high, conventional debridement of the wound should be considered. The excision of vital tissue should not be initiated until expert medical or health physics advice is obtained. Retain debrided or excised tissue for dose assessment.

Perform decontamination in the following order of priority: wounds, orifices, skin areas with a high level of contamination and, finally, skin areas with a lower level of contamination.

4.1.3. Decontamination of body orifices

Contaminated body orifices, such as the mouth, nose, eyes and ears, need special attention because absorption of radioactive material is likely to be much more rapid in these areas than through the skin. Table 14 is a guide for the decontamination of facial orifices.

4.1.4. Decontamination of intact skin

Use warm water, never hot water. Cold water tends to close the pores, trapping radioactive material within them. Hot water causes vasodilatation with increased area blood flow, opens the pores and enhances the chance of absorption of the radioactive material through the skin.

If washing with plain water is ineffective, use a mild soap (neutral pH) or surgical scrub soap. Scrub the area for 3–4 min. Avoid aggressive rubbing, which tends to cause abrasion and erythema. Rinse two to three times and blot dry. Check the contaminated area with a radiation monitor. Repeat steps (including monitoring between scrubbing and rinsing) if necessary. Stop decontamination when the radiation level cannot be further reduced or if skin irritation is evident.

Complete decontamination, with a survey monitor reading at levels comparable to the background, is not always possible as some radioactive material can remain fixed on the skin surface. Decontamination need only be as thorough

TABLE 14. GUIDE FOR DECONTAMINATION OF FACIAL ORIFICES
(adapted from Ref. [21])

Contamination area	Method	Technique	Remarks
Eyes	Flushing with water or saline solution	Roll back eyelid. Rinse the eye by directing the stream of water from the inner canthus to the outer canthus of the eye while avoiding contamination of the nasolacrimal duct.	Ideally performed by trained personnel.
Ears	Flushing	Rinse the external part of the ear. Clean the opening of the ear channel with cotton swabs. Use an ear syringe to rinse the auditory canal.	Be cautious not to damage the tympanic membrane.
Mouth	Flushing	Encourage the patient to brush the teeth with toothpaste and frequently rinse the mouth.	If the pharyngeal region is also contaminated, advise the victim to gargle with a 3% hydrogen peroxide solution. Warn the patient not to swallow. If radioactive material is swallowed, apply gastric lavage.

as is practical. For contamination that is not removable, cover the area with cotton bandages and a thin plastic cover (for hands use a cotton glove covered with a plastic or rubber glove). Wait 1–2 h for sweating to take place, then remove the covers, clean the area again and survey. Repeat the procedure if necessary.

Decontaminate using a sink, basin or shower depending on the area of contamination. Caution the patient to avoid splashing water into the eyes, nose, mouth or ears. Repeat washing, if necessary. Provide clean towels for drying after each wash. If necessary, the water may be discharged into the sewer. External deposits of beta emitting radionuclides on the skin (like ^{137}Cs) can produce beta burns.

4.2. INTERNAL CONTAMINATION

Internal contamination occurs when radioactive material is taken into the body through different pathways, as occurred during the radiological accident at Goiânia when a sealed ^{137}Cs source was opened and several persons were internally and externally contaminated [5]. Internal contamination is usually checked by monitoring biological samples taken from the person or by direct measurement. When patients present internal contamination only, they do not represent a direct hazard to other persons unless the internal contamination is extremely high and involves gamma emitters. In that case, medical personnel and other people around (patients, relatives) might be subject to external exposure as a result of internal contamination of the patient. However, such exposure has been low in past occurrences [5, 6].

There are five potential pathways through which persons may become internally contaminated with radionuclides. These are: (i) inhalation of radioactive particles or gases; (ii) ingestion of radioactive material (dust or contaminated food/water or solutions); (iii) absorption of radioactive material through wounds; (iv) absorption of radioactive material through intact skin; and (v) injection of radioactive material into the body. Once it enters the body, the radioactive material undergoes a series of physiological processes. The way radioactive material is retained or released from organs and tissues depends on factors such as its physical and chemical forms, the intake pathway and physiological conditions.

Although in certain instances internal contamination with specific radionuclides could demand a prompt and appropriate intervention to avoid or minimize incorporation, in cases where there is an associated life threatening condition present, the main priority is to stabilize and provide medical support for the patient. Dose estimations, decontamination procedures and decorporation therapy are secondary priorities in this eventuality.

In general terms, activities that involve the use of unsealed radioactive sources imply a risk for internal contamination with radionuclides for the exposed individuals. Depending on the circumstances, a malicious act with radioactive material may cause internal and external contamination (for instance, the detonation of a radiological dispersion device, also known as a ‘dirty bomb’).

Considering the very low potential for radiation exposure, the health risks for professionals handling a patient contaminated with radionuclides are practically negligible, assuming protective clothes are used and universal biosafety standards are adhered to. Comparatively, the radiological risk to health care personnel assisting such a patient is similar to or lower than the biological hazard resulting from ordinary medical practice [102].

In general, internal contamination with radionuclides does not cause immediate clinical manifestations, unless it is associated with toxic material of another kind, such as chemicals.

4.2.1. Phases

Internal contamination with radionuclides has four phases [102]:

(i) *Intake:* The act or process of taking radionuclides into the body by inhalation or ingestion or through the skin. The word 'intake' also denotes the activity of the radionuclides incorporated into the body in a given time period or as a result of a given event. In some publications, the term 'incorporation' is used to denote this phase of internal contamination with radionuclides. Much less frequently, the word 'internalization' is used for the same purpose.
(ii) *Uptake:* The process by which radionuclides enter systemic circulation (body fluids) from the respiratory or gastrointestinal tract, or directly through the skin, especially through wounds. The term is also used to refer to the fraction of an intake entering the systemic circulation.
(iii) *Deposition:* The ingress of the radionuclide into the cells of its target organ or tissue (e.g. thyroid for radioiodines) after uptake or the contact of radioactive material with regions of the respiratory tract in the case of inhalation as an intake process.
(iv) *Decorporation:* The natural, or therapy stimulated, excretion of radioactive material from the body.

4.2.2. Health consequences

Health risks derived from internal contamination with radionuclides are influenced by the following factors:

— The amount of radioactive material that enters the body (burden);
— The chemical form of the radioactive material (this influences solubility and hence uptake);
— The kind of emission and half-life of the contaminant radionuclide (alpha emitters have a greater internal radiotoxicity);
— The radiosensitivity of the organ or tissue where, after uptake, the radionuclide is deposited (target organ or tissue);
— The patient's age (younger people have higher radiosensitivity and a longer life expectancy, so the probability of cancer is higher);
— Individual physiological factors that make excretion more difficult (such as kidney failure);

— The contamination pathway (contamination with soluble materials through wounds can directly lead to uptake).

The main health concern for internal contamination with radionuclides is the stochastic late effect of cancer development. Risk coefficients for cancer development after internal contamination with different radionuclides have been established [103].

In rare cases, internal contamination with radionuclides could lead to ARS (when very radiotoxic nuclides such as ^{210}Po [104] or massive internal burdens [105] are involved).

4.2.3. Diagnosis and assessment

The initial diagnosis of internal contamination with radionuclides will in most instances be presumptive and based on circumstances and preliminary findings (like counting of orifice swabs). Internal contamination occurs when unprotected personnel ingest, inhale or have wounds contaminated with radioactive material. Externally contaminated individuals who did not have respiratory protection should be evaluated for internal contamination. Internal contamination is more likely when significant contamination is found on the face, in/around the nostrils or mouth, or in/around open wounds.

Internal doses are assessed differently than external doses. The two primary differences are as follows:

(a) Internal doses are calculated assuming a certain biokinetic model for the radioactive substance in different organ and tissues.
(b) The doses are committed doses. Internal doses are compared to the intake, or the amount of radioactive material that initially enters the body [27].

Definitive diagnosis and assessment rely on such procedures as internal dose assessment by bioassay (mainly excreta bioanalyses), whole body counting and gamma camera measurement (for some radionuclides).

Generally, urine and faeces bioassays are the most feasible methods for assessing intake. Because of its convenience, urine is the preferred sample for bioassay measurements for internal contamination with soluble compounds. Samples should be collected and labelled to record the time of sampling. Urine bioassay can be used to measure a wide range of radionuclides. In general, 24 h samples are preferred because biokinetic models used to interpret data are based on daily excretion rates [102].

When a bioassay is performed, one can ascertain the activity concentration in the urine, for example, at that time. Calculations are then performed to

determine how much activity initially entered the body. The same applies to whole body counts, lung counts or other methods for internal dose assessment [27].

The assessment of internal contamination provides information on the nature of the radionuclide and quantifies the incorporation of the radioactive material into the body, to estimate the committed effective dose[6]. The concept of committed dose accounts for the fact that internal doses are protracted. The assessment helps determine whether or not long term treatment is needed. The participation of specialized laboratories and physicists is always necessary for this purpose.

When the radioactive material deposits into an organ, it remains there until it decays or the body removes it through normal biokinetic processes. These two processes can coexist and are generally independent from each other. The effective half-life takes radioactive decay and biological elimination into account. It is calculated by dividing the product of the biological and radioactive half-lives by their sum [27].

In many instances, the medical decision for immediate decorporation treatment will be based on the strength of the evidence, preliminary early assessments and clinical judgement. For a decision regarding the long term use of decorporating drugs, it is essential to undertake a comprehensive evaluation of the intake using a multidisciplinary approach.

4.2.4. Treatment

There might be instances when the physician must decide whether to begin treatment based on the available data on the events and patients. Bioanalyses for the identification and quantification of radionuclides in the body (urine, faeces, blood samples) are time consuming, requiring between 24 and 48 h (especially when activities are very small). Whole body counters are not easily available and their use in emergency conditions is limited on technical and operational grounds. Consequently, the following will support the clinical judgement to initiate the treatment, even without confirmatory tests available:

— History of the accident, including time of occurrence, radionuclide(s) possibly involved, circumstances and results of the dose estimations;
— Contamination pathway (worst scenario: through wounds);

[6] The committed effective dose is the committed radiation weighted dose to tissues over the integration of time and the tissue weighting factor for a determined tissue. When the time is not specified, it will be taken to be 50 years for adults and up to 70 years for intakes by children. Simply put, this is the dose that the body will incur over the years if the radioactive material remains in it and is just physically and biologically eliminated [26].

— Solubility of the contaminant radioactive material (if known);
— Radiotoxicity of the contaminant (if known);
— Patient's age and his/her specific clinical conditions (pregnancy, liver function, kidney function);
— Toxicity of the drug to be used for decorporation;
— Initial analyses from nasal or oral swabs;
— Wound contamination level.

