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No. 2



DIAGNOSIS
AND
TREATMENT
OF RADIATION
INJURIES



DIAGNOSIS AND TREATMENT OF
RADIATION INJURIES

SAFETY REPORTS SERIES No. 2

DIAGNOSIS AND TREATMENT OF RADIATION INJURIES

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FOREWORD

In the publication of the International Atomic Energy Agency entitled Manual on Early Medical Treatment of Possible Radiation Injury (Safety Series No. 47, 1978) first aid and early medical treatment of workers who might have received external or internal radiation exposure in an accident are discussed.

In the IAEA publication Medical Handling of Accidentally Exposed Individuals (Safety Series No. 88, 1988) a set of general criteria and recommendations are presented to aid specialists involved in the medical handling of overexposed persons.

Many lessons have been learnt from the accidents at Chernobyl (Ukraine, 1986) and Goiânia (Brazil, 1987), and also from those at San Salvador (El Salvador, 1989), Soreq (Israel, 1990) and Nesvizh (Belarus, 1991), on the early medical handling of radiation injuries. These lessons have been incorporated into this report, which is intended to help all those physicians who may be involved in the early medical handling of radiation victims with prompt diagnostic measures and emergency treatment. Special attention is drawn to the localized radiation injuries which are the most frequently observed direct health effects of ionizing radiation.

The participation of all the members of the Advisory Group meeting (April 1993) and of the consultants meetings (May 1993 and April 1996) in drafting the report is appreciated. The major contribution of A. Barabanova (Institute of Biophysics, Russian Federation) is especially acknowledged.

The Scientific Secretary responsible for preparation of this publication was I. Turai of the Division of Radiation and Waste Safety.

EDITORIAL NOTE

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1. INTRODUCTION

1.1. BACKGROUND

According to the International Basic Safety Standards an accident is “any unintended event, including operating errors, equipment failures or other mishaps, the consequences or potential consequences of which are not negligible from the point of view of protection or safety” [1].

A radiological accident is defined as an unforeseen event involving overexposure or contamination of persons and/or the environment by radioactive material. Exposure may have actually occurred or only be suspected. This distinction is important because experience has shown that it is safer and less costly to put an accident plan into operation when an accident is suspected, rather than wait until its occurrence is established. Although infrequent compared to conventional accident situations, occurrences over the past five decades have provided sufficient data to develop guidelines for medical management of radiation casualties.

Although the March 1979 incident at Three Mile Island in the United States of America created tremendous public concern, it caused no radiation injuries. Because of the integrity of the containment vessel, and in spite of a fuel meltdown, the contamination outside the reactor building and the release of radioiodine were negligible. By contrast, the major nuclear and radiological accidents at Chernobyl, Ukraine, and Goiânia, Brazil, have provided important information for the diagnosis, monitoring and treatment of radiation injuries. The explosion of vapour in April 1986 at the Chernobyl nuclear power plant, which had no containment vessel, resulted in the hospitalization of 237 patients identified as having been overexposed. Of these, 134 developed acute radiation syndrome (ARS); 28 of these patients eventually died of ARS associated with extensive radiation burns [2].

In September 1987, a shielded radioactive ^{137}Cs source (50.9 TBq) was removed from the protective housing of an abandoned teletherapy machine in Goiânia, Brazil. Subsequently, the source was ruptured. As a result, many people incurred large doses of radiation by both external and internal contamination. Four of the casualties eventually died and 28 people developed local radiation injuries. A total of 249 cases of radioactive contamination were detected, 129 of whom had both internal and external contamination [3]. There was extensive contamination of homes, other buildings and surface soil in the urban area of Goiânia. This incident is discussed in greater detail in Annex II.

In 1989 a radiological accident occurred at an industrial sterilization facility in San Salvador, El Salvador. The accident occurred when the ^{60}Co source became stuck in the open position. Three workers were exposed to high radiation doses and developed ARS. The immediate acute effects were limited by specialized treatment.

Nonetheless, two of the men were so seriously injured that their legs had to be partly or completely amputated. The most highly exposed worker died six months later, death being attributed to residual lung damage and other injuries [4].

The International Atomic Energy Agency has provided detailed reports on these accidents in various publications [3–6]. The report on the accident at Tammiku, Estonia, is currently being prepared for publication by the Agency.

1.2. OBJECTIVE

This publication is directed at medical professionals who may be involved in the management of radiation injuries starting from the first few hours or days after an exposure of undefined severity (i.e. those handling the emergency situation may not know the extent and severity of the accident). Experience has shown that in addition to occupational physicians, the complete management of an emergency case involves other professionals such as haematologists, oncologists, plastic surgeons, dermatologists, vascular surgeons, psychiatrists and consultants in other medical specialties. The principal aim of this publication is to provide guidelines to enable medical professionals to carry out prompt diagnostic measures and to offer emergency treatment.

1.3. SCOPE

This report provides information in tabulated form on clinical criteria for dose assessment. Additionally, it discusses the appropriate dose–effect relationship in cases of external radiation involving either total body or local exposures, as well as internal contamination. It is not within the scope of this report to provide details of conventional treatment procedures. However, indications as to when to perform specific therapies are provided. The underlying principles of radiobiology and radiation pathology are not discussed.

1.4. STRUCTURE

Section 2 covers the different types and modes of accidental exposure and their medical management including triage, which is an important step to establish priorities for medical treatment and hospitalization. Sections 3 and 4 deal with the medical management following external exposure and internal contamination, reviewing diagnosis and treatment. Section 5 provides a classification of combined radiation injuries and their treatment. Section 6 offers information on a consulting system from which advice and assistance can be obtained in the event of a radiation accident, and Section 7 gives instructions on how to collect data relating to patient care. Annex I contains a set of record form samples for data collection. Annex II gives a description of the diagnosis and treatment used at Goiânia.

2. TYPES OF ACCIDENTAL EXPOSURE AND THEIR MEDICAL MANAGEMENT

2.1. TYPES OF ACCIDENT

An accident is called a nuclear accident when it involves a nuclear facility, especially a nuclear reactor. A radiological accident involves a sealed or unsealed radiation source and leads to an uncontrolled release of ionizing radiation or radioactive materials into the environment. Such radiation sources include X ray equipment, sealed radioactive isotope sources (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.

Potential accident types include the following:

- (a) A radioactive source may be misplaced, lost or stolen. An obvious example might be a γ radiography source container and source found to be missing. One problem here is that the container may come into the possession of people who decide to dismantle or otherwise interfere with it, thereby exposing themselves and possibly others to an unshielded source.
- (b) A radioactive source may become unshielded as the result of a failure during routine operations. Again, γ radiography provides an example: after making an exposure an operator may find it impossible to retract the source into its container.
- (c) A radioactive material may be dispersed. For example, a vial containing a radioactive solution might develop a leak during storage. Another example would be a violent release of radioactive substances from a radiochemical facility.

In all these cases, there is a possibility of uncontrolled exposure of persons unless appropriate protective measures are taken. From a planning point of view, it is helpful to classify accidents according to their severity, the number of individuals injured (e.g. more than five is considered a major accident), and their radiological consequences, such as external exposure, external and internal contamination and their combination.

2.2. RADIATION SOURCES AND MODES OF EXPOSURE

The facilities in which X rays and radionuclides are either produced or used, the types of radiation source, and the levels of activity have to be identified in order to

TABLE I. COMMON RADIATION SOURCES, FACILITIES AND EXPOSURE MODES

Group	Source and/or facility	External exposure	Contamination	Mixed
I	Critical assembly	Yes	Yes	Yes
	Reactor	Yes	Yes	Yes
	Fuel element manufacture	Yes	Yes	Yes
	Radiopharmaceutical manufacture	Yes	Yes	Yes
	Fuel reprocessing plant	Yes	Yes	Yes
II	Radiation device, e.g.			
	Particle accelerator	Yes	^a	^a
	X ray generator	Yes	No	No
III	Sealed source (intact)	Yes	No	No
	Sealed source (leaking)	Yes	Yes	Yes
IV	Nuclear medicine laboratory	Yes	Yes	Yes
	In vitro assay laboratory	Yes	Yes	Yes
V	Source transportation	Yes	Yes	Yes
VI	Radioactive wastes	Yes	Yes	Yes

^a Neutrons may induce radioactivity within the body (see text).

provide information that can be used in advance preparation of proper medical arrangements for dealing with an accident. The most frequently encountered radiation sources are listed in Table I.

Group I includes nuclear facilities such as power reactors and industrial and research facilities. Group II sources are encountered in both industrial and medical facilities. Sealed sources in Group III are widely used in industry and medicine. The most common accidents occur in industries using sealed sources. Very serious injuries and some deaths have occurred in this group, although many of these have not yet been reported in the medical literature. Group IV consists of the largest number of facilities, but serious accidents are unlikely because of the low levels of activity and the use of radionuclides with short half-lives.

In Groups IV–VI, only one individual or a very small number of people have been involved in the accidents described in most published accounts. Although the potential for accidents in transportation (Group V) is important, they occur only rarely.