Appropriate specialized treatment will be given to any person who develops a severe deterministic effect (tissue reaction) or with a committed effective dose that indicates a higher risk for stochastic effects. Some individuals with low levels of intake may not need any kind of treatment. However, other patients with low levels of intake of very radiotoxic nuclides, such as ^{241}Am or ^{239}Pu, could incur significant health risks and require treatment. Since no treatment is completely free of side effects, a decision based on a benefit to risk analysis must be made before initiating a treatment course.

When a wound is contaminated and the radionuclide is not removed, the radionuclide may be absorbed and metabolized into the body. Therefore, copious irrigation with physiological saline solution, or possibly with diethylenetriaminepentaacetatic acid (DTPA) (depending on the case), is indicated. Depending on the radionuclide involved in the contamination of a wound, the possibility of systemic therapy needs to be considered; for instance, internal contamination of an individual with plutonium or other actinides could be treated with chelation therapy (DTPA) [105].

When nasal or oral swabs are indicative of an inhalation of radionuclides, additional studies may be required to determine the burden of the intake and the need for decorporation treatment. However, some situations, such as intakes of plutonium or americium, may require the prompt administration of DTPA before a substantial deposition in organs can occur [102, 106].

In the case of ingestion of radionuclides, there will be a transit time through the gastrointestinal tract prior to absorption (uptake) into the blood stream. Some actions can reduce the amount of radionuclide absorbed, such as the administration of alginates, barium sulphate and aluminium containing compounds. These drugs bind some chemical elements (such as strontium), reducing their uptake [106].

The immediate treatment goals for cases with internal contamination are:

— To impede or reduce uptake of the radionuclide into the blood and deposition into target organs or tissues;
— To enhance as much as possible the excretion of radionuclides from the body;
— To minimize the absorbed dose by the most effective method.

The overall goal of the treatment is to reduce the stochastic or long term risk of radiation induced cancer. After a radionuclide becomes retained in tissues with a slow cell turnover, the effectiveness of treatment is significantly reduced. It is therefore generally accepted that treatment is most effective when administered as soon as internal contamination occurs.

Treatment procedures and methods for internal contamination with radionuclides are generally included in the following categories [102]:

— Unspecific measures: These are oriented towards reducing or inhibiting uptake of radionuclide from the gastrointestinal tract. Examples are gastric lavage, emetics and laxatives, gastric alkalization and wound irrigation. Ideally, such general measures (as well as specific procedures, such as the administration of decorporating drugs) would be most effective if commenced within the first hour after intake. In many instances, gastric lavage and the use of laxatives or emetics are not feasible (as in a mass casualty emergency) or can even be contraindicated for clinical or toxicological reasons.
— Specific measures, including the following:
    - *Blocking:* Blocking agents reduce the body's uptake of a radionuclide by saturating tissues, organs and metabolic processes with a stable isotope (an identical non-radioactive element). The most commonly known blocking agent is potassium iodide (KI), which is used to prevent or treat contamination with radioiodines. If promptly administered, KI will saturate the thyroid with non-radioactive iodine so that the radioactive iodine isotope, either inhaled or ingested, will 'pass through' the body instead of being taken up by the thyroid and subsequently irradiating it. KI is most effective if taken shortly before the potential exposure (less than 12 h) or shortly after the internal contamination occurs (less than 6 h).
    - *Isotopic dilution:* Isotopic dilution consists of the administration of large quantities of a stable isotope to accelerate the process of eliminating the radionuclide. Tritium contamination can be treated by forced fluid intake. Enhanced fluid intake (e.g. water, tea, milk) will increase excretion and can reduce the time tritium stays in the body.
    - *Displacement:* Displacement has essentially the same principle as blocking and dilution therapies, but in this instance a non-radioactive element with a different atomic number is used. This non-radioactive element competes for the uptake sites, displacing the radioisotope from the receptor. An example is calcium gluconate competing for bone deposition with radiostrontium.
    - *Ion exchange:* Radioactive caesium follows the enterohepatic circulation, so ferric hexacyanoferrate, known as Prussian blue,

is used to capture recycling caesium through an ion exchange mechanism long after contamination has occurred. Prussian blue was extensively and successfully used for ^{137}Cs decorporation in the Goiânia accident [107–109].

- *Mobilization:* This refers to the increase in the natural turnover process to release radionuclides from body tissues and to enhance the elimination rate. Ammonium chloride, for example, when given orally, results in acidification of the blood and increases the elimination of incorporated radiostrontium. Other examples include diuretics and parathyroid extract.
- *Chelation:* Chelating agents are organic or inorganic compounds capable of binding metal ions to form complex, ring-like structures called 'chelates'. Chelating agents possess 'ligand' binding atoms that form two covalent linkages, one covalent and one coordinate linkage, or two coordinate linkages in the case of bidentate chelates, and can be easily excreted by kidneys or other organs [110]. Chelating agents firmly bind to metals (including radioactive metals) to eliminate them from the organism. The formation of radionuclide complexes, leading to greater excretion via the kidneys and/or intestines, is proven effective for actinides and lanthanides, such as plutonium and americium. The chelating agent with the greatest potential range of use in radiotoxicology is DTPA. This drug is usually administered intravenously, but an aerosol form is also available in some countries. Normally, DTPA can only be used under medical supervision in specialized centres. It is indicated, for example, for internal contamination with ^{241}Am or plutonium. DTPA is often used in formulations with calcium or zinc. Zn-DTPA is preferred for longer term administration. Other important chelating agents that might be used for decorporation of radioactive metals are dimercaprol, dimercaptosuccinic acid and deferoxamine.
- *Excision:* Wound debridement and excision for removal of fixed contamination may also be necessary. This demands a well established evaluation of the condition by specialized personnel to assist in making a sound medical decision based on the advantages and disadvantages of the surgical procedure.
- *Lung lavage:* This is an invasive procedure that implies the same risk as that for general anaesthesia. It would be indicated in a very limited number of cases. A thorough medical and dosimetric evaluation, among other elements, is mandatory for indicating this kind of treatment for internal contamination with insoluble radioactive material deposited in the lungs. Parameters that are used to evaluate the indication of

lung lavage include clinical status, patient's age, the existence of comorbidities, radiotoxicity of the contaminant, its burden and dose assessments. For some patients, lung lavage can be conducted to avoid deterministic effects (tissue reactions) at lung doses above 6 Gy anticipated within a 30 d period, though on a case by case basis [111].

Table 15 provides information on initial treatment for internal contamination with selected radionuclides.

TABLE 15. INITIAL TREATMENTS FOR SELECTED RADIONUCLIDES

Radionuclide (any radioisotope of concern)	Drug of choice	Usual dosage
Americium, cobalt, indium, iridium, plutonium	DTPA	0.5–1 g, administered by slow intravenous injection over a period of 3–4 min or by intravenous infusion diluted in 100–250 mL of 5% dextrose in water (D5W), Ringer's solution or normal saline. Only a single initial dose of Ca-DTPA is recommended.
Caesium	Prussian Blue	1–3 g three times a day orally in a little water. The duration of treatment after exposure is dictated by the level of contamination and clinical judgement, based on urine and faeces bioassays.
Gallium	Penicillamine	Adults: 1–3 capsules, 250 mg, three times a day.
Iodine	KI	Adults 18–40 years: 130 mg/d, oral route. Pregnant and lactating women, adolescents 12–18 years (weight <70 kg) and children 3–12 years: 65 mg/d, oral route. Children: 1 month–3 years: 32 mg/d, oral route. Newborns up to 1 month: 16 mg/d, oral route.
Polonium	Dimercaprol	Adults: 2–3 mg/kg body weight, administered by intramuscular injection every 4 h. First injection limited to 50 mg; injections ideally not to be given for more than 3 d and under hospital conditions; individual sensitivity should be tested at the time of the first injection (quarter of an ampoule).

TABLE 15. INITIAL TREATMENTS FOR SELECTED RADIONUCLIDES (cont.)

Radionuclide (any radioisotope of concern)	Drug of choice	Usual dosage
Technetium	Potassium perchlorate	Adults: 200–400 mg, oral route. The maximum dose will not exceed 1 g. Administer with as much water as possible to avoid gastric irritation.
Tritium	Forced fluids	Oral or intravenous (water diuresis).
Uranium	Sodium bicarbonate	To alkalize the urine (pH8–9). Aqueous isotonic solution with a concentration of 14 g/L (1.4%). Sodium bicarbonate is available commercially from many companies in 150, 500 and 1000 mL bottles and in ampoules of 10 and 20 mL (other concentrations are available as well). Contraindication and adverse effects: blood pH and electrolytes will be monitored. Sodium bicarbonate can cause or aggravate hypokalaemia. This can be prevented by means of potassium supplementation. Possible drug associations will be considered: there are many alkaline related non-compatible conditions. Contraindications are alkalosis, respiratory acidosis and sodium retention. A risk of a sodium bicarbonate overdose exists in the following situations: metabolic alkalosis with respiratory depression, hypokalaemia, acute pulmonary oedema and heart failure.

4.2.5. Protective measures to avoid the spread of contamination

A patient with external contamination (and potentially also a patient with internal contamination, via excreta) could contaminate the transporting vehicles, hospital rooms and other premises, as well as other persons and attending personnel. Table 16 summarizes measures to avoid the spread of contamination.

TABLE 16. GENERAL BASIC MEASURES TO PREVENT THE SPREAD OF RADIOACTIVE CONTAMINATION

Area	Measures
For attendants	Protective clothes are to be issued and used by all personnel involved (i.e. coveralls with hood, protective goggles, face masks and gloves). Tape the edges of both masks and gloves. Paramedic and ambulance personnel need to be surveyed for contamination after handling and transporting a patient with possible external or internal contamination.
Setting up the treatment area	An isolated room would ideally be used, or the emergency room needs to be set up in such a manner as to reduce the possibility of spreading radioactive contamination, including the floor, the walls and equipment. Provide containers for wastewater and any contaminated materials, and plastic bags. Restrict the treatment area to authorized personnel only. Prior to the patient's arrival, survey the treatment area with a contamination monitor (Geiger–Müller or proportional counter) or other survey instrument to determine the background radiation level. Remove the patient's clothes very carefully (if this was not done previously) and place them in containers or bags with plastic protection and proper labels with the patient's name and the day and hour of the procedure. Clothes are ideal for the identification of the contaminant radionuclides. In the first hour after an event, nasal (from each nostril separately) and oral swabs can be obtained and can be initially counted with handheld instrumentation, providing additional information which could help in early medical management when the samples are positive. In case of negative results, internal contamination may not be excluded. These samples will be sent for further radiological measurements.
Survey meter	A well maintained Geiger–Müller counter with beta and gamma detection capability is usually sufficient. A full scale meter deflection indicates a high exposure rate, and a high range instrument (ion chamber) may be required. The survey will be conducted at a distance of about 25 mm from the person's body, moving the detector no faster than 50 mm/s. A quick head to toe radiological survey is to be performed by a radiation protection officer (or by a trained individual) with appropriate equipment, and will include a careful examination of the wounds. The wounds should be surveyed with a Geiger–Müller detector and the count rate used to initially estimate intake (based on the activity in the wound). This can provide sufficient evidence of the presence or absence of gross contamination.