TABLE II. RADIOLOGICAL AND NUCLEAR ACCIDENTS RESULTING IN RADIATION INJURY

Area of application	Source, radionuclide	Part of body exposed	Possible number of persons injured
Industry			
Sterilization	Co-60, Cs-137	Whole body, hands	1-3
Radiography	Ir-192, Cs-137	Hands, other parts	1-10
Gauging	Ir-192, Cs-137	Hands, other parts	1-2
Medicine			
Diagnostics	X ray generators	Hands, face	1-10
Therapy	Co-60, Cs-137 and accelerators	Whole body, hands and other parts	1-10 (more in extremely rare cases)
Research	Broad spectrum of sources, including reactors	Hands, face, other parts	1-3 (more at research reactors)
Spent sources	Co-60, Cs-137 and others	Hands, other parts	1-20 (more in extremely rare cases)
Nuclear reactors	Cs-137, Sr-90 I-131 Pu-210	Whole body Thyroid gland Lung	1-500 (usually much less than the number of persons affected)

Table II categorizes radiological and nuclear accidents according to the radioisotopes involved, the parts of the body exposed and the possible number of persons injured.

The most important exposure routes in the early stage of an accident are:

- direct radiation from the source or facility and from any radioactive material released;
- inhalation of airborne material (volatiles, aerosols, particulates);
- direct radiation from ground or surface deposition;
- contamination of skin and clothing.

For these exposure routes it has been shown that direct radiation from the source is the strongest contributor to the doses received [7, 8]. In particular, accidents associated with γ radiography are likely to have significant radiological consequences. In nuclear accidents the radioactive plume may act as a main source of external radiation, while radioactive airborne material, especially radioactive isotopes of iodine, may significantly contribute to the internal dose of the thyroid gland.

2.3. SORTING (TRIAGE) OF INJURED PERSONS

Triage refers to the sorting of patients into classes on the basis of their injury and/or disease, for the purpose of expediting clinical care and maximizing the use of the available clinical services and facilities. One of its main tasks is to determine the level of emergency care required. If the accident produces only a small number of casualties, medical management should not cause major problems in most countries. An accident involving tens or hundreds of individuals exposed, or suspected of having been exposed, would cause great difficulties, especially regarding hospitalization. Thus, planning is very important and should be adapted to the system of medical care contemplated for catastrophic event situations. This chain of sorting and care becomes crucial when both relief personnel and facilities are limited. Triage is widely employed in all kinds of catastrophe; radiation injury is not unique in this regard.

The organization of medical treatment should be assessed on the basis of whether an injury constitutes an emergency or not. Emergency treatment will be determined initially by conventional injuries such as trauma, wounds and thermal or chemical burns. Contamination with radionuclides is a problem in relatively few cases. Persons contaminated either externally or internally should be identified and treated immediately and specifically. In all other cases the need for treatment of radiation injuries does not constitute a medical emergency, although some early essential actions should be taken (such as blood sampling for assessing the degree of severity of the exposure and for human lymphocyte antigen (HLA) typing).

The early clinical symptoms serve as a basis for sorting persons exposed to radiation and deciding upon proper medical care at an individual level. The most important prodromal early clinical signs are nausea, vomiting, diarrhoea, and skin and mucosa erythema. The decision on hospitalization, in cases of whole body exposure (WBE) or local exposure (LE), depends on the presence of early clinical signs as described in Table III.

2.4. MEDICAL MANAGEMENT OF INDIVIDUALS

The first task is to divide the persons exposed (or suspected of having been exposed) into groups, taking into account the estimated severity of the radiation

TABLE III. GUIDE FOR THE MANAGEMENT OF RADIATION INJURIES BASED ON EARLY SYMPTOMS

Clinical signs		Corresponding dose (Gy)		Decision
WBE	LE	WBE	LE	
No vomiting	No early erythema	<1	<10	Outpatient with five week surveillance period (blood, skin)
Vomiting 2–3 h after exposure	Early erythema or abnormal sensation 12–24 h after exposure	1–2	8–15	Surveillance in a general hospital (or outpatient for 3 weeks followed by hospitalization if necessary)
Vomiting 1–2 h after exposure	Early erythema or abnormal sensation 8–15 h after exposure	2–4	15–30	Hospitalization in a haematological or surgical (burns) department
Vomiting earlier than 1 h after exposure and/or other severe symptoms, e.g. hypotension	Early erythema, within the first 3–6 h (or less) after exposure, of skin and/or mucosa with oedema	>4	>30	Hospitalization in a well equipped haematological or surgical department with transfer to a specialized centre for radiopathology

induced injuries and the type and level of medical care needed. Three main categories of exposed persons can be distinguished.

The first category includes those individuals, whether overexposed or suspected of overexposure, that display signs of conventional injuries such as trauma, wounds, burns and/or chemical contamination. These individuals should be managed as in any medical emergency. In addition, they should undergo specific testing without delay (blood cell counts, blood sampling for cytogenetic studies and HLA typing), in order to assess the severity of the exposure and to provide the basis for treatment initiation. If a sufficient number of first aid personnel are available, then specific testing on-site should be implemented as soon as feasible.

The second category includes individuals who are likely to have been exposed externally or who have external or internal contamination, or who are suspected of having been exposed at such dose levels that they may require a certain degree of medical management. For this category, preplanned actions are required. These

victims should be regrouped in a treatment centre where a secondary triage into three subcategories should be carried out. These subcategories include: persons whose whole body has been exposed; those whose body has been locally exposed; and those who have been contaminated with radionuclides. Simultaneously, the availability of medical facilities at regional and/or national level should be determined. In the days immediately following the exposure, most victims can be handled by physicians, to ensure that examinations and follow-up are carried out properly. These basic examinations should be listed on a special protocol drawn up by the medical centre responsible for handling the accident. In a second phase, a further classification into categories of severity will be based on clinical and biological findings.

The last category comprises individuals who are likely to have received only low doses and are free from any other injury. These individuals should be registered and monitored as outpatients for a few days.

The severity of the injury depends on the dose level incurred, the dose rate, the radiosensitivity of the tissues involved, the area of the body exposed and the extent of exposure suffered by the organ system. The severity of the injury is greater when the whole body is exposed; partial body exposure to the same dose has less impact on health. An absorbed radiation dose of about 3.5 Gy is generally expected to result in the death of 50% of the exposed population group within two months if there is no medical treatment. This LD_{50/60} value can be increased to about 5.0–6.0 Gy with adequate supportive treatment. Table IV presents the main diagnostic methods used in cases of whole body exposure.

TABLE IV. METHODS FOR EARLY DIAGNOSIS OF RADIATION INJURIES^a

Procedure	Finding	Time of onset	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 count	Absolute lymphocyte count ^b < 1 G/L	Within 24–72 h	~0.5
Cytogenetics ^c	Dicentrics, rings, fragments	Within hours	~0.2

^a Partly from Ref. [9].

^b Lymphocytes may decrease within hours. The baseline count should be obtained as soon as possible and the counting repeated daily. Lymphocyte count (G/L) expressed as 10⁹ cells/L.

^c Requires 48–72 h for analysis.

The severity of the exposure will usually be assessed in an iterative manner:

- (a) A very early classification will be based on clinical symptoms such as nausea, vomiting, diarrhoea, erythema and fever. These signs, as well as the time of their appearance, their frequency and their severity, should be carefully recorded. This permits the classification of victims into two categories according to whether the absorbed dose is greater or less than 2 Gy.
- (b) Confirmation and more precise classification will be based on haematological counts, including, in particular, tests to observe the decline of lymphocytes within the first two days, allowing a more detailed classification within the category where the dose exceeded 2 Gy.
- (c) Further confirmation will be effected in hospital, on the basis of the evolution of clinical and laboratory findings, and of more specific means of analysis such as haematological examinations, and biological (cytogenetic) and physical dosimetry.

To meet the requirements of this assessment (a–c), planning a medical response and training the necessary medical personnel are of prime importance. Planning efficiency depends mainly upon the incorporation of a catastrophic event medical response action into the medical plan, with regular drills to test the performance of the medical response team. The medical management of large groups of victims in the wake of large scale accidents will depend upon local and national capabilities and available resources. The need for specialized units and/or personnel may require international collaboration.

3. EXTERNAL EXPOSURE

3.1. TYPES OF EXTERNAL EXPOSURE

The prognosis and medical handling of individuals exposed to external radiation depend upon whether the whole body has been exposed, or whether exposure has been localized. It is very important for the prognosis and choice of treatment to know how the absorbed dose has been distributed within the body. The dose distribution depends on the condition of exposure and the circumstances of the accident.

If a source, small in size, were very close to the body — in a pocket or touched by the hand — only local exposure could take place. Conversely, if an individual were relatively far from the source and/or the size of the source were commensurate with the person's body size and he/she moved around the source, then this would result in a whole body exposure with a more or less uniform dose distribution. The farther away the source, and the more movements made by the person, the more uniform the dose distribution.

If a source were located relatively close to the body and there were some shielding, partial or local exposure would result. The closer the source to the body, the smaller the area exposed.

The duration of the exposure, or dose rate, is also important. If the same dose were delivered within a shorter time (higher dose rate) a more severe radiation effect would be observed.

3.2. DIAGNOSIS AND TREATMENT OF LOCAL RADIATION INJURY

Local radiation injury (LRI) is much more frequent than WBE and hence described in detail in the specialized literature [10]. LRI caused by high doses of radiation (>8–10 Gy) produces signs and symptoms similar to a thermal burn except for the striking delay in the onset of clinical changes, from several days to a week or longer. The severity of LRI depends not only on the dose and type of radiation, but also on the location and size of the area exposed. Although not usually life threatening, its delayed effects can result in serious impairment.