TABLE 16. GENERAL BASIC MEASURES TO PREVENT THE SPREAD OF RADIOACTIVE CONTAMINATION (cont.)

Area	Measures
Personal dosimeter	A personal dosimeter is needed, as a minimum requirement. Even when a direct reading personal dosimeter is available, providing immediate information to personnel, local authorities may require the use of passive dosimeters. Exposures will be kept as low as reasonably achievable and kept within the limits set by the national competent authorities.

4.2.6. Medical follow-up

In principle, follow-up and surveillance after internal contamination with radionuclides is aimed at the early detection of possible related malignancies. This should be established on an individual basis.

4.2.7. Case study: The radiological accident in Goiânia, Brazil

Four patients died from ARS in the Goiânia accident. Autopsies, which were legally required, showed that all bodies had internal and external contamination with ^{137}Cs [5]. A six year old girl had massive internal contamination and the initial dose rate close to her skin reached 2.5 mSv/h [5, 109, 112]. Information on the medical, pathological and radiological conditions of the deceased individuals is given in Table 17 [5, 17].

Planning the autopsies was essential to avoid the spread of contamination and to minimize radiation exposure. Pathologists, coroners, morgue technicians, radiation medicine doctors and radiation protection personnel met and planned the procedures. For example, personnel were rotated every ten minutes during the autopsies and the outer gloves were changed frequently [5, 6].

All radiation protection measures, including the kind of protective clothing to be used, were determined by radiation protection personnel. Respiratory protection other than surgical masks was not judged necessary. Otherwise, conventional biosafety techniques were fully adopted.

The autopsy room team members used personal dosimeters (including dosimetry rings) and dose rates were constantly monitored. No one received any significant radiation dose and no radiological contamination or occupational accident occurred. The autopsy room was appropriately prepared to avoid contamination [17].

TABLE 17. MEDICAL, PATHOLOGICAL AND RADIOLOGICAL CONDITIONS OF THE DECEASED INDIVIDUALS IN THE GOIÂNIA RADIOLOGICAL ACCIDENT

Case	Death (days after initial exposure)	Cause of death	Cs-137 burden (MBq)	Mean cytogenetic estimated dose (Gy)
LNF: 6 years old, female	29	Diffuse haemorrhaging of multiple organs, sepsis	1677	4.4
IBS: 22 years old, male	34	Acute pulmonary oedema, bilateral bronchopneumonia, sepsis	60	2.9
MGF: 36 years old, female	34	Diffuse haemorrhaging of multiple organs, sepsis	34	3.9
AAS: 18 years old, male	35	Lung collapse, lobar pneumonia, sepsis	120	3.7

5. COMBINED RADIATION INJURIES

Combined radiation injuries (CRIs) consist of physical, thermal and/or chemical trauma combined with radiation exposure. CRI may be expected in a radiation mass casualty event. Patients with CRIs have a worse overall prognosis; evidence predicts that the resulting morbidity and mortality will be greater than the sum of both injuries [113].

CRI is a potentially severe and lethal form of multiple trauma. To care for these patients, it is necessary to be familiar with the effects of radiation on the human body, and how these effects influence the management of trauma victims; the lethality increases significantly in these cases [113, 114]. Their diagnosis, treatment and prognosis are more complex [8].

There are some potential problems in the diagnosis of CRIs. Results of laboratory tests, for example haematological indices, and other information can be altered in a way that makes diagnosis of the radiation component of combined injuries difficult. Results of particular cytogenetic techniques (micronucleus

assay) may also be influenced by toxic chemicals, making their use more complex for radiation dose assessment.

The primary effect of trauma is the physical disruption of tissues and organs, which compromises the structural and functional integrity of the affected systems. In addition, trauma, such as ionizing radiation, unleashes a cascade of inflammatory and neurohormonal events that have systemic repercussions [115]. Because of the burns and trauma in CRI patients there is a complicated activation of cascades of numerous cytokines (such as interleukin 6 and tumour necrosis factor), producing systemic effects which enhance the radiation injury and result in more severe perturbations of haemodynamic and haematological function [115].

Cases of CRI were observed after the Chernobyl accident, where some firefighters died as a result of the combination of exposure to radiation and thermal burn injuries. CRI would be a major issue following a nuclear detonation, as was seen in Hiroshima and Nagasaki [116].

Experts therefore recommend triaging these patients and taking a different approach to treating them since they are more susceptible to infection and cardiovascular collapse, requiring modified handling at lower radiation doses for earlier wound repair [115, 116], and more prompt consideration of the use of cytokines (such as G-CSF) and HSCT.

If surgery is contemplated for CRI patients, it is preferable to perform it prior to the eventual onset of the different cytopenias (if expected). The use of bone marrow growth factors and blood products are valuable tools before and after surgery.

Life saving actions and the medical handling of conventional trauma have the highest priority. Treatment has to be individualized according to the nature and severity of the combined injuries [117].

Since the manifestations of radiation injuries occur after a latent period, all necessary medical interventions for the non-radiation injuries in CRI need to be carried out as soon as possible, before the development of aplasia (if expected based on the estimated absorbed dose for the patient).

6. EMERGENCY COMMUNICATION AND MENTAL HEALTH ASPECTS

This section provides an introduction to the importance of the communication and mental health aspects of a radiation emergency, and offers some recommendations on interventions that could be initiated by the medical

community. It is important to note that the medical community is not necessarily responsible for emergency communications and that there are different professionals responsible for this task during an emergency.

Experience from past nuclear and radiological emergencies confirms that public communication is one of the most important elements in emergency management. Sometimes, an event may not be considered an emergency by experts or responders but is perceived very differently by the public. The differences in the risk perception among experts, responders and the public can be mitigated by effective communication of risks, which consequently can reduce the psychosocial effects related to emergencies (communications strategy) [118, 119].

Communicating effectively with the public about radiation emergencies will help the public to understand the risk and to distinguish between the actual and perceived risk, supporting the implementation of protective actions and contributing to the alleviation of negative psychological impacts [119]. Effective risk communication involves two parts:

(a) *The exchange process:* A two way exchange process fosters a dialogue between those who may be affected by the risk and those who are in charge of controlling it.
(b) *The actual information about the risk:* The risk perception considers the difference between how risk is perceived by the public and how the risk is assessed and measured. The goal of risk communication is not to force a change between the divergent views of the expert and the public, but rather to develop an understanding of these factors so that they may be considered and addressed. This requires an understanding of the underlying factors on which public perception of risk is based [119].

Psychological effects in the affected population and among responders are among the most important non-radiological public health consequences caused by an emergency, intervention or both [21]. Immediate, short term and long term actions need to be implemented to mitigate these effects. Immediate and short term actions include the following:

— Providing counselling to response teams regarding issues of fear, grief, disorientation and active participation, and measures to support the psychosocial well-being of health and relief workers;
— Setting up systems for communication and re-establishing links with family and social supports;
— Providing psychological ‘first aid’ at general health care facilities and evacuation centres/information points;

— Re-establishing recreational activities, schooling and religious activities to facilitate community support structures;
— Providing training in preparedness and the complex range of responses needed.

As described earlier, communication, risk perception and the impact on mental health of radiation emergencies are related factors. The long term actions will include medical and mental health follow-up and assistance to the population as part of public health actions. Long term interventions may be important as the medium term and long term effects of exposure to chemical, biological, radiological or nuclear agents are often very hard to predict. The implementation of a surveillance and monitoring programme for the affected population is necessary. Also needed are outreach activities in communities to disseminate clear information and promote positive ways of coping.

The impact on mental health, risk behaviour and demand for health services may vary dramatically over time. Long term public health follow-up is necessary for several reasons: to provide information about the seriousness of health problems; to identify earlier radiation induced health effects; and to reduce the uncertainty about the long term effects of contamination, which creates fear and anxiety in the population. Rumours and distortions exaggerating the consequences are common after a large scale radiation accident.

Social assistance is necessary for the affected population (social adaptation measures, material support from the authorities, long term rehabilitation programmes), especially for those evacuated or relocated. Adequate social assistance can prevent the development of additional stress or restore people's self-confidence. It can also restore confidence in the activities of the authorities.

6.1. EMERGENCY COMMUNICATION DURING RADIATION EMERGENCIES

Emergency communication consists of messages that include the sense of urgency related to crisis situations. The main objective of emergency communication is to provide the public with information that will help them make the best decision possible, taking into account the existence of challenging constraints during radiation emergencies. Emergency communication also aims at: (a) managing public response; and (b) establishing the responsible organization(s) as the main source(s) of information.

Communication in an emergency has the following unique characteristics [120, 121]:

— The role of communication in managing human behaviour is a significant component of overall emergency management.
— The need for constant communication is high.
— The need to monitor other communication channels is high.
— The stress of crisis circumstances related to risk perception factors (the uncertain knowledge of radiation in the general population) is high.

The early messages and actions of an emergency response will have a significant impact on how people respond, their perception of risk and their attitude about the emergency response organization. Those will form the initial foundations of their perception of the whole event. These foundational moments are critical to the overall emergency response and its ability to manage public behaviour. Communication is a key tool at this stage.

People will be demanding information, and various sources will be providing it constantly. It is important to maintain a constant flow of information from the responsible organization, providing updates on the emergency situation even when there is no change [120]. It is also important that the information be provided in such a way that it can be well understood by the people in distress. This means that all responsible stakeholders must demonstrate the requisite respect and empathy for the situation at hand.

Physicians must always keep in mind that explanations during an emergency must be simple and clear. Simple advice based on internationally endorsed guidance will reduce the psychological effects on the population [119]. In this regard, the following actions can improve communication during an emergency [122]:

— Be first. Responding quickly is important because crises are time sensitive.
— Be right. Being right builds credibility. The information that needs to be provided will ideally include:
    • What is known;
    • What is not known;
    • What is being done to fill in the gaps.
— Be credible. Honesty is necessary to maintain credibility.
— Express empathy. People who suffer need to be acknowledged. Empathy builds trust.
— Promote action. Action calms anxiety by keeping the individual occupied with meaningful and useful actions, while promoting their sense of control after a frightening incident.

— Show respect. Respect promotes cooperation.

6.2. MENTAL HEALTH ASPECTS OF RADIATION EMERGENCIES

Psychosocial effects can be both widespread and long lasting, constituting some of the most significant and challenging consequences of a radiation emergency. Consideration of psychosocial factors needs to be an integral part of radiation accident training, preparedness and response. Serious events may have profound psychosocial effects. Risk perception plays a pivotal role in the population's reactions to the assumed/expected consequences of any emergency, even if these have not yet materialized.

The psychosocial effects during radiation emergencies have often been underestimated or even ignored. However, experience shows that fear may be an important driver of human actions during dangerous situations and may have powerful public health implications [123]. For instance, studies of the accident at the Fukushima Daiichi nuclear power plant revealed that the psychosocial impact is a major consequence [124, 125]. Following the Chernobyl accident, psychosocial effects caused by the accident were a major public health problem, and they remain an important issue today [126]. For this reason, it is important for physicians to have a good general understanding of the psychosocial aspects of radiation emergencies [127].

Emotional reactions play a role in how people feel and perceive the risk (Table 18 [128]). A clear and direct message will help to reduce the stress level and limit the risk perception in the population. Understanding the emotional factors that contribute to those perceptions is a basic part of any risk communication programme [120]. Prolonged periods of psychological stress can result in physiological changes, psychosomatic and mental health problems and cognitive effects [21]. Table 18 contains different elements to help health care professionals recognize the emotional reactions of persons under stress.

6.2.1. Psychosocial considerations related to the affected population

Mental health assistance requires the involvement not only of mental health professionals, but also of general practitioners and other professionals. Psychological support may be needed during the entire period of the emergency and may need to be continued thereafter. Some individuals might need mental health counselling for long periods. After the accident, several measures are available to reduce the psychological consequences for the affected population.

Basic principles that guide initial psychological support include the following [129, 130]:

TABLE 18. EMOTIONAL REACTIONS IN INDIVIDUALS UNDER STRESS [128]

Type	Reaction
Cognitive	Impaired concentration, disorganization, forgetfulness, difficulty in making decisions, diminished attention
Emotional	Shock, disbelief, fear, anxiety and worry, irritability, anger, denial, hopelessness, helplessness, feeling overwhelmed
Behavioural	Sleep disturbances, appetite disturbances, isolation from others, difficulties being alone, restlessness, increased substance use (i.e. drugs or alcohol)
Physical	Sweating, hyperarousal, increased heart rate, dizziness, elevated blood pressure, fatigue, headaches, gastrointestinal distress, nausea, medically unexplained physical symptoms
Spiritual	Feelings of uncertainty, feeling abandoned, diminished or lost belief in a just world and the goodness of others, struggles with notion of evil, shattered assumptions about safety

— How to understand and offer help in an emergency situation:
  - Check for safety.
  - Check for people with obvious urgent basic needs.
  - Check for people with serious distress reactions.
— How to understand the specific needs of affected people:
  - Approach people who may need support.
  - Ask about people's needs and concerns.
  - Listen to people and help them to feel calm.
— How to provide information and practical support:
  - Help people address basic needs and get access to services.
  - Help people cope with problems.
  - Give information.
  - Connect people with loved ones and social support.

Physicians need to understand the role they can play in tackling not only the physical but also the psychological effects and impacts of radiation emergencies on the mental health of affected individuals, workers and the public in general.

The lessons learned also indicate that the psychological impact of the treatment of radiation induced injuries needs to be minimized, and therefore the treatment will be provided as close to the individual's home as possible, or in a

region with the same language and culture. Provision needs to be made for family members to accompany the patient if treatment is in another country [131].

Religious, cultural or other social considerations will be addressed when performing surveys, decontamination or other procedures. Make arrangements for assistance to both males and females [21].

6.2.2. Psychosocial considerations related to responders

Stress also affects emergency responders (firefighters, police, monitoring teams, emergency medical responders) during a radiation emergency. They are expected to perform their usual duties in addition to duties that are not an ordinary part of their job (i.e. monitoring, decontamination, evacuations). Factors that need to be considered by responders include the following:

— Staff and volunteers are affected, and they are worried about their families and relatives.
— Wearing personal protective equipment may cause distress due to constraints on senses, breathing, movement and communication.
— Responders are faced with death, fear, chaos and uncertainty, and occasionally unclear roles and responsibilities.
— Responders need support in order to help others.

Periodic health examinations of responders, conducted by physicians and psychologists, are advisable. Responders need to be encouraged to meet in groups to discuss the problems they face and any distress they might have experienced. Information on real risk for emergency responders needs to be regularly provided and discussed as a central element for proper psychological management.

7. RECORD KEEPING

Detailed record keeping is essential not only for patient care and subsequent dosimetric and medical follow-up, but also for medico-legal considerations. Record keeping during or after an emergency is relevant for future actions.

Information about the identification and notification of the emergency, the related circumstances and the individuals involved is very important. The assistance of radiation protection officers can be very useful for the collection of such data. Depending on the circumstances, the radiation protection officer will be in a position to provide information on the exposure rate and possible surface

contamination, the type of accident, sources and kind of radioactivity, dosimetry of affected subjects and contamination of the environment.

Table 19 provides some of the information to be recorded in the event of a radiation emergency.

TABLE 19. INFORMATION TO BE RECORDED IN THE EVENT OF A RADIATION EMERGENCY

Identification and notification	
All cases	Identification of the individual(s) (name, sex, age, contact details) Number of individuals involved Notification to national/international authorities Exposure conditions Use of personal dosimeter (if occupationally exposed workers are involved)
Circumstances of the emergency	
External irradiation	Activity of the source Time of exposure Duration of the exposure Distance from the source Estimation of dose rate and dose to the patient (to the whole body or tissues)
External irradiation	Exposed parts of the body Exposure to a sealed or open radioactive source (is there any information about the breakage of the container of the radioactive source?)
External contamination	Radionuclides involved (if known) Levels of activity concentration on the body surface Body area involved Potential internal contamination
Internal contamination	Activity of the source Time of exposure Duration of the exposure Intake Pathway: Inhalation Ingestion Through wounds Through intact skin

TABLE 19. INFORMATION TO BE RECORDED IN THE EVENT OF A RADIATION EMERGENCY (cont.)

Relevant medical information on individuals/patients	
Health conditions and clinical manifestations	Associated trauma Consciousness and neurological manifestations Comorbidities
Health conditions and clinical manifestations	Nausea and vomiting Diarrhoea Anorexia Asthenia Fever Skin lesions (erythema, blisters)
Tests and procedures	Laboratory tests (CBC[a], amylase, polymerase chain reaction or other samples) Biodosimetry and bioassay samples Drug administration (conventional and decorporating drugs) Decontamination procedures performed Personal items for physical dosimetry (dosimeter, if available, or, if possible, buttons, cell phones, watches, pendants, etc.) Photograph/diagrams of the facility/practice involved

[a] CBC: complete blood count.

Appendix I

MEDICAL PREPAREDNESS FOR RADIATION EMERGENCIES

Requirement 12 of GSR Part 7 [1] states:

"**The government shall ensure that arrangements are in place for the provision of appropriate medical screening and triage, medical treatment and longer term medical actions for those people who could be affected in a nuclear or radiological emergency.**"

In view of the very infrequent occurrence of nuclear and radiological accidents, it is not the purpose of this report to encourage the proliferation of medical centres equipped and staffed for the sole purpose of treating patients during radiation emergencies [24]. Nevertheless, preparedness is essential to mitigate the consequences to the population, the individuals affected and emergency workers.

A significant number of radiation emergencies were discovered by physicians treating the individuals affected (most of them in emergency preparedness categories III and IV). Examples of these are (category III): the accident involving radiotherapy patients in Costa Rica [15]; and the accident involving workers in the irradiation facility in San Salvador [36]. The accidents in Brazil [5], Thailand [7] and Turkey [11] were also discovered by physicians. As local physicians are inexperienced in the diagnosis of radiation injuries, it has often taken some time before radiation exposure was suspected. Early diagnosis of the cause of the injuries may have prevented further injuries or deaths [131].

Based on the analysis of previous emergencies, the medical aspects of the preparedness and response to radiation emergencies have demonstrated gaps that need to be addressed. Most of these gaps are related to the diagnosis and treatment of patients exposed to ionizing radiation. Specific weaknesses include the following [5, 10, 11, 24, 130–132]:

— Lack of training of medical professionals in recognizing radiation induced injuries and understanding the specifics of treating these patients.
— Lack of appropriate medical assessment relating the severity of radiation dose with the clinical manifestations.
— Lack of knowledge of the processes for notifying the national authorities.
— Lack of availability of a sufficient number of medical staff to deal with the projected number of victims affected in a radiation emergency.

— Lack of provisions in the national emergency plan for promptly requesting emergency assistance from international organizations (under the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency) for dealing with victims.
— Lack of established criteria for determining the groups which have been highly exposed and should be subject to long term medical follow-up to detect the early appearance of cancer and other effects.

Emergency medical response needs to be planned and organized in accordance with the potential consequences of different radiation emergencies (hazard assessment). The basic medical preparedness requirements for responding to a radiation emergency will consider: the evaluation of possible types of emergency according to the local circumstances [22]; training of health care professionals; the provision of simplified dosimetry services (a dose rate meter at the 'pre-hospital' stage); capabilities for detecting radiation and containing the spread of contamination; basic preparations for receiving exposed or contaminated patients; and simple medical procedures to be undertaken by non-specialized staff (e.g. first aid, lifesaving actions by trained non-professional care providers).

In addition, the planning of the medical response needs to include: medical and radiological triage; an initial medical examination; clinical, laboratory and dose assessments; designation of medical institutions for management of patients; treatment in specialized medical centres (for severe radiation injuries); and medical follow-up.

The establishment of reference centres and identification of hospitals to be designated for the medical management of patients affected by radiation emergencies must consider a number of factors such as: the population density in the affected area; the availability of staff with experience in the medical treatment of radiation emergency patients; familiarity with decontamination techniques; and experience in the decorporation (removal) of radioactive contaminants from the human body [131].

Different types of institution — or different departments and laboratories — must be designated and prepared over a reasonable period of time for: dose assessment; medical management on-site (at the scene) and in hospitals; decontamination and decorporation of radioactive material from the body of the affected persons; and training and capacity building. The medical response organization in a radiation emergency is schematically presented in Fig. 13.