3.2.1. The clinical picture

A gradual, incremental development of skin reaction with underlying tissue involvement is a typical feature of LRI. In general, the higher the dose received, the more rapid the development of pathological symptoms and the more severe the prognosis. Intractable pain of increasing intensity is a typical symptom and poses a challenge to patient management. Table V illustrates the dose range and time delays observed for the onset of clinical signs in situations where skin has been exposed to γ radiation or high energy X rays.

TABLE V. TIME OF ONSET OF CLINICAL SIGNS OF SKIN INJURY DEPENDING ON THE DOSE RECEIVED

Stage/symptoms	Dose range (Gy)	Time of onset (d)
Erythema	3–10	14–21
Epilation	>3	14–18
Dry desquamation	8–12	25–30
Moist desquamation	15–20	20–28
Blister formation	15–25	15–25
Ulceration (within skin)	>20	14–21
Necrosis (deeper penetration)	>25	>21

TABLE VI. CLINICAL SIGNS OF LRI TO THE HAND FOLLOWING LOW ENERGY RADIATION EXPOSURE

Period of onset of clinical signs in the acute phase					Time and evolution of late phase effects (d)	Delayed effects	Estimated dose range (Gy)
Primary erythema	Secondary erythema	Blisters	Erosion, ulceration	Necrosis			
None or 12–24 h	12–20 d				30–35 Dry desquamation	None	12–18 ^a 10–15 ^b
6–12 h	6–14 d	8–15 d			40–50 Moist desquamation, epithelialization	None, or slight atrophy	20–30 ^a 18–25 ^b
4–6 h	3–7 d	5–10 d	10–18 d		50–70 Epithelialization	Atrophy, depigmentation, telangiectasia	35–80 ^a 30–70 ^b
1–2 h	0–4 d	3–5 d	6–7 d	6–10 d	60–80 Scar formation, no healing without surgery	Atrophy, depigmentation, telangiectasia, possible functional incapacity	>80

^a Fingers only.

^b Whole hand.

Skin exposure to β radiation or low energy X rays is characterized by an earlier appearance of all clinical signs, but the prognosis is not as severe (Table VI).

3.2.2. Main diagnostic procedures

Physical dosimetry is very important, since no appropriate biodosimetric method is available for the early stages of local radiation injury. A detailed history of the accident should be taken and recorded. As regards physical examination, skin reaction should be observed daily with the aid of serial colour photo documentation.

In the case of LRI, the use of electron spin resonance methods can be helpful to estimate the dose incurred when applied to teeth, clothes, buttons, earrings, or any organic substance exposed [11, 12]. During the first week following an accident, daily blood counts can help to discount the possibility of whole body exposure, since in LRI only certain non-specific changes can be observed such as mild leucocytosis or increase of the erythrocyte sedimentation rate [13]. Chromosomal aberration can be

found in only a small number of cultured lymphocytes at a local exposure with a dose range of 5–10 Gy [14] and provides qualitative rather than quantitative information.

Two diagnostic procedures can be used to assess the severity of local over-exposures: thermal and radioisotopic methods. Both are most reliable when the irradiated area can be compared with a corresponding unirradiated one.

Thermography can be used to identify any injury and to determine its extent. It is a useful and sensitive technique for detecting local radiation injuries, especially in the early and latent phases when clinical symptoms are not evident [15]. Additionally, both contact thermography and infrared telethermvision are useful. Although the latter technique is possibly superior in the diagnosis of a partial body irradiation, principally when the extremities are affected, it is also significantly more expensive. A radioisotopic method can be used to record the vascular circulation in an organ or part of the body when $^{99}\text{Tc}^{\text{m}}$ pertechnate is injected intravenously, the distribution being monitored with a scintillation camera [16].

Thermography and the radioisotopic method are complementary. They do not permit an exact assessment of the dose, but can assist in assessing the clinical severity of the injury. Promising new techniques, such as hair cortical cell counting, are being studied, as indicators of radiation exposure to parts of the human body [17].

3.2.3. Treatment

Erythema and dry desquamation can be treated symptomatically. Lotions or sprays containing hydrocortisone can be used to relieve the symptoms associated with severe erythema accompanied by oedema. To treat moist desquamation, daily dressings and bathing of the affected skin in antiseptic solutions is helpful. Antibiotic creams can also be used.

For ulceration, isolation of the limb in a sterile environment or daily dressing and bathing of the ulcer in antiseptic solutions is recommended. Analgesics or stronger opioids may be necessary. In the event of suspected or verified secondary infection, topical or systemic antibiotic therapy should be considered.

For necrosis, only surgical treatment is effective. This consists of the excision of a deep necrosis followed by skin grafts or other kinds of grafting. The extent, timing and type of surgical intervention should be assessed on a case by case basis. Skin grafting is possible only when the underlying vasculature is stable, otherwise a myocutaneous flap or pedicle flap should be made. Surgery is justified whenever irreversible alterations appear which require ulcerectomy, necrectomy and amputation.

In practice, in almost all cases of γ exposure with a local dose in excess of 20–25 Gy, surgical treatment might be justified, since spontaneous recovery may not be possible. Healing is not expected, even after superficial epithelialization, as a secondary ulcer may appear in the higher dose range. When irreversible alterations

are clinically evident, the operation should be undertaken as soon as possible, after the necessity of the procedure has been explained to the patient. Indications for amputation include very severe lesions with destruction of underlying tissues, including vascular damage, intractable pain and lack of infection control. Table VII illustrates the clinical aspects and the diagnostic and therapeutic options available for acute local radiation injuries and their chronic evolution [18].

3.3. DIAGNOSIS AND TREATMENT OF ACUTE RADIATION SYNDROME

3.3.1. Diagnosis

Diagnosis of ARS is based on clinical and laboratory data. The prodromal phase may occur within hours after exposure and is characterized by anorexia, nausea and vomiting (Table VIII). In this phase of ARS, laboratory evidence of haematopoietic damage can already be observed after an exposure of about 0.5 Gy (Table IX). There is usually a remission in the symptoms, allowed by a relatively asymptomatic latent phase that lasts one to three weeks, depending upon the dose incurred (Table X). The latent phase is followed by the critical phase (Table XI).

The circulating lymphocytes are one of the most radiosensitive cell lines, and a fall in the absolute lymphocyte count is the best and most useful laboratory test to determine the level of radiation exposure in the early phase of observation (Tables IX–XI). Immunological dysfunction appears within 48 h. Gastrointestinal symptoms are observed at doses in excess of 10–15 Gy, and sometimes even with a lower dose, overlapping the bone marrow syndrome. Accelerated prodromal and shortened latent phases may be followed by diarrhoea. Neurovascular syndrome occurs after exposures exceeding 20 Gy and is characterized by the immediate onset of severe prodromal signs, leading to vasomotor collapse and death within one to two days.

Among the assays for biological dosimetry, the chromosomal aberration analysis from cultured circulating lymphocytes is the most widely accepted and reliable one. The dose–response relationships are well established in many laboratories around the world [14, 19–21]. The sensitivity of the technique depends on the dose and radiation qualities. The lower limit of detection of a dose by using this cytogenetic method is approximately 0.2 Gy of γ rays or X rays and approximately 10–20 mGy of fission spectrum neutrons [22–24].

There are limitations for using this technique in cases of partial body irradiation [25, 26]. The presence of chromosomal aberrations might indicate the radiation injury but does not permit a precise dose assessment. In addition, doses from internal radiation sources cannot always be assessed, owing to the varying distributions of different radionuclides.

TABLE VII. CLINICAL AND DIAGNOSTIC ASPECTS, AND THERAPEUTIC OPTIONS FOR LOCAL RADIATION INJURIES:
ACUTE PHASE


Irradiation 		Dose estimation	}	History	Vascular thermography
		Routine examinations		Physical dosimetry	
Specialized studies	Accident reconstruction	Biological dosimetry			
		end of ↓ 1st day	end of ↓ 1st week	end of ↓ 1st month	
		PRODROMAL PHASE	LATENT PHASE	ACUTE PHASE	
Clinical picture	Symptoms	Heat sensation Itching Tenderness	Minor (itching, pain), if any	Pain Itching Paresthesia Hyperalgia	
	Signs	Transient erythema	Minor epilation, if any	Erythema Oedema Blistering Moist desquamation	
Treatment		Symptomatic	Avoidance of trauma Analgesics Hydration emulsion (sweet almond oil)	Pain relief Non-steroidal anti-inflammatory drugs (NSAIDs) Local antibiotics Vasodilators Healing drugs Anti-adherent platelet drugs Epidermal growth factors Debridement	

TABLE VII. (cont.) CLINICAL AND DIAGNOSTIC ASPECTS, AND THERAPEUTIC OPTIONS FOR LOCAL RADIATION INJURIES: CHRONIC PHASE (continued time-scale)

Vascular scintigraphy Thermography Biopsy (histo- and immunocytochemical studies)	Vascular scintigraphy Bone scan Thermography	Vascular scintigraphy Bone scan Thermography
_____ 1st year		_____ 2nd year _____
HEALING OR CHRONIC EVOLUTION (SCLEROSIS AND FIBROSIS) (SECONDARY INFECTION POSSIBLE)		
Pain	Injury Reopening Vasculitis (possible) Pain Late erythema	Pain Altered tactile and thermal sensitivities Paresthesia Skin dryness
Ulceration Necrosis	Oedema Ulcer Necrosis (spontaneous healing impossible)	Atrophy, telangiectasia, pigmentary changes, keratoses, epilation or problems with hair, deformity (ankilosis), functional incapacity
Surgery (necrectomy, skin grafts, amputation)	Conservative Analgesics NSAIDs Surgery (necrectomy)	Avoidance of trauma Rehabilitation Superoxide dismutase (liposomal and topical) Surgery

TABLE VIII. PRODROMAL PHASE OF ACUTE RADIATION SYNDROME

Symptoms and medical response	ARS degree and the approximate dose of acute WBE (Gy)				
	Mild (1–2 Gy)	Moderate (2–4 Gy)	Severe (4–6 Gy)	Very severe (6–8 Gy)	Lethal ^a (>8 Gy)
<i>Vomiting</i>					
Onset	2 h after exposure or later	1–2 h after exposure	Earlier than 1 h after exposure	Earlier than 30 min after exposure	Earlier than 10 min after exposure
% of incidence	10–50	70–90	100	100	100
<i>Diarrhoea</i>	None	None	Mild	Heavy	Heavy
Onset	—	—	3–8 h	1–3 h	Within minutes or 1 h
% of incidence	—	—	<10	>10	Almost 100
<i>Headache</i>	Slight	Mild	Moderate	Severe	Severe
Onset	—	—	4–24 h	3–4 h	1–2 h
% of incidence	—	—	50	80	80–90
<i>Consciousness</i>	Unaffected	Unaffected	Unaffected	May be altered	Unconsciousness (may last seconds/minutes)
Onset	—	—	—	—	Seconds/minutes
% of incidence	—	—	—	—	100 (at >50 Gy)
<i>Body temperature</i>	Normal	Increased	Fever	High fever	High fever
Onset	—	1–3 h	1–2 h	<1 h	<1 h
% of incidence	—	10–80	80–100	100	100
<i>Medical response</i>	Outpatient observation	Observation in general hospital, treatment in specialized hospital if needed	Treatment in specialized hospital	Treatment in specialized hospital	Palliative treatment (symptomatic only)

^a With appropriate supportive therapy individuals may survive whole body doses as high as 12 Gy [36].

TABLE IX. CHANGE OF LYMPHOCYTE COUNTS (G/L) IN THE INITIAL DAYS OF ACUTE RADIATION SYNDROME DEPENDING ON THE DOSE OF ACUTE WHOLE BODY EXPOSURE

Degree of ARS	Dose (Gy)	Lymphocyte counts (G/L) ^a after 6 d since first exposure
Pre-clinical phase	0.1–1.0	1.5–2.5
Mild	1.0–2.0	0.7–1.5
Moderate	2.0–4.0	0.5–0.8
Severe	4.0–6.0	0.3–0.5
Very severe	6.0–8.0	0.1–0.3
Lethal	>8.0	0.0–0.05

^a Expressed as 10^9 cells/L.

Analysis of the results can take three days, as a 48 h culturing of lymphocytes is necessary to obtain enough metaphases to evaluate the frequency of chromosomal aberrations. Moreover, the scoring is time consuming and requires considerable expertise.

For a faster screening of injured persons, an assay for the detection of lymphocytic micronuclei is possible [27–29]. This technique also involves the culturing of lymphocytes, but the scoring is quicker and easier. In particular, automation of the assay with the aid of computerized image analysis requires less effort than for metaphase chromosome analysis [30].

3.3.2. Treatment

Treatment should be based on actual symptoms, signs, and the results of routine laboratory tests (see Tables VII–XII). The initial symptoms and signs are non-specific. Careful observation and repeated laboratory studies are the only means of evaluation until further information is gathered and clinical manifestations become apparent [31–36]. The most useful single laboratory test to rule out severe injury within the first 48 h is the absolute lymphocyte count (Table X).

Patients in the emergency room suffering nausea and vomiting should be treated symptomatically and should be monitored with daily blood counts. Victims who have received external doses of less than 1 Gy may be followed up as outpatients if the laboratory test (absolute lymphocyte count) results and dose estimate indicate this to be appropriate. Patients exposed to radiation doses exceeding 1 Gy should be observed. The principal therapeutic measures corresponding to different degrees of ARS severity are summarized in Table XII.

The guiding principle in the further treatment of ARS is to prevent complications arising from bone marrow depression. This approach has replaced that of

TABLE X. LATENT PHASE OF ACUTE RADIATION SYNDROME

	Degree of ARS and approximate dose of acute WBE (Gy)				
	Mild (1–2 Gy)	Moderate (2–4 Gy)	Severe (4–6 Gy)	Very severe (6–8 Gy)	Lethal (>8 Gy)
Lymphocytes (G/L) (days 3–6)	0.8–1.5	0.5–0.8	0.3–0.5	0.1–0.3	0.0–0.1
Granulocytes (G/L)	>2.0	1.5–2.0	1.0–1.5	≤0.5	≤0.1
Diarrhoea	None	None	Rare	Appears on days 6–9	Appears on days 4–5
Epilation	None	Moderate, beginning on day 15 or later	Moderate or complete on days 11–21	Complete earlier than day 11	Complete earlier than day 10
Latency period (d)	21–35	18–28	8–18	7 or less	None
Medical response	Hospitalization not necessary	Hospitalization recommended	Hospitalization necessary	Hospitalization urgently necessary	Symptomatic treatment only

TABLE XI. CRITICAL PHASE OF ACUTE RADIATION SYNDROME

	Degree of ARS and approximate dose of acute WBE (Gy)				
	Mild (1–2 Gy)	Moderate (2–4 Gy)	Severe (4–6 Gy)	Very severe (6–8 Gy)	Lethal (>8 Gy)
Onset of symptoms	>30 d	18–28 d	8–18 d	<7 d	<3 d
Lymphocytes (G/L)	0.8–1.5	0.5–0.8	0.3–0.5	0.1–0.3	0–0.1
Platelets (G/L)	60–100 10–25%	30–60 25–40%	25–35 40–80%	15–25 60–80%	<20 80–100% ^a
Clinical manifestations	Fatigue, weakness	Fever, infections, bleeding, weakness, epilation	High fever, infections bleeding, epilation	High fever, diarrhoea, vomiting, dizziness and disorientation, hypotension	High fever, diarrhoea, unconsciousness
Lethality (%)	0	0–50 Onset 6–8 weeks	20–70 Onset 4–8 weeks	50–100 Onset 1–2 weeks	100 1–2 weeks
Medical response	Prophylactic	Special prophylactic treatment from days 14–20; isolation from days 10–20	Special prophylactic treatment from days 7–10; isolation from the beginning	Special treatment from the first day; isolation from the beginning	Symptomatic only

^a In very severe cases, with a dose >50 Gy, death precedes cytopenia.

TABLE XII. PRINCIPAL THERAPEUTIC MEASURES FOR ACUTE RADIATION SYNDROME ACCORDING TO DEGREE OF SEVERITY

Whole body dose (Gy)	1–2	2–4	4–6	6–8	>8
Degree of severity of ARS	Mild	Moderate	Severe	Very severe	Lethal
Medical management and treatment	Outpatient observation for maximum of one month	Hospitalization			
		Isolation, as early as possible			
		G-CSF or GM-CSF as early as possible (or within the first week)		IL-3 and GM-CSF	
		Antibiotics of broad spectrum activity (from the end of the latent period) Antifungal and antiviral preparations (when necessary)			
		Blood components transfusion: platelets, erythrocytes (when necessary)			
		Complete parenteral nutrition (first week) Metabolism correction, detoxication (when necessary)			
		Plasmapheresis (second or third week) Prophylaxis of disseminated intravascular coagulation (second week)			
			HLA-identical allogene BMT (first week)	Symptomatic therapy only	

Note: BMT: bone marrow transplantation; G-CSF: granulocyte-colony stimulating factor; GM-CSF: granulocyte macrophage-colony stimulating factor; IL-3: interleukin.

administering prophylactic antibiotics and transfusing blood products (platelets and erythrocytes). Platelet and erythrocyte transfusions are used prophylactically when the platelet count is less than 20 G/L (1 G/L = 10^9 cells/L) and the haemoglobin is less than 100 g/L. The use of prophylactic antibiotics and the administration of blood products are decided after isolation in an antiseptic ward and careful clinical observation for symptoms of fever, bleeding, oropharyngeal ulceration, and neurological and vascular changes. Microbiological monitoring provides guidelines for an efficient treatment of infection. Blood culture should be performed whenever the fever is higher than 38°C (98.6°F).

Symptomatic and supportive treatment is also necessary. This may include the use of tranquilizers and drugs to relieve pain, supportive fluids and adequate nutrition. Intravenous routes should be employed as needed to supply fluid, electrolyte and nutrition. Barriers to prevent hospital infection are desirable, as is the use of sterile food. Raw vegetables and raw fruits should be avoided.