Supporting capabilities for the medical response, including international cooperation for assistance, are expected to be in place and tailored to each country's needs, taking into account the following:

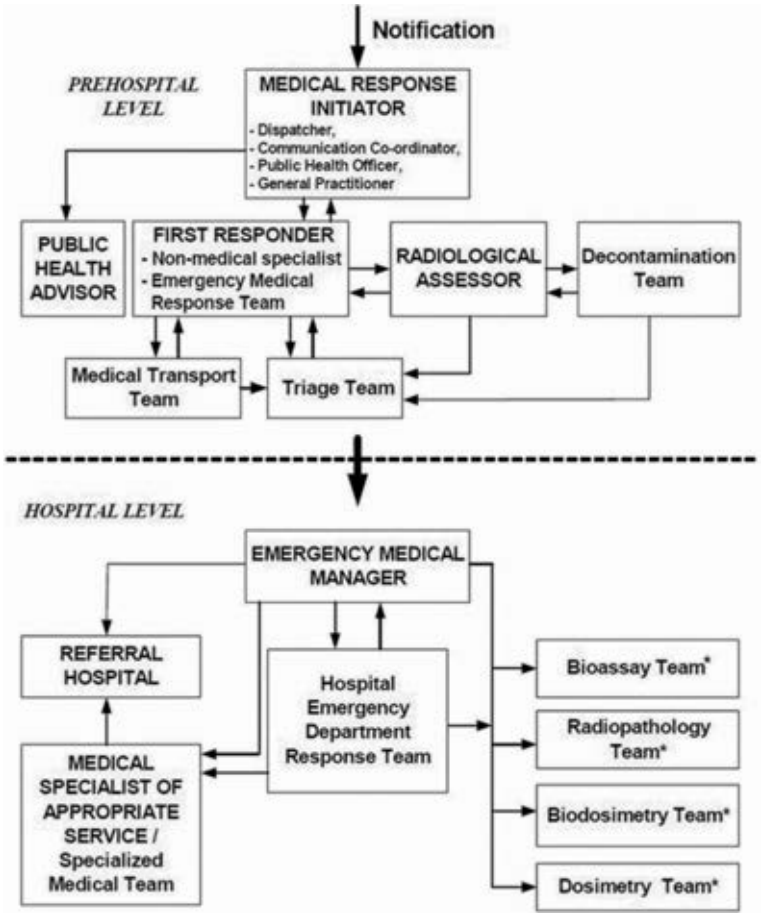


FIG. 13. Representation of the medical response organization in a radiation emergency [21]. The asterisks indicate teams that are not necessarily located in the hospital but are part of the hospital response.

— Dose assessment: cytogenetic methods and ESR [23, 133];
— Specialized medical treatment for patients with severe ARS [131];
— Specialized medical treatment for patients with severe LRI [132];
— Advising on and executing decontamination, bioassays and decorporation of radioactive material from the human body [102];
— Advising on public health actions and countermeasures [134].

Training of all medical personnel, including the designated medical and paramedical personnel and other health care professionals, to recognize, treat and safely manage individuals overexposed to radiation or contaminated with

radioactive material can be considered the most important component of the preparedness for medical response to radiation emergencies [19]. The training ideally has to consider theoretical and practical aspects. Practical skills in contamination monitoring and decontamination procedures need to be taught through exercises [24].

Appendix II

BIOLOGICAL EFFECTS OF IONIZING RADIATION: BASIC INFORMATION FOR THE GENERAL PRACTITIONER

II.1. INTRODUCTION

Radioactivity is the phenomenon whereby atoms undergo spontaneous disintegration, usually accompanied by the emission of radiation. Radiation is the transmission of energy through space and is of two types: ionizing and non-ionizing.

Depending on the range in the electromagnetic energy spectrum, it is possible to characterize non-ionizing radiation such as heat, microwaves, visible light or others, and ionizing radiation such as X rays and gamma rays. These waves are characterized essentially by their energy, which varies inversely to the wavelength.

Ionizing radiation may be emitted in the process of decay of unstable nuclei or by de-excitation of atoms and their nuclei from natural sources like the sun, the stars or cosmic radiation. It may also be produced by X ray machines, nuclear reactors, cyclotrons and other devices. During radioactive decay, gamma (γ) rays are often produced alongside other types of radiation, such as alpha (α) or beta (β) particles.

When a nucleus emits an alpha or beta particle, the daughter nucleus is sometimes left in an excited state which, after de-excitation, returns to a lower energy level by emitting a gamma ray in much the same way that an atomic electron can, in most cases, jump to a lower energy level by emitting visible light [135].

Ionizing radiation can strip electrons from atoms and break the bonds between the atoms of a molecule. The density of energy deposition in a material such as tissue is called the linear energy transfer of the radiation. It is defined as the average energy deposited per unit length of track of radiation; the unit is keV/μm [133]. Ionizing radiation can be divided into low and high linear energy transfer radiation (as a guide to its relative biological effectiveness[7]), or into strongly penetrating radiation and weakly penetrating radiation (as an indication of its ability to penetrate shielding or human body tissues).

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[7] Relative biological effectiveness is defined as a factor used to compare the biological effectiveness of different types of ionizing radiation (i.e. the ratio of survival fractions (the fraction of cells surviving after irradiation) produced by the same doses of two different radiations) [136].

The characteristics of the four major types of radiation emitted by radioactive material, namely, alpha, beta, gamma and neutron radiation, are as follows:

— Alpha radiation has a relatively short range, travelling only a few centimetres in air. It can be stopped by a sheet of paper and cannot penetrate the outer layers of intact human skin. For this reason, alpha radiation becomes a hazard only if an alpha-emitter radionuclide is taken into the body. Examples of alpha particle emitters are americium-241 (^{241}Am) and polonium-210 (^{210}Po) [102].
— Beta radiation can travel several metres in air and can penetrate inadequately protected skin. Beta radiation emitters are considered primarily an internal hazard, but the deposition on the skin of radionuclides emitting beta particles of sufficient energy (such as caesium-137 (^{137}Cs)) can give rise to 'skin burns'.
— Gamma radiation is highly penetrating and can pass through most materials, including the human body. For this reason, gamma radiation is considered an external hazard as well as an internal hazard. Examples of gamma radiation emitters are iridium-192 (^{192}Ir) and cobalt-60 (^{60}Co).
— Neutrons are emitted in the processes of nuclear fission and reaction, or when some radioactive material undergoes spontaneous decay.

II.2. RADIATION CONCEPTS, DOSES AND UNITS

Radiation exposure, in physical terms, is a measure of radiation based on its ability to produce ionization in air under standard temperature and pressure. This quantity is indicated by many radiation detectors such as ionization (i.e. Geiger–Müller) chambers [133]. The International System of Units (SI) unit for exposure is coulombs/kg in air (or röntgen, R, in 'old' units: 1 R = 2.58 × 10^{-4} C/kg air). The unit of exposure is only defined for air and cannot be used to describe dose to tissue. Nevertheless, ionization chambers are widely used to calibrate medical radiation devices and conversion factors to calculate absorbed dose from exposure have been carefully documented for different radiation energies and tissues [27, 133, 136].

The old unit for measuring activity was the curie (Ci), first defined to correspond to the activity of 1 g of ^{226}Ra, and defined more recently as:

$$1\ \text{Ci} = 3.70 \times 10^{10}\ \text{radioactive decays per second} \quad (1)$$

The SI unit replacing the curie is the becquerel (Bq):

$$1 \text{ Bq} = 1 \text{ radioactive decay per second} = 2.703 \times 10^{-11} \text{ Ci} \quad (2)$$

When ionizing radiation interacts with the human body, it deposits its energy in organs and tissues. The amount of energy absorbed per unit weight of the organ or tissue is called ‘absorbed dose’ and is expressed in units of gray (Gy). One Gy of absorbed dose is equivalent to one joule of radiation energy absorbed per kilogram of organ or tissue mass. Equal absorbed doses from different types of ionizing radiation are not equally harmful. Alpha particles produce greater harm than do beta particles, gamma rays and X rays for a given absorbed dose. To account for this difference, radiation dose is expressed as equivalent dose in units of sieverts (Sv).

The equivalent dose in Sv is equal to absorbed dose multiplied by a radiation weighting factor (see Table 20).

II.3. BACKGROUND RADIATION

The term ‘background radiation’ can have different meanings, depending on whether an ambient radiation dose is being considered, or it is necessary to differentiate between an incidental background and a particular source of

TABLE 20. RADIATION WEIGHTING FACTORS
(modified from Ref. [137])

Radiation type	Radiation weighting factor
Gamma rays and X rays	1
Photons	1
Electrons and muons	1
Beta particles	1
Neutrons	A continuous function of neutron energy
Alpha particles, fission fragments, heavy ions	20

Note: All values are related to the radiation incident on the body or, for internal sources, emitted from the incorporated radionuclide(s). Equivalent dose in Sv = absorbed dose in Gy × radiation weighting factor.

radiation. Natural radiation background normally refers to dose rates or activity concentrations associated with natural sources [26, 138].

Most of the human absorbed radiation doses arise from natural sources such as cosmic and terrestrial sources, and from inhalation or intake of radioactive isotopes. Gamma radiation emitted from natural sources is largely due to primordial radionuclides, mainly the ^{232}Th and ^{238}U series, and their decay products, as well as ^{40}K, which exist at trace levels in the Earth's crust. Their concentrations in soil, sands and rocks depend on the local geology of each region in the world.

The average dose received by people from natural background radiation is around 2.4 mSv/a (see Table 21) [139]. This varies depending on the geology and altitude where people live; it generally ranges between 1 and 10 mSv/a, but can be more than 50 mSv/a. The highest known level of background radiation affecting a substantial population is in Kerala and Tamil Nadu states in India [138, 139].

TABLE 21. ANNUAL AVERAGE DOSES AND RANGES OF INDIVIDUAL DOSES OF IONIZING RADIATION BY NATURAL SOURCE OF EXPOSURE

(modified from Ref. [139])

Source or mode	Annual average dose worldwide (mSv)	Typical range of individual doses	Comments
Inhalation (radon gas)	1.26	0.2–10	The dose is much higher in some dwellings
External terrestrial	0.48	0.3–1	The dose is higher in some locations
Ingestion	0.29	0.2–1	
Cosmic radiation	0.39	0.3–1	The dose increases with altitude
Total natural	2.4	1–13	Sizeable population groups receive 10–20 mSv

II.4. DETERMINISTIC EFFECTS OF IONIZING RADIATION

Health effects resulting from the extensive changes in cellular function at high radiation doses are called ‘deterministic effects’, or ‘tissue effects’, because they are predetermined to occur above a threshold level of equivalent dose. Deterministic effects, therefore, are not clinically expressed at low radiation doses.