Because the care is directed towards preventing the consequences of agranulocytosis and loss of immune competence, help from a haematologist/oncologist is desirable.

3.3.3. Bone marrow transplantation

Bone marrow transplantation (BMT) seems to be a logical treatment for victims of accidental whole body irradiation when the dose is sufficiently high to make spontaneous bone marrow recovery impossible [2, 8, 35]. Nevertheless, BMT has many limitations. These include identification of histocompatible donors, age constraints, HLA typing in lymphogenic patients, the need for additional immunosuppression and the risk of graft versus host disease.

Information gained from the accidents at Chernobyl and the Soreq irradiation facility in Israel [2, 37] strongly suggests that BMT has a limited role for the treatment of victims of radiation accidents and would benefit only a small number of exposed individuals. Given these experiences, transplants should probably be considered only for victims receiving doses in the range of 8–12 Gy, uniformly distributed, without serious skin injuries, and in the absence of severe internal contamination and conventional injuries.

The timing of grafting is important and all arguments favour early marrow transplantation, even within the first week after exposure. Grafting in the peak period of immunosuppression may reduce the chance of graft rejection. This circumstance underscores the importance of reliable clinical, biological and dosimetric findings to assess the dose level and dose distribution within the body. In the absence of reliable physical dosimetry and haematological parameters, the use of allogenic bone marrow transplantation is unjustified.

3.3.4. Use of haematopoietic growth factors

Granulocyte-colony stimulating factors (G-CSF) and granulocyte macrophage-colony stimulating factors (GM-CSF) increase the rate of haematopoietic recovery in patients after radiation exposure and may obviate the need for BMT when stem cells are still viable [38–40]. Interleukins (IL-1 and IL-3) act in synergy with GM-CSF.

During the past decade, these factors have been suggested as having the potential to accelerate bone marrow recovery after radiation exposure in the lethal range. They have been used successfully for radiation victims of the Goiânia, San Salvador, Soreq and Nesvizh accidents [3, 4, 37, 41].

3.3.5. Criteria for choice of therapy

On the basis of Tables IX–XI, the therapeutic recommendations are as follows:

- (a) If the lymphocyte count during the first week is within 0.2–0.5 G/L (200–500 cells/ μ L), spontaneous recovery is possible. Therapy comprises isolation, antibiotics, and supportive treatment, including platelet infusion. Growth factors can be used.
- (b) If the lymphocyte count in the first week is lower than 0.2–0.5 G/L, the stem cells are probably irreversibly damaged. Therapy as above. Additional growth factor therapy is a method of choice.
- (c) If the lymphocyte count within the first week is less than 0.1 G/L, treatment with growth factors and BMT has to be considered.

It is necessary to observe the HLA compatibility for allogenic BMT. This therapy may be recommended to patients exposed to whole body doses exceeding 9 Gy [42, 43].

4. CONTAMINATION WITH RADIONUCLIDES

Radioactive contamination can be external or internal. The biological and possible health consequences depend on the following:

- (a) Mode of entry;
- (b) Pattern of distribution;
- (c) Site of deposition of radionuclides in the organs;
- (d) Nature of the radiation emission from the contaminating radionuclide;
- (e) Amount of radioactivity on/in the body;
- (f) Physicochemical nature of the contaminant.

This information is essential for the adequate evaluation, assessment and medical management of a contaminated individual.

4.1. DIAGNOSIS

In the case of external contamination, physical measuring equipment such as surface contamination monitors (Geiger–Müller detectors, etc.) can be used (Table XIII). In addition, swab samples have to be taken from body surfaces and orifices and measured. In the case of internal contamination, which may have happened through inhalation, ingestion, or wounded or apparently undamaged skin, physical measurement includes thyroid monitoring, whole body counting, gamma camera measurement, and blood and excreta analysis. For the latter, all urine and faecal samples have to be collected and labelled to record the time of sampling (Table XIV).

The purpose of contamination diagnosis is to obtain information on the time of intake, the nature of the radioisotopes involved and the distribution of the

TABLE XIII. GUIDELINES FOR PROTECTIVE MEASURES

For attendants	Protective clothes should be issued to all personnel involved, i.e. coverall with hood, mask and gloves. The edges of both mask and gloves should be taped. Paramedic and ambulance personnel should be surveyed for contamination before going off duty.
Room setting	An isolated room or a room away from the general emergency area should be used. Air circulation should be prevented and a tub or table with a drainage system provided. Other useful items include containers for waste water and any contaminated materials, and plastic bags.
Survey meter	A well maintained Geiger–Müller counter with β and γ 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 should be conducted at a distance of about 25 mm from the person's body, moving the detector no faster than 50 mm/s.
Personal dosimeter	A film badge or thermoluminescent dosimeter should be regarded as a minimum requirement, although a direct reading, personal dosimeter is preferable. Exposures should be kept as low as reasonably achievable, but in any case should be within the limits set by the national competent authorities.

radioisotopes on the surface of, and within, the organism. In the event of simple contamination, with one or several radionuclides, there will be no clinical manifestations initially.

4.2. TREATMENT

The radionuclide should be removed by washing, dissolution or application of strippable material to the skin. The spread of contamination through the body should be prevented at all cost. The rule is to avoid abrasion of the skin. Products that could facilitate the passage of material through the skin should not be used and preliminary decontamination of the skin should be carried out on the spot. Verification of removal of contamination and, if necessary, more elaborate treatment to remove residual or fixed contamination should be carried out in the medical facility at the workplace. If radioactive contamination is found, measures are required to protect attendants and to minimize the spread of radioactive contamination at the accident site, during transportation of patients, and at the medical facility (Tables XIII and XIV).

In cases where internal contamination is known or suspected, decorporation procedures must be started as soon as possible.

4.2.1. Decontamination

An initial and important consideration in the emergency room is to prevent the spread of radioactivity and provide for appropriate decontamination (Table XV).

TABLE XIV. INITIAL CONTAMINATION SURVEY AND LABORATORY TESTS

External contamination	Use instrumental contamination monitoring. Use cotton swabs for skin, nostrils, ear canals, wounds or any contaminated object. Each swab should be placed in a labelled test tube for counting. ^a
Internal contamination	Use instrumental detection methods such as whole body counting, gamma camera, thyroid counting. Radionuclides may be in the blood or excreted in the faeces or urine. Excreta should be placed in appropriate containers and blood samples in test tubes for counting.

^a Every specimen should be clearly labelled and include the patient's name, the type of specimen taken, and the date and time the specimen was obtained.

TABLE XV. DECONTAMINATION PROCEDURES

Materials	Lukewarm water, soap or ordinary detergent, soft brush, sponges, plastic sheets, tape, towels, sheets, iodine tablets or solution.
Procedural priority	Remove all clothing and place in plastic bags. Carry out life saving measures first. Identify contaminated areas, mark clearly and cover until decontamination takes place. Start with decontamination of the wound, when present, and move on to the most contaminated area.
Wound	Irrigate the wound with a normal saline solution repeatedly. Surgical debridement might be considered in some instances. Eyes and ears may be irrigated gently with isotonic saline solution.
Local contamination	Cover uncontaminated area with plastic sheet and tape edges. Soak the contaminated area, gently scrub with soap, and rinse thoroughly. Repeat the cycle and observe changes in activity. One cycle should not last longer than about 2–3 min. Avoid vigorous scrubbing. A stable isotope solution may facilitate the process.
Extensive contamination	Shower for those not seriously injured. Bathing on the operating table or stretcher for the seriously injured. Soak–scrub–rinse cycle should also be observed.
Expected outcome	Radionuclide activity is no longer detectable or is decreasing.
Prophylactic measures	Cover areas still contaminated with plastic sheet and tape edges. Gloves can be used for hands. Repeat washing after allowing the skin to rest.

Prior notification of the arrival of a potentially contaminated person is a great aid in preparation. Absorption of the radionuclide, especially when in ionic or other soluble form, is very rapid in areas where the capillary network is directly exposed. Nasal and buccal mucosae are other ready entry sites of radionuclides, and gentle nasal or oral irrigation with isotonic solutions may reduce the level of contamination and absorption.

The recommended procedure for local surface contamination is to cover the surrounding uncontaminated area with a plastic sheet, tape its edges, and then wash the affected area with soap or detergent. The contaminated surface should then be

blotted dry. Immersing the patient in a bath or complete showering as an initial measure is not recommended because such steps often spread contamination to clean areas. Note that fingertips, hair, nostrils and ear canals are regions in which decontamination is more difficult.

Clipping nails facilitates the process, and cutting or shaving hair may be considered when shampooing does not sufficiently remove the contaminant. Sweating of extremities by covering with plastic or rubber gloves overnight may be helpful. Surgical debridement may be necessary to remove embedded matter from highly contaminated wounds.

Caution is needed to avoid excessive vigour in decontamination. Patients very rarely, if ever, suffer deleterious effects from contamination except from very high exposures to skin, such as those occurring at Chernobyl in 1986 and in the accident in Goiânia in 1987. The goal of decontamination is to prevent development of late stage deleterious effects and at the same time avoid damage from efforts of decontamination and decorporation.