Deterministic effects of ionizing radiation (also called tissue reactions) are produced by extensive killing of cells, have a dose threshold typically of several Gy, are specific to particular tissues, and have a severity of effect that is dependent on the dose (the higher the dose, once the threshold is overcome, the more severe is the effect). Examples of deterministic effects include ARS, LRIs, radiation induced cataracts, hypothyroidism, infertility, and effects in the embryo and fetus (abortions and teratogenesis).

II.5. STOCHASTIC EFFECTS OF IONIZING RADIATION

Stochastic effects are assumed to have no dose threshold and depend on DNA damage, not on cell death. In contrast to deterministic effects, the severity of harm is not dose dependent. The probability of a stochastic effect increases as the effective dose increases.

Unrepaired DNA damage may produce modified but viable stem cells. If the modified cell is a somatic cell, it can be the initiator of a long and complex process that may lead to cancer. Alternatively, if the cell is a germ cell, the mutation could be transmitted to the progeny of exposed persons. These effects, both somatic and hereditary, deriving from a cell modification, are called ‘stochastic’ because their expression is of a random nature. Hereditary effects have not been demonstrated in human populations exposed to ionizing radiation; however, exposure to radiation increases the frequency of spontaneous mutations in people [140].

Although the exact cause of most cancers remains unknown or poorly understood, exposure to agents such as tobacco smoke, asbestos and ultraviolet radiation, as well as ionizing radiation, is known to play a role in inducing certain types of cancer. The development of cancer is a complex, multistage process that usually takes many years. Radiation appears to act principally at the initiation stage by introducing certain mutations in the DNA of normal cells in tissues. These mutations allow a cell to enter a pathway of abnormal growth that can sometimes lead to the development of a malignancy [138–141].

Epidemiological and other studies of survivors of Hiroshima and Nagasaki are the main sources for the association of irradiation and the development of

cancers [138]. A significant increase in papilliferous thyroid cancer was also observed in children and teenagers exposed to radioiodine after the Chernobyl accident in 1986 [141].

REFERENCES

[1] FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, INTERNATIONAL ATOMIC ENERGY AGENCY, INTERNATIONAL CIVIL AVIATION ORGANIZATION, INTERNATIONAL LABOUR ORGANIZATION, INTERNATIONAL MARITIME ORGANIZATION, INTERPOL, OECD NUCLEAR ENERGY AGENCY, PAN AMERICAN HEALTH ORGANIZATION, PREPARATORY COMMISSION FOR THE COMPREHENSIVE NUCLEAR-TEST-BAN TREATY ORGANIZATION, UNITED NATIONS ENVIRONMENT PROGRAMME, UNITED NATIONS OFFICE FOR THE COORDINATION OF HUMANITARIAN AFFAIRS, WORLD HEALTH ORGANIZATION, WORLD METEOROLOGICAL ORGANIZATION, Preparedness and Response for a Nuclear or Radiological Emergency, IAEA Safety Standards Series No. GSR Part 7, IAEA, Vienna (2015).

[2] INTERNATIONAL ATOMIC ENERGY AGENCY, The Chernobyl Accident: Updating of INSAG-1, Safety Series No. 75-INSAG-7, IAEA, Vienna (1992).

[3] ILYIN, L.A., Chernobyl: Myth and Reality, Megapolis, Moscow (1995).

[4] THE CHERNOBYL FORUM, Chernobyl's Legacy: Health, Environmental and Socio-Economic Impacts and Recommendations to the Governments of Belarus, the Russian Federation and Ukraine, 2nd revised version, IAEA/PI/A.87 Rev.2/06-09181, IAEA, Vienna (2006).

[5] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Goiânia, IAEA, Vienna (1988).

[6] INTERNATIONAL ATOMIC ENERGY AGENCY, Dosimetric and Medical Aspects of the Radiological Accident in Goiânia in 1987, IAEA-TECDOC-1009, IAEA, Vienna (1998).

[7] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Samut Prakarn, IAEA, Vienna (2002).

[8] INTERNATIONAL ATOMIC ENERGY AGENCY, WORLD HEALTH ORGANIZATION, Diagnosis and Treatment of Radiation Injuries, Safety Reports Series No. 2. IAEA, Vienna (1998).

[9] INTERNATIONAL ATOMIC ENERGY AGENCY, Categorization of Radiation Sources, IAEA-TECDOC-1191, IAEA, Vienna (2000).

[10] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Tammiku, IAEA, Vienna (1998).

[11] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Istanbul, IAEA, Vienna (2000).

[12] COEYTAUX, K., et al., Reported radiation overexposure accidents worldwide, 1980–2013: A systematic review, PLoS One **10** 3 (2015).

[13] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident at the Irradiation Facility in Nesvizh, IAEA, Vienna (1996).

[14] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Yanango, IAEA, Vienna (2000).

[15] INTERNATIONAL ATOMIC ENERGY AGENCY, Accidental Overexposure of Radiotherapy Patients in San José, Costa Rica, IAEA, Vienna (1998).
[16] WORLD HEALTH ORGANIZATION, Emergency Triage Assessment and Treatment (ETAT): Manual for Participants, WHO, Geneva (2005).
[17] INTERNATIONAL ATOMIC ENERGY AGENCY, Medical Preparedness and Response for a Nuclear or Radiological Emergency: Training Materials, EPR-Medical/T-2014, IAEA, Vienna (2014).
[18] TURAI, I., VERESS, K., GÜNALP, B., SOUCHKEVITCH, G., Medical response to radiation incidents and radionuclear threats, Br. Med. J. **328** (2004) 568–572.
[19] TURAI, I., KÖTELES, G., "Sugárorvostan – személyi sérülésekkel járó sugárbalesetek és tanulságaik, felkészülés az ellátásukra", Sugáregészségtan (TURAI, I., KÖTELES, G., Eds), Medicina, Budapest (2014) 159–187.
[20] GUSEV, I.A., GUSKOVA, A.K., METTLER, F.A., BARABANOVA, A.V. (Eds), Medical Management of Radiation Accidents, 2nd edn, CRC Press, Boca Raton, FL (2001) 225.
[21] INTERNATIONAL ATOMIC ENERGY AGENCY, Generic Procedures for Medical Response During a Nuclear or Radiological Emergency, EPR-Medical, IAEA, Vienna (2005).
[22] METTLER, F.A., VOELZ, G.L., Major radiation exposure: What to expect and how to respond, New Engl. J. Med. **346** (2002) 1554–1561.
[23] INTERNATIONAL ATOMIC ENERGY AGENCY, Cytogenetic Dosimetry: Applications in Preparedness for and Response to Radiation Emergencies, EPR-Biodosimetry, IAEA, Vienna (2011).
[24] INTERNATIONAL ATOMIC ENERGY AGENCY, Convention on Early Notification of a Nuclear Accident and Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency, Legal Series No. 14, IAEA, Vienna (1987).
[25] INTERNATIONAL ATOMIC ENERGY AGENCY, Joint Radiation Emergency Management Plan of the International Organizations, EPR-JPLAN, IAEA, Vienna (2017).
[26] INTERNATIONAL ATOMIC ENERGY AGENCY, IAEA Safety Glossary: Terminology Used in Nuclear Safety and Radiation Protection, 2018 Edition, IAEA, Vienna (2019).
[27] RADIATION EMERGENCY ASSISTANCE CENTER/TRAINING SITE, The Medical Aspects of Radiation Incidents, Oak Ridge Institute for Science and Education, Oak Ridge, TN (2017).
[28] DANIAK, N., et al., Literature review and global consensus on management of acute radiation syndrome affecting nonhematopoietic organ systems, Disaster Med. Public Health Prep. **5** 3 (2011) 183–201.
[29] DANIAK, N., et al., First global consensus for evidence-based management of the hematopoietic syndrome resulting from exposure to ionizing radiation, Disaster Med. Public Health Prep. **5** 3 (2011) 202–212.
[30] BERTHO, J.M., GRIFFITHS, N.M., GOURMELLON, P., "The medical diagnosis and treatment of radiation overexposed people", Proc. 11th Int. Congr. International Radiation Protection Association, Madrid, 2004, IRPA, Madrid (2004).

[31] INSTITUT DE RADIOPROTECTION ET DE SÛRETÉ NUCLÉAIRE, De nouvelles voies de traitement pour les brûlures radiologiques? AKTIS **18** (2014).
[32] INTERNATIONAL ATOMIC ENERGY AGENCY, Investigation of an Accidental Exposure of Radiotherapy Patients in Panama, IAEA, Vienna (2001).
[33] INTERNATIONAL ATOMIC ENERGY AGENCY, Accidental Overexposure of Radiotherapy Patients in Białystok, IAEA, Vienna (2004).
[34] HERRERA REYES, E.D., et al., Medical response to radiological accidents in Latin America and international assistance, Radiat. Res. **185** 4 (2016) 359–365.
[35] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Nueva Aldea, IAEA, Vienna (2009).
[36] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in San Salvador, IAEA, Vienna (1990).
[37] PETER, R.U., "Management of skin injuries in radiation accidents: The cutaneous radiation syndrome", The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims (RICKS, R.C., BERGER, M.E., O'HARA, F.M., Jr., Eds), The Parthenon Publishing Group, New York (2002) 225–229.
[38] RYAN, J.L., Ionizing radiation: The good, the bad, and the ugly, J. Invest. Dermatol. **132** (2012) 985–993.
[39] HEALTH PROTECTION AGENCY, High Dose Radiation Effects and Tissue Injury: Report of the Independent Advisory Group on Ionising Radiation, Rep. RCE-10, HPA, Chilton (2009).
[40] PANIZZON, R.G., GOLDSCHMIDT, H., "Radiation reactions and sequelae", Modern Dermatologic Radiation Therapy (GOLDSCHMIDT, H., PANIZZON, R.G., Eds), Springer, New York (1991).
[41] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in Lilo, IAEA, Vienna (2000).
[42] BEY, E., Emerging therapy for improving wound repair of severe radiation burns using local bone marrow-derived stem cell administration, Wound Repair Regen. **18** 1 (2010) 50–58.
[43] BAST, F., GROSS, A., LARS, H., SCHROM, T., Etiology and treatment of osteonecrosis of the mandible, Contemp. Oncol. (Pozn) **17** 3 (2013) 281–285.
[44] LATAILLADE, J.J., et al., New approach to radiation burn treatment by dosimetry-guided surgery combined with autologous mesenchymal stem cell therapy, Regen. Med. **2** 5 (2007) 785–794.
[45] OKUNIEFF, P., et al., Pentoxifylline in the treatment of radiation-induced fibrosis, J. Clin. Oncol. **22** 11 (2004) 2207–2213.
[46] IDDINS, C.J., et al., Management of ionizing radiation injuries and illnesses, Part 5: Local radiation injury, J. Am. Osteopath. Assoc. **114** (2014) 840–848.
[47] DIEHL, C., Use of topical superoxide dismutase in the management of radiation-induced fibrosis: A neglected opportunity? J. Cancer Therapeut. Res. (2012).
[48] GEORGE, T.C., HUZAR, T.F., CROSS, J.M., Exposure to an iridium-192 source in an industrial safety worker, J. Burn Care Res. **35** 3 (2014).
[49] BEY, E., et al., Irradiation aiguë localisée: Chirurgie et thérapie cellulaire — A propos de deux cas, Bull. Acad. Natl Med. **191** 6 (2007) 971–978.

[50] BENDERITTER, M., et al., New emerging concepts in the medical management of local radiation injury, Health Phys. **98** 6 (2010) 851–857.
[51] KOTENKO, K.V., et al., Cell technologies in the treatment of radiation burns: Experience Burnasyan Federal Medical Biophysical Centre, Cell. Transplant. Tissue Eng. **7** 2 (2012) 97–102 (in Russian).
[52] FLYNN, D., "Advances in the diagnosis and management of acute radiation syndrome, cutaneous radiation syndrome, and acute local radiation injuries", The Medical Basis for Radiation Accident Preparedness: Medical Management (CHRISTENSEN, D.M., SUGARMAN, S.L., O'HARA, F.M., Jr., Eds), Oak Ridge Associated Universities, Oak Ridge, TN (2013) 109–112.
[53] AKITA, S., et al., Autologous adipose-derived regenerative cells are effective for chronic intractable radiation injuries, Radiat. Prot. Dosim. **151** (2012) 656–660.
[54] INTERNATIONAL ATOMIC ENERGY AGENCY, Report on the Preliminary Fact Finding Mission Following the Accident at the Nuclear Fuel Processing Facility in Tokaimura, Japan, IAEA, Vienna (1999).
[55] MIQUEL MACIÀ I GARAU, A., CALDUCH, A.L., LÓPEZ, E.C., Radiobiology of the acute radiation syndrome, Rep. Pract. Oncol. Radiother. **16** 4 (2011) 123–130.
[56] GOURMELON, P., MARQUETTE, C., AGAY, D., Involvement of the central nervous system in radiation-induced multi-organ dysfunction and/or failure, Br. J. Radiol. Suppl. **27** (2005) 62–68.
[57] GAUGLER, M.-H., A unifying system: Does the vascular endothelium have a role to play in multi-organ failure following radiation exposure? Br. J. Radiol. Suppl. **27** (2005) 100–105.
[58] WASELENKO, J.K., et al., Medical management of acute radiation syndrome: Recommendations of the Strategic National Stockpile Radiation Working Group, Ann. Int. Med. **140** 12 (2004) 1037–1051.
[59] VALVERDE, N.J., et al., "The acute radiation syndrome in the 137Cs Brazilian accident, 1987", The Medical Basis for Radiation Accident Preparedness II: Clinical Experience and Follow-up Since 1979 (RICKS, R.C., FRY, S.A., Eds), Elsevier North-Holland, New York (1990) 89–107.
[60] GUNTER-SMITH, P.J., "Effect of ionizing radiation on gastrointestinal physiology", Military Radiobiology (CONKLIN, J.J., WALKER, R.I., Eds), Academic Press, Orlando, FL (1987) 135–151.
[61] HALL, E.J., "Acute effects of total-body irradiation", Radiobiology for the Radiologist, 5th edn (HALL, E.J., Ed.), Lippincott Williams and Wilkins, Philadelphia, PA (2000) 124–135.
[62] ROJAS-PALMA, et al. (Eds), TMT Handbook: Triage, Monitoring and Treatment of People Exposed to Ionising Radiation Following a Malevolent Act, Lobo Media, Oslo (2009).
[63] DEMIDENKO, E., WILLIAMS, B.B., SWARTZ, H.M., Radiation dose prediction using data on time to emesis in the case of nuclear terrorism, Radiat. Res. **171** 3 (2009) 310–319.

[64] HUET, C., et al., Physical dose reconstruction in case of radiological accidents: An asset for the victims' management, Proc. 12th Int. Congr. International Radiation Protection Association, Buenos Aires, 2008, IRPA, Buenos Aires (2008).
[65] BARRET, A., et al., Changes in serum amylase and its isoenzymes after whole body irradiation, Br. Med. J. (Clin. Res. Ed.) **285** 6336 (1982) 170–171.
[66] MONROY, R.L., "Radiation effect on the lymphohematopoietic system: A compromise in immune competency", Military Radiobiology (CONKLIN, J.J., WALKER, R.I., Eds), Academic Press, Orlando (1987) 111–134.
[67] AKASHI, M., et al., European Approach for the Medical Management of Mass Radiation Exposure (2007), https://sremc.files.wordpress.com/2018/07/ebmt-nuclear-accident-committee-pocket-guide-2017.pdf
[68] JUNGLEE, D., et al., Salivary amylase and pancreatic enzymes in serum after total body irradiation, Clin. Chem. **32** 4 (1986) 609–610.
[69] HENNEQUIN, C., et al., L'amylasemie: Un marqueur biologique des irradiations accidentelles, Bull. Cancer **76** 6 (1989) 617–624.
[70] DUBRAY, B., et al., Post-irradiation hyperamylasemia as a biological dosimeter, Radiother. Oncol. **24** 1 (1992) 21–26.
[71] BERTHO, J.M., et al., Level of Flt3-ligand in plasma: A possible new bio-indicator for radiation-induced aplasia, Int. J. Radiat. Biol. **77** (2001) 703–712.
[72] ROY, L., et al., Biochemical approach to prediction of multiple organ dysfunction syndrome, Br. J. Radiol. Suppl. **27** (2005) 146–151.
[73] OSSETROVA, N.I., SANDGREN, D.J., BLAKELY, W.F., C-reactive protein and serum amyloid A as early-phase and prognostic indicators of acute radiation exposure in nonhuman primate total-body irradiation model, Radiat. Meas. **46** 9 (2011) 1019–1024.
[74] LUTGENS, L.C., et al., Plasma citrulline concentration: A surrogate end point for radiation-induced mucosal atrophy of the small bowel, A feasibility study in 23 patients, Int. J. Radiat. Oncol. Biol. Phys. **60** 1 (2004) 275–285.
[75] SWARTZ, H., et al., In vivo EPR dosimetry to quantify exposures to clinically significant doses of ionizing radiation, Radiat. Prot. Dos. **120** 1–4 (2006) 163–170.
[76] BRUSTOLON, M., GIAMELLO, E. (Eds), Electron Paramagnetic Resonance: A Toolkit for Practitioners, Wiley, Hoboken, NJ (2009).
[77] ROMANYUKHA, A., REYES, R.A., TROMPIER, F., "Electron spin resonance in the diagnosis of acute radiation syndrome: The state of the art", The Medical Basis for Radiation Accident Preparedness: Medical Management (CHRISTENSEN, D.M., SUGARMAN, S.L., O'HARA, F.M., Jr., Eds), Oak Ridge Associated Universities, Oak Ridge, TN (2013) 61–79.
[78] WILLIAMS, B.B., et al., In vivo EPR tooth dosimetry for triage after a radiation even involving large populations, Radiat. Environ. Biophys. **53** 2 (2014) 335–346.
[79] COSSET, J.M., et al., "Medical management during the prodromal and latent periods", The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims (RICKS, R.C., BERGER, M.E., O'HARA, F.M., Jr., Eds), The Parthenon Publishing Group, New York (2002) 45–51.

[80] NAIR, V., et al., Allogeneic hematopoietic stem cell transplantation: The Army hospital experience. Natl Med. J. India **26** 1 (2013) 6–11.
[81] FREIFELD, A.G., et al., Clinical practice guideline for use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America, Clin. Infect. Dis. **52** 4 (2011) e56–e93.
[82] HUGHES, W.T., "Use of antimicrobial agents for treatment of infection in the neutropenic immunocompromised patient", The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims (RICKS, R.C., BERGER, M.E., O'HARA, F.M., Jr., Eds), The Parthenon Publishing Group, New York (2002) 117–129.
[83] DANIAK, N., GENT, N., "Evidence-based recommendations for clinical management of radiation-associated injury to bone marrow", The Medical Basis for Radiation Accident Preparedness. Medical Management (CHRISTENSEN, D.M., SUGARMAN, S.L., O'HARA, F.M., Jr., Eds), Oak Ridge Associated Universities, Oak Ridge, TN (2013) 51–60.
[84] HERODIN, F., DROUET, M., Cytokine-based treatment of accidentally irradiated victims and new approaches, Exp. Hematol. **33** (2005) 1071–1080.
[85] FLIEDNER, T.M., BEYRER, K., Medical Management of Radiation Accidents: Manual on the Acute Radiation Syndrome, British Institute of Radiology, London (2001).
[86] HÉRODIN, F., MAYOL, J.-F., MOURCIN, F., DROUET, M., Which place for stem cell therapy in the treatment of acute radiation syndrome?, Folia Histochem. Cytobiologica **43** 4 (2005) 223–227.
[87] GEORGES, G.E., STORB, R.F., "Experimental and clinical experience with hematopoietic stem cell transplants", The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims (RICKS, R.C., BERGER, M.E., O'HARA, F.M., Jr., Eds), The Parthenon Publishing Group, New York (2002) 73–93.
[88] MASON, K.A., WITHERS, H.R., McBRIDE, W.H., DAVIS, C.A., SMATHERS, J.B., Comparison of the gastrointestinal syndrome after total-body or total-abdominal irradiation, Radiat. Res. **117** (1989) 480–488.
[89] WILLIAMS, J.P., Animal models for medical countermeasures to radiation exposure, Radiat. Res. **173** 4 (2010) 557–578.
[90] WITHERS, H.R., ELKIND. M.M., Dose-survival characteristics of epithelial cells of mouse intestinal mucosa, Radiol. **91** (1968) 998–1000.
[91] POTTEN, C.S., HENDRY, J.H., Radiation and Gut, Elsevier Science, Amsterdam (1995).
[92] DENHAM, J., HAUER-JENSEN, M., PETERS, L., Is it time for a new formalism to categorize normal tissue radiation injury? Int. J. Radiat. Oncol. Biol. Phys. **50** (2001) 1105–1106.
[93] MOUSSA, L., Bowel radiation injury: Complexity of the pathophysiology and promises of cell and tissue engineering, Cell Transpl. **25** 10 (2016) 1723–1746.
[94] HUI-JU CH'ANG et al., ATM regulates target switching to escalating doses of radiation in the intestines, Natl Med. **11** (2005) 484–490.
[95] QUASTLER, H., The nature of intestinal radiation death, Radiat. Res. **4** (1956) 303–320.
[96] GERACI, J.P., JACKSON, K.L., MARIANO, M.S., The intestinal radiation syndrome: Sepsis and endotoxin, Radiat. Res. **101** (1985) 442–450.