4.2.2. Decorporation

The procedures recommended for the treatment of persons with acute, internally deposited radionuclides are intended to reduce the absorbed radiation dose and hence the risk of possible future health effects (Table XVI). These aims can be accomplished by reducing absorption, thereby preventing incorporation and internal deposition within organs, and promoting elimination or excretion of absorbed nuclides, which is more effective when started at the earliest opportunity. Reduction of gastrointestinal absorption can be performed through application of stomach lavage, mild emetics, purgatives to accelerate the removal of radioisotopes, activated charcoal, Prussian blue (against caesium), aluminium containing antacids (against strontium) and barium sulphate to absorb the radioactive materials.

TABLE XVI. DECORPORATION PROCEDURES

Principle	Dilution, blocking, chelation, mobilization and elimination of the contaminant.
Inhalation	Irrigate nasopharynx and mouth.
Ingestion	Administer cathartics for insoluble materials; diuresis by forcing fluids for soluble contaminants.

Specific decorporation procedures can be used depending on the type and metabolic pathway of the contaminating radionuclides. These include blocking, diluting and displacement agents. For radioiodine, which concentrates mostly in the thyroid, the blocking of the gland with stable iodine (e.g. potassium iodide) will prevent the uptake of radioiodine. The effectiveness of this treatment is strongly time dependent. Administration of the thyroid blocking dose of a stable iodine compound 4 h after the radioiodine intake will result in only a 50% decrease of the thyroid dose. Thyroid blocking on the day following radioiodine inhalation is ineffective. The daily single dose of potassium iodide should be given as rapidly as possible following an accidental radioiodine intake, depending on the age of the patient as follows: 10–20 mg to infants (those not breast fed); 20–50 mg to children of 1–10 years of age; 50–100 mg to children of 11–18 years of age; and 100–300 mg to adults. This treatment may be continued over a few days, according to the risk of ingestion of ^{131}I contaminated food, such as cow's milk and leafy vegetables or fresh fruit [44–47].

In the case of tritium intake, a large amount of fluids (water, tea) should be administered as a dilutant over a period of one week. At the same time, diuretics may also be given [48].

Mobilizing (displacement) agents are compounds that increase a natural turnover process, thereby enhancing the elimination of radionuclides from body tissues. These agents are more effective if they are administered soon after exposure. However, some are still effective if they are administered within weeks. Chelating agents such as diethyltriamidopentaacetate (DTPA) (in the form of aerosols in the case of inhalation), desferrioxamine, etc., can be used systematically or locally, either by application to the skin or when performing lung lavage. This last procedure should be performed only if large amounts of contaminant have been identified and then only performed by very well trained specialists.

5. COMBINED RADIATION INJURIES

Combined radiation injuries (CRIs) occur whenever radiation effects are combined with mechanical, thermal or chemical injuries. Such combinations may worsen the prognosis. Lethality increases significantly in the presence of CRIs. Understandably, diagnosis, treatment and prognosis are much more complex in this case. There are some peculiarities in the diagnosis of CRI. Laboratory tests, haematological indices and others can be affected in a way that makes diagnosis of the radiation component of combined injuries difficult. Cytogenetics can also be influenced by toxic chemicals, and thus may not be useful for precise assessment.

5.1. CLASSIFICATION

According to the combination of the radiation dose with other factors, CRIs can be classified as follows:

- (a) Thermal CRI: external and/or internal irradiation with thermal burns.
- (b) Mechanical CRI: external and/or internal irradiation with wound or fracture, or with haemorrhage.
- (c) Chemical CRI: external and/or internal irradiation with chemical burns or chemical intoxication.

5.2. TREATMENT

The medical handling of conventional trauma and life saving activities have the highest priority. Treatment has to be individualized according to the nature and grade of the combined injuries. Since a radiation injury is characterized by a latent period, all important treatments of the non-radiation component of CRI should be carried out during the first two or three weeks. Later efforts will be necessary for the treatment of bone marrow and skin radiation injuries.

6. CONSULTING SYSTEM

In a particular radiation accident involving injuries to patients, an urgent need may arise for expert medical consultation and help. For cases where this is not available nationally, the World Health Organization (WHO) has designated a number of collaborating centres around the world from which help can be obtained. These are listed below. General advice and assistance can also be obtained from the IAEA and WHO headquarters.

WHO Headquarters

WHO,
CH-1211 Geneva 27, Switzerland
Fax: +41 22 791 0746
Tel: +41 22 791 3763

WHO Collaborating Centres and Liaison Institutions

Argentina	Department of Health Physics, P.O. Box 3268, Buenos Aires Fax: +541 382 5680 or +541 381 0971 Tel: +541 382 5680
Armenia	Research Centre of Radiation Medicine and Burns, 375078 Davidasben, Yerevan Fax: +3742 340 800 Tel: +3742 341 144
Australia	Radiation Protection and Radiation Emergency, Yallambia, Victoria 3093 Fax: +613 9432 1835 Tel: +613 9433 2211
Brazil	Radiation Protection and Medical Preparedness for Radiological Accidents, Avenida Salvador Allende (vio9), Jocorepogu, CP 37750, CEP 22780, Rio de Janeiro Fax: +5521 442 2539 or +5521 442 1950 Tel: +5521 442 1927 or +5521 442 9614
China	Institute of Radiation Medicine, 27, Tai Ping Road, 100850 Beijing Fax: +8610 821 4653 Tel: +8610 821 3044 or +8610 821 4653
France	Centre international de radiopathologie, B.P. 34, Bâtiment 01, F-92269 Fontenay-aux-Roses Fax: +331 4638 2445 Tel: +331 4554 7266
Germany	Institute for Occupational Health, University of Ulm, Pf. 2060, D-8900 Ulm Fax: +49 731 502 3415 Tel: +49 731 502 3400

India	<p>Bhabha Atomic Research Centre, 400085 Mumbai Fax: +9122 556 0750 Tel: +9122 551 1677</p>
Japan	<p>Radiation Effects Research Foundation, 5-2 Hijiyama Park, Minami-ku, J-732, Hiroshima Fax: +11 8182 263 7279 Tel: +11 8182 261 3131</p>
Russian Federation	<p>State Research Centre – Institute of Biophysics, 46, Zhivopisnaya, 123182 Moscow Fax: +7095 190 3590 Tel: +7095 190 5156</p> <p>Central Research Institute of Roentgenology and Radiology, Pesochnij 2, 189646 St. Petersburg Fax: +7812 437 8787 Tel: +7812 437 8781</p> <p>All-Russian Centre on Ecological Medicine, 17, Botkinskaya, 194175 St. Petersburg Fax: +7812 541 8805 Tel: +7812 248 3419</p> <p>Medical Radiological Research Centre, 4, Koroliev, 249020 Obninsk Fax: +7095 956 1440 Tel: +7095 956 1439</p> <p>Urals Research Centre for Radiation Medicine, Medgorodok, F1B, 454076 Chelyabinsk Fax: +73512 344 321</p>
United Kingdom	<p>National Radiological Protection Board, Chilton, Didcot, Oxfordshire OX11 0RQ Fax: +441235 822 630 Tel: +441235 822 612</p>

United States of America Radiation Emergency Assistance, REAC/TS,
Oak Ridge, TN 37831-0117
Fax: +1 615 576 9522
Tel: +1 615 576 3450

IAEA Headquarters

IAEA,
Wagramer Strasse 5, P.O. Box 100, A-1400 Vienna, Austria
Fax: +431 20607
 +431 2060 29309 (for emergency service during office hours)
 +431 239270 (for 24 h emergency service)
Tel: +431 2060

7. RECORD KEEPING

Detailed record keeping is essential, not only for patient care and subsequent dosimetric and medical follow-up, but also for medical and legal considerations. Record keeping is the responsibility of the respective employer or governmental authority.

The assistance of the radiation protection officer of the facility where an accident has occurred is essential for the collection of data and for consultations with the physicians and governmental authorities involved. The officer will be in a position to provide information on the type of accident, sources and kinds of radioactivity, and dosimetry of the affected subjects and the environment. The following approaches might be suggested:

- (a) Use of a still camera (preferably colour) as serial, frequent and dated photos are of great value;
- (b) Use of a video camera and tape recorder for the preservation of patient interviews and narrative, and for a reconstruction of events;
- (c) Computerization of all data.

Annex I provides examples of record forms for the collection of data. Careful use of these forms, together with the use of the technical devices listed above, will be of great value in the often lengthy clinical treatment of the injured.