[97] CARR, K.E., Effects of radiation damage on intestinal morphology, Int. Rev. Cytol. **208** (2001) 1–119.
[98] POTTEN, C.S., "Radiation injury to the gastrointestinal epithelium: Current research on treatment, management and prevention", The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims (RICKS, R.C., BERGER, M.E., O'HARA, F.M., Jr., Eds), The Parthenon Publishing Group, New York (2002) 139–160.
[99] HOND, E.D., et al., Effect of long-term oral glutamine supplements on small intestinal permeability in patients with Crohn's disease, J. Parenter. Enteral. Nutr. **23** (1999) 7–11.
[100] FASANO, A. "Pathophysiology and management of radiation injury of gastrointestinal tract", The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims (RICKS, R.C., BERGER, M.E., O'HARA, F.M., Jr., Eds), The Parthenon Publishing Group, New York (2002) 149–160.
[101] FLIEDNER, T.M., DORR, H.D., MEINEKE, V., Multi-organ involvement as a pathogenetic principle of the radiation syndromes: A study involving 110 case histories document in SEARCH and classified as the bases of hematopoietic indicators of effect, Br. J. Radiol. Suppl. **27** (2005) 1–8.
[102] INTERNATIONAL ATOMIC ENERGY AGENCY, Medical Management of Persons Internally Contaminated with Radionuclides in a Nuclear or Radiological Emergency: A Manual for Medical Personnel, EPR-Internal Contamination, IAEA, Vienna (2018).
[103] UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, Cancer Risk Coefficients for Environmental Exposure to Radionuclides: Federal Guidance Report No. 13, Rep. EPA 402-R-99-001, EPA, Washington, DC (1999).
[104] HARRISON, J., LEGGETT, R., LLOYD, D., PHIPPS, A., SCOTT, B., Polonium-210 as a poison, J. Radiol. Prot. **27** (2007) 17–40.
[105] NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENTS, Development of a Biokinetic Model for Radionuclide-contaminated Wounds and Procedures for Their Assessment, Dosimetry and Treatment, Rep. 156, NCRP, Bethesda, MD (2006).
[106] NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENTS, Management of Persons Contaminated with Radionuclides, 2 vols, Rep. 161, NCRP, Bethesda, MD (2008).
[107] LIPSZTEIN, J.L., et al., Application of in-vitro bioassay for ^{137}Cs during the emergency phase of the Goiânia accident, Health Phys. **60** 1 (1991) 43–49.
[108] LIPSZTEIN, J.L., BERTELLI, L., OLIVEIRA, C.A., DANTAS, B.M., Studies of Cs retention in the human body related to body parameters and Prussian blue administration, Health Phys. **60** 1 (1991) 57–61.
[109] FARINA, R., BRANDÃO-MELLO, C.E., OLIVEIRA, A.R., Medical Aspects of 137Cs decorporation: The Goiânia radiological accident, Health Phys. **60** 1 (1991) 63–66.
[110] FLORA, S.J., PACHAURI, V., Chelation in metal intoxication, Int. J. Environ. Res. Public Health **7** (2010) 2745–2788.
[111] MORGAN, C., BINGHAM, D., HOLT, D.M., JONES, D.M., LEWIS, N.J., Therapeutic whole lung lavage for inhaled plutonium oxide revisited, J. Radiol. Prot. **30** (2010) 735–746.

[112] OLIVEIRA, A.R, et al., “Skin lesions associated with the Goiânia accident”, The Medical Basis for Radiation Accident Preparedness II: Clinical Experience and Follow-up Since 1979 (RICKS, R.C., FRY, S.A., Eds), Elsevier North-Holland, New York (1990) 173–181.
[113] BOWERS, G.J., “The combined injury syndrome”, Military Radiobiology (CONKLIN, J.J., WALKER, R.I., Eds), Academic Press, Orlando (1987) 191–217.
[114] LEDNEY, G., ELLIOTT, T., Combined injury: Factors with potential to impact radiation dose assessments, Health Phys. **98** (2010) 145–152.
[115] COLEMAN, N., et al., Medical planning and response for a nuclear detonation: A practical guide, Biosecur. Bioterrorism **10** 4 (2012) 346–371.
[116] KIANG, J., et al., Wound trauma alters ionizing radiation dose assessment, Cell Biosci. **2** 20 (2012).
[117] ZOU, Z., LUO, C., Progress in research on radiation combined injury in China, Radiat. Res. **169** (2008) 722–729.
[118] INTERNATIONAL ATOMIC ENERGY AGENCY, Communication with the Public in a Nuclear or Radiological Emergency, EPR-Public Communications, IAEA, Vienna (2012).
[119] INTERNATIONAL ATOMIC ENERGY AGENCY, Communication with the Public in a Nuclear or Radiological Emergency: Training Materials, EPR-Public Communications/T, IAEA, Vienna (2012).
[120] INTERNATIONAL ATOMIC ENERGY AGENCY, Method for Developing a Communication Strategy and Plan for a Nuclear or Radiological Emergency, EPR-Public Communication Plan, IAEA, Vienna (2015).
[121] REYNOLDS, B., SEEGER, M., Crisis and Emergency Risk Communication: 2014 Edition, Centers for Disease Control and Prevention, Atlanta, GA (2014).
[122] ROPEIK, D., GRAY, G., Risk: A Practical Guide for Deciding What’s Really Safe and What’s Really Dangerous in the World Around You, Houghton Mifflin Harcourt, New York (2002).
[123] INTERNATIONAL ATOMIC ENERGY AGENCY, The Fukushima Daiichi Accident, Technical Volume 3: Emergency Preparedness and Response, IAEA, Vienna (2015).
[124] WORLD HEALTH ORGANIZATION, Health Risk Assessment from the Nuclear Accident after the 2011 Great East Japan Earthquake and Tsunami, Based on a Preliminary Dose Estimation, WHO, Geneva (2013).
[125] UNITED NATIONS, Levels and Effects of Radiation Exposure due to the Nuclear Accident after the 2011 Great East Japan Earthquake and Tsunami (Report to the General Assembly), UN, New York (2013).
[126] INTERNATIONAL FEDERATION OF RED CROSS AND RED CRESCENT SOCIETIES, “Psychosocial interventions”, Nuclear and Radiological Emergency Guidelines: Preparedness, Response and Recovery, IFRC, Geneva (2015).
[127] NEW YORK STATE DEPARTMENT OF HEALTH, Disaster Mental Health: Assisting People Exposed to Radiation, SUNY New Paltz (2015), www.ct.gov/dmhas/lib/dmhas/publications/DMH-RadiationXposure.pdf
[128] WORLD HEALTH ORGANIZATION, Psychological First Aid: Guide for Field Workers, WHO, Geneva (2011).

[129] AUSTRALIAN PSYCHOLOGICAL SOCIETY, Psychological First Aid: An Australian Guide to Supporting People Affected by Disaster, APS, Melbourne (2013).
[130] INTERNATIONAL ATOMIC ENERGY AGENCY, Lessons Learned from the Response to Radiation Emergencies (1945–2010), EPR-Lessons Learned, IAEA, Vienna (2012).
[131] INTERNATIONAL ATOMIC ENERGY AGENCY AND WORLD HEALTH ORGANIZATION, Planning the Medical Response to Radiological Accidents, Safety Reports Series No. 4, IAEA, Vienna (1998).
[132] HEADS OF THE EUROPEAN RADIOLOGICAL PROTECTION COMPETENT AUTHORITIES, Emergency Preparedness Practical Guidance: Practicability of Early Protective Actions, HERCA, Brussels (2011), www.herca.org/documents/Practical%20Guidance%20-Practicability%20of%20Early%20Protective%20Actions_20110630.pdf
[133] INTERNATIONAL ATOMIC ENERGY AGENCY, Radiation Biology: A Handbook for Teachers and Students, Training Course Series No. 42, IAEA, Vienna (2010).
[134] CANADIAN CENTRE FOR OCCUPATIONAL HEALTH AND SAFETY, Radiation: Quantities and Units of Ionizing Radiation (2019), www.ccohs.ca/oshanswers/phys_agents/ionizing.html
[135] SHAHBAZI-GAHROUEI, D., GHOLAMI, M., SETAYANDEH, S., A review on natural background radiation, Adv. Biomed. Res. **2** (2013) 65.
[136] GONZÁLEZ, A.J., Biological effects of low doses of ionizing radiation: A fuller picture, IAEA Bull. (April 1994).
[137] INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, The 2007 Recommendations of the International Commission on Radiological Protection, ICRP Publication 103, Elsevier, Oxford (2007).
[138] INTERNATIONAL ATOMIC ENERGY AGENCY, Radiation, People and the Environment, IAEA, Vienna (2004).
[139] UNITED NATIONS, Sources and Effects of Ionizing Radiation: United Nations Scientific Committee on the Effects of Atomic Radiation, UNSCEAR 2008 Report to the General Assembly with Scientific Annexes, Vol. 1, UN, New York (2008).
[140] HALL, E.J., GIACCIA, A.J., Radiobiology for the Radiologist, Wolters Kluwer, Philadelphia, PA (2018).
[141] IVANOV, V.K., et al., Radiation-epidemiological studies of thyroid cancer incidence in Russia after the Chernobyl accident (estimation of radiation risks, 1991–2008 follow-up period), Radiat. Prot. Dosim. **151** (2012) 1–11.

ABBREVIATIONS

ARS	acute radiation syndrome
CBC	complete blood count
CRI	combined radiation injury
DTPA	diethylenetriaminepentaacetatic acid
ESR	electron spin resonance
G-CSF	granulocyte colony stimulating factor
GIT-ARS	gastrointestinal type of acute radiation syndrome
GM-CSF	granulocyte macrophage colony stimulating factor
HEPA	high efficiency particulate air
HLA	human leukocyte antigen
HT-ARS	haematopoietic type of acute radiation syndrome
HSCT	haematopoietic stem cell transplantation
LRI	local radiation injury
MSC	mesenchymal stem cell
NVT-ARS	neurovascular type of acute radiation syndrome
PCC	premature chromosome condensation

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