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Annex I

ACCIDENTAL EXPOSURE FORM SAMPLES

Sample Accident Information Form

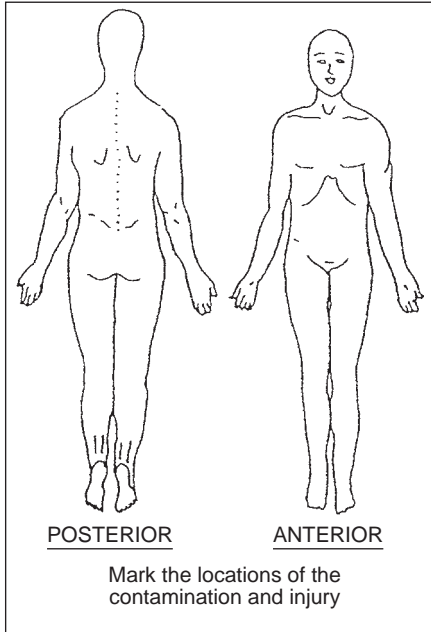
(To be filled in by physician)

1. Identification of informant
2. Number and condition of uncontaminated patients
3. Number and condition of contaminated patients
4. Description and extent of accident
 - (a) Irradiation condition
 - Source
 - Distance
 - Time
 - Estimated dose
 - (b) Contamination (external)
 - Radionuclides involved
 - Activity level
 - Body area involved
 - (c) Contamination (internal)
 - Ingestion
 - Inhalation
 - (d) Contaminated wound
 - (e) Whether initial decontamination done
5. Expected time of arrival of patients at the place of special medical care

Date

Signature

Sample Identity Tag for Accidental Exposure (front and rear view)



**IDENTITY TAG
(FIRST AID POST)**

Name	
Dept.	
Contamination	Y/N
Site of contamination	
Injury	Y/N
Site of injury	
Overexposure	Y/N
Preliminary actions taken	
Treatment	
First aid	
Decontamination	
To: PERSONNEL DECONTAMINATION CENTRE/SITE HOSPITAL	

Note: The contamination level should be expressed in disintegrations per minute/100 cm² or over the affected area if less than 100 cm². Both α and β contamination levels should be indicated. If β - γ contamination levels are high, they may be given in mGy/h measured with a Geiger-Müller probe with an open window. An estimate of the total contamination should be given wherever possible. Both the initial level of contamination and the level of contamination at the time the patient is referred to the personnel decontamination centre/site hospital should be provided.

Weakness	Yes	No	
Headache	Yes	No	
Nausea	Yes	No	
Vomiting	Yes	No	frequency
Diarrhoea	Yes	No	frequency
Temperature			
Pulse			
Blood pressure			
Consciousness	normal	abnormal	agitation delirium sleepiness coma
Equilibrium disturbance		Yes	No
Co-ordination disturbance		Yes	No
Skin and mucosa			
Oedema		Yes	No
Erythema		Yes	No
Other			

6. TREATMENT AND INVESTIGATIONS

6.1. MEASURES TAKEN

Undressing	Yes	No
Decontamination	Yes	No

DTPA administration	Yes	No
If yes, administration pathway	aerosol bathing intravenous	
Stable iodine administration (in thyroid blocking dose)	Yes	No

6.2. LABORATORY TESTS

Blood samples

First sample (if possible, before the third hour)

Date	Time
------	------

Blood cell count

Cytogenetic sample (10 mL) taken	Yes	No
Sample for radioactivity measurement	Yes	No

Second sample (if possible, 2 hours after the first one)

Date	Time
------	------

Blood cell count

HLA typing	Yes	No
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Urine samples

(If applicable, for radioactivity measurement)	Yes	No
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Is it the first urination after the accident?	Yes	No
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7. REFERRAL OF THE PATIENT (IF SENT FOR FURTHER TREATMENT)

8. PHYSICIAN'S CONCLUSIONS

Date	Signature
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Annex II

DIAGNOSIS AND TREATMENT OF PERSONS EXPOSED TO CAESIUM-137: THE GOIÂNIA EXPERIENCE*

As a consequence of the Goiânia accident, 249 individuals were directly affected by radiation, receiving slight to severe external whole body or partial body irradiation, in addition to significant internal and external contamination. Of this total, 14 patients exhibited some degree of bone marrow suppression, eight clearly manifested the clinical symptoms of the haematological form of acute radiation syndrome, and four eventually died of infectious and haemorrhagic complications. Twenty-eight people suffered acute, localized radiation induced injuries ranging from first to third degree, which required conservative and surgical treatment. Internal contamination due to ingestion and/or absorption of ^{137}Cs was removed efficiently by means of Prussian blue.

II-1. THE ACCIDENT

The Goiânia radiological accident was caused by the removal of a ^{137}Cs source, formerly used in a radiotherapy unit, from an abandoned clinic in Goiânia, Brazil. The caesium source, with an activity of 50.9 TBq (1375 Ci), was in the form of powder, compacted into a steel capsule within the shielding container of the unit. Persons who handled the capsule were exposed to γ radiation attenuated by the steel. Those who handled the caesium powder directly were contaminated internally and externally, and exposed to a mixed β and γ radiation field.

The exact duration of each exposure could not be established as the patients were exposed to the source several times each day in different ways. The source–subject geometry was extremely variable and for many patients there was external contamination due to direct contact with the body surface. Part of the caesium powder was removed and rubbed on patients' bodies. The body irradiation was of a heterogeneous character and the corporal distribution of localized radiation induced lesions concentrated mainly on the extremities, especially the palms of hands and the fingers.

* Annex II is based upon information supplied by A.R. Oliveira.

II-2. EARLY MEDICAL RESPONSE

II-2.1. Medical response at the accident site

A specialized medical team from Rio de Janeiro arrived in Goiânia ten hours after the severity of the accident was established and began preliminary examinations and treatment at the Olympic Stadium. Clinical and laboratory evaluations (blood counts) were performed, as well as external decontamination, when necessary, with warm water and neutral soap. The medical team promptly adapted a ward in the Goiânia General Hospital to receive the patients and set up a control point to avoid spreading the contamination. The ward was divided into controlled, supervised and clean areas. To assess the severity of each patient's condition the procedures adopted included collection of clinical and accident histories and of haematological data, as well as monitoring body surfaces to determine the presence of external and/or internal contamination.

It was apparent that the accidental exposure of the majority of the victims had a heterogeneous and protracted character. The patients had received significant whole body and localized irradiation and suffered internal and external contamination. It was clear from the outset that precise dose estimation, a very important parameter for treatment and prognosis, would be a major problem.

II-2.2. Triage of victims

The triage of injured persons was based on the following criteria:

- (a) Severity of the haematopoietic syndrome, based on peripheral lymphocyte and neutrophil counts;
- (b) Severity of local radiation injuries: intensity and precocity of cutaneous reactions, i.e. erythema, blisters and bulla formation;
- (c) Intensity of internal and external contamination, based on accident history, surface radiation monitoring and, subsequently, in vitro bioassays.

The main purpose of triage was the identification and referral of the most seriously injured individuals to the appropriate medical unit in Rio de Janeiro. Additionally, it was helpful in identifying those victims who should be hospitalized immediately in the Goiânia General Hospital.

II-3. CLINICAL OBSERVATIONS

II-3.1. Acute radiation syndrome

At least 14 of the 20 hospitalized patients showed varying degrees of bone marrow suppression. The patients most affected were in poor general health when admitted to the hospital. Eight patients developed the classical manifestations of the prodromal phase of ARS, i.e. anorexia, nausea, vomiting, fluid diarrhoea, headache and fever, with the onset of the symptoms varying from two to four hours after exposure. Local signs of radiation exposure, such as conjunctival hyperemia and transient erythema, were also observed.

The critical phase was basically characterized by infectious and haemorrhagic phenomena. Infection was documented in eight patients who developed bone marrow suppression and was a principal factor in the four deaths. Opportunistic infections, caused by fungal specimens, developed in six patients, affecting oral, oesophageal, vaginal and perineal mucosae. Neither herpesvirus nor cytomegalovirus infections were documented, although a preventive antiviral therapy had been instituted.

Haemorrhagic phenomena were recognized in four out of the eight most seriously ill patients and were an associated cause of death in two cases. Haematemesis, melaena and epistaxis were the major bleeding manifestations. The autopsies showed multiple haemorrhagic areas throughout the entire skeletal musculature and within various organs.

In the fourth and fifth weeks following initial exposure, four patients died from ARS complications. The other patients attained almost full recovery from haematopoietic syndrome.

II-3.2. Local radiation induced injuries

Local symptoms appeared a few hours after contact between the source and the skin surface. Pain, sensation of local heat, burning and itching, as well as changes in sensitivity, were the most frequent complaints. Some patients reported the simultaneous appearance of transient erythema in the affected regions.

After a period of latency, ranging from a few days to two weeks, a second wave of localized disturbances erupted, characterizing the 'critical phase', which was represented by stronger pain and oedema, always preceded by secondary erythema, resembling a classical thermal burn. Soon thereafter, blisters or bullae developed, coinciding in general with the swollen region. This phase of bullous epithelitis lasted approximately two weeks. In some cases the bullae were so tense and painful that drainage was required to relieve the symptomatology and allow movement of the extremity.

The resection of dead tissues disclosed a raw and extremely painful dermis, with a swollen aspect and sparse evidence of epithelialization. This phase was followed by a fairly slow regeneration process, characterized by tissue granulation beginning at the outer edges of the injury and progressing towards the middle, a process requiring months to complete. Generally, the scar tissue was thin, translucent and very sensitive to touch.

The final aspect of the injury was generally poor, owing mainly to its retractile appearance. Some patients received such intense local irradiation that recovery was never achieved. In such cases, the dermis was covered with a relatively thin layer of fibrin, lightly fixed to the underlying dermis. The necrotic aspect of the injury was observed in at least four patients. Seven patients developed more severe local radiation induced injuries, resulting in areas of superficial necrosis caused by attenuated (shielded) γ rays plus β emissions of caesium and in deeper necrotic injuries of a darker tone, both requiring surgery. In these cases, a clear reduction in the evolutionary phase was noticed.

II-4. MEDICAL MANAGEMENT OF RADIATION INJURIES IN GOIÂNIA

II-4.1. Acute radiation syndrome

All 20 patients hospitalized were subjected to a daily clinical evaluation complemented by serial assessment of blood counts. Serum chemical profiles and hepatic and renal functions were evaluated twice a week or every other day, when indicated. Chest X rays, electrocardiograms and stool examinations were performed on a routine basis, or when indicated by clinical findings. Ophthalmological examinations (fluoresceinographic studies) evidenced changes in the retinal veins in the most affected patients. In one 56 year old patient, who received an estimated dose of 5.0 Gy, signs of lenticular opacity were observed a year after the accident. In those patients who agreed to undergo gonadal function tests (sperm counts), a severe reduction, if not a total disappearance, of seminal cells was observed.

Medical care was provided round the clock. All patients were kept in individual or two-bed rooms with reverse isolation. Trimethoprim and sulphamethoxazole, and subsequently norfloxacin, were used for gut decontamination. Ketoconazole was administered to treat fungal infections and acyclovir to prevent herpesvirus activation. Patients with granulocytopenia and fever were given comprehensive treatment with antibiotics. Initially, two or three antibiotics were administered and, in accordance with clinical and bacteriological data, antibiotics were shifted. Oral moniliasis was prevented by use of nistatin, and for cases unresponsive to this drug, amphotericin B was given. Two patients received parenteral nutrition through a central access line. All food was cooked and raw vegetables were avoided.

Patients were given total blood transfusions or red packed cells in order to maintain the level of haemoglobin within safe limits. Platelet transfusions were performed to keep these elements at a level above 20 G/L or whenever bleeding occurred in patients with a platelet count of less than 60 G/L.

GM-CSF was used for treating eight individuals with bone marrow suppression. After administration of GM-CSF (doses of 500 $\mu\text{g}/\text{m}^2$ of body surface per day), four patients responded well to the therapy with a clear myeloproliferative recovery, reflected in the peripheral blood by a rapid and acute rise in the number of neutrophils. One patient died of infectious complications, although showing overt signs of bone marrow recovery. The other patients who died, two females and one young male, showed marked bone marrow involvement and multiple organ failure. No relation was established between GM-CSF administration and the behaviour of platelets and haemoglobin.

II-4.2. Local radiation injuries

Patients with significant local radiation injuries underwent specialized procedures to determine the extent of their lesions and to orient medical management. In one particular case, $^{99}\text{Tc}^{\text{m}}$ red blood pool imaging studies showed no vascularization in the affected area of a severe radionecrosis located in the right forearm. An amputation was performed to minimize the consequences of this injury to the blood economy. In another patient, this same procedure indicated areas of increasing blood supply during the critical period, thus characterizing an inflammatory reaction. A computerized tomographic scan of an injury located at the lateral aspect of a patient's thigh demonstrated an oedema and swelling in the muscle and adjacent structures of the affected limb. Magnetic resonance imaging (MRI) studies of this injury showed compromise of the deep muscular tissue and marked perivascular oedema involving the femoral artery. The segment of bone marrow directly affected by radiation was also compromised, showing a modified density in relation to the unaffected tissues. Only images compatible with an infiltration process and oedema of the subcutaneous tissue were assessed.

Baseline X rays of extremities performed on patients with severe local radiation induced injuries showed a pattern compatible with osteoporosis. In one patient, a late radioinduced and pathological fracture in a segment of the distal falange was identified and the fragment later removed surgically. Pain relief required much patience and dedication from the medical team. Along with local analgesics, central action analgesics were employed, either per os or parenterally. Meperidine, chlorpromazine and promethazine were also administered in cases of intense and unbearable pain. Continuous peridural anaesthesia was used for one patient who complained of excruciating and sharp pain and who manifested suicidal intentions.

To reduce skin dryness, hands and fingers were immersed in boric acid solution. With some patients, in order to avoid excessive administration of narcotics, iced water was sprinkled on the areas surrounding the lesion, which provided pain relief. Creams and ointments with healing and anti-inflammatory properties were applied freely on the raw surfaces of the injuries. Attempts to increase blood flow to the bed of the injury were made by using a peripheral vasodilator and a drug intended to improve the flow properties of blood, by decreasing its viscosity, with action at microcirculation level (Pentoxifylline). When blisters and bullae ruptured the exposed surfaces were protected with non-adherent dressings coated with neomycin. Although the majority of lesions presented bacterial colonization, in only a few instances did infection develop during hospitalization.

All patients with deep ulceration or necrosis on hands, feet and thighs underwent repair surgery. The success of the surgery depended essentially on the location and depth of the lesion, as well as the viability and integrity of the tissue over which the grafted tissue was applied.

Extensive lesions involving thick, fatty or muscular regions required removal of all necrotic and infected tissues until reaching an area of good blood supply. Only then could the bed of the wound be covered with a good quality split skin graft. In two cases, lesions on the palms of the hand required ample debridement, practically to the level of the flexor muscles and tendons, followed by coverage of the ulcer bed with an abdominal flap. Surgical treatment of finger lesions consisted of resection of the damage followed by coverage with a skin graft. In one case it was necessary to perform microsurgery, transferring a segment of tissue with the intact vascular pedicle to be anastomosed to the finger vessels. In two patients, the development of necrosis and mummification of fingers necessitated amputation as soon as the irreversibility of the damage was confirmed on clinical and laboratory grounds. Finally, in a patient with a severe injury of the lateral aspect of the right thigh, excision was performed followed by coverage of the wound bed with a skin graft of the contralateral limb one year after exposure. An attempt to use a dermoexpansor to increase the skin surface, which would assist closure of the wound, failed. Unfortunately, dehiscence and infection occurred during expansion, demanding interruption of the procedure.

II-4.3. Caesium-137 decorporation

A total of 46 individuals were treated with Prussian blue in doses varying from 1 to 10 g. The drug was given orally two, three, six or ten times a day, depending on the total dose, with a minimum of 2 h between doses. With the administration of Prussian blue, the expected pattern of caesium elimination changed and removal via the faeces became predominant, owing to the efficiency of Prussian blue in binding caesium ions in the lumen of the gut, thereby interrupting its enteric cycle and preventing subsequent reabsorption. With the use of the drug, caesium half-lives in

adults were reduced to one third of the normal value, which is consistent with the reduction of half-lives obtained in previous studies.

II-4.4. Body surface decontamination

Conventional decontamination techniques were employed during the first two days of the patients' hospitalization to avoid further incorporation of ^{137}Cs , to reduce the equivalent dose received by the patients, and to reduce contamination of the ward. Any contamination was easily confirmed by measuring hot spots caused by β and γ radiation on the skin surface. Such measurements were complicated by the high γ dose rate generated from internal contamination. The following techniques were utilized to decontaminate the patients:

- (a) Repeated baths in warm water with neutral soap, which reduced the contamination levels substantially.
- (b) Use of acetic acid for increasing the solubility of caesium and thus facilitating its removal.
- (c) Applications of titanium dioxide associated with hydrated lanolin, in cases where a great amount of radioactive material was present on palms and soles. Owing to its mildly abrasive action, titanium dioxide, after repeated applications, was able to remove considerable quantities of caesium from non-superficial skin layers.
- (d) Additional mechanical methods for decontamination, such as callus abraders, rigid bristle nylon brushes and pumice stone, were used for patients with severe sole contamination.
- (e) Later, after all the above described means were exhausted, use was made of an ion exchange resin, substituting caesium for potassium. The resin was placed inside gloves and plastic overshoes, where hands or feet would remain in contact with it for at least 20 min. As a consequence, a 50% removal of residual caesium was achieved.

II-5. FINAL REMARKS

The Goiânia accident is considered to be the worst radiological accident to have occurred and is of interest from various standpoints. The difficulties confronted by the emergency teams stemmed mainly from the delay in recognizing and identifying the nature and severity of the accident. The fact that fragments of the caesium source were dispersed among many persons and over many places made a proper reconstruction of the events following the removal of the capsule containing ^{137}Cs impossible.

As for the acute radiation syndrome, the therapeutic strategy adopted was to treat the patients conservatively. Use of GM-CSF was based on the assumption that

residual stem cells existed and that a factor able to stimulate their proliferation and differentiation might play an important role in recomposing the natural defence mechanisms of the irradiated patients.

Regarding local radiation injuries, it became evident that conventional treatment did not greatly modify the clinical evolution of severe radiation injuries. Unfortunately, the detailed extent of radiation damage can be accurately established only a few months after exposure, when it is possible to choose a more definitive therapy. The two problems challenging physicians are determining the extent of the damage and deciding which tissues will inevitably be destroyed, and choosing the most suitable moment to perform surgery. Data provided by MRI, computerized tomography, vascular scintigraphy, and histochemical and immunocytochemical studies of biopsy material, as well as topographic dosimetry, including in-depth distribution of the doses, and clinical evolution should all be taken into consideration.

Prussian blue proved to be an excellent antidote in cases of caesium contamination, even when administered several days after contamination. The optimum dose suggested is 3 g/d, administered at regular intervals, i.e. in doses of 1 g (two capsules) every 8 h, in order to maintain its gastrointestinal availability throughout the day. The drug can be used over long periods of time, for months if necessary. Definitive suspension of the drug is indicated when no more caesium is detected in the excreta.

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