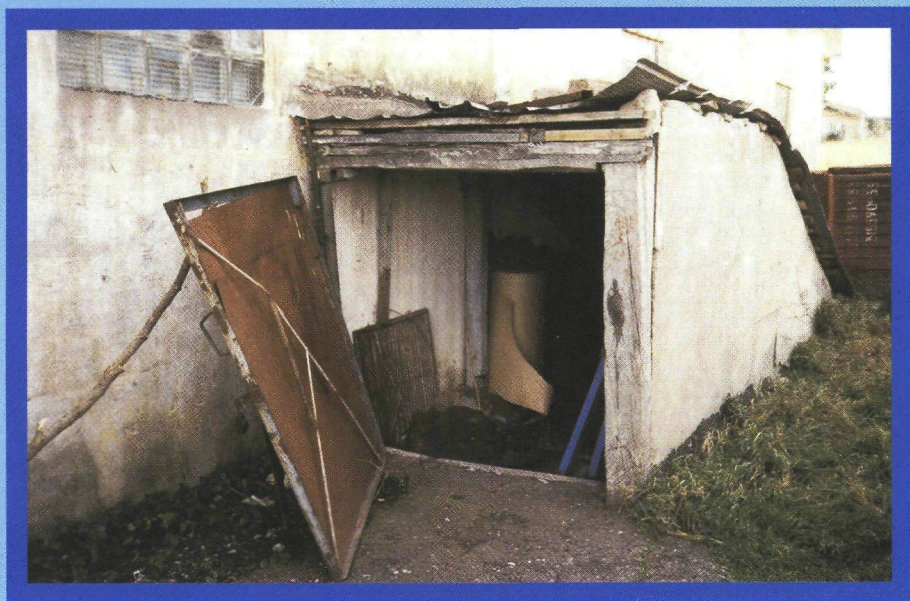


# The Radiological Accident in Lilo





THE RADIOLOGICAL ACCIDENT  
IN LILO



# THE RADIOLOGICAL ACCIDENT IN LILO

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## FOREWORD

The use of nuclear technologies has fostered new, more effective and efficient medical procedures and has substantially improved diagnostic and therapeutic capabilities. However, in order that the benefits of the use of ionizing radiation outweigh the potential hazards posed by this medium, it is important that radiation protection and safety standards be established to govern every aspect of the application of ionizing radiation. Adherence to these standards needs to be maintained through effective regulatory control, safe operational procedures and a safety culture that is shared by all.

Occasionally, established safety procedures are violated and serious radiological consequences ensue. The radiological accident described in this report, which took place in Lilo, Georgia, was a result of such an infraction. Sealed radiation sources had been abandoned by a previous owner at a site without following established regulatory safety procedures, for example by transferring the sources to the new owner or treating them as spent material and conditioning them as waste. As a consequence, 11 individuals at the site were exposed for a long period of time to high doses of radiation which resulted inter alia in severe radiation induced skin injuries.

Although at the time of the accident Georgia was not an IAEA Member State and was not a signatory of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency, the IAEA still provided assistance to the Government of Georgia in assessing the radiological situation, while the World Health Organization (WHO) assisted in alleviating the medical consequences of the accident.

The two organizations co-operated closely from the beginning, following the request for assistance by the Georgian Government. The IAEA conducted the radiological assessment and was responsible for preparing the report. The WHO and its collaborating centres within the Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) assessed the medical aspects of the accident and provided the diagnosis and treatment of the patients in associated specialized hospitals in France and Germany. The Governments of France and Germany provided financial support for the medical treatment of the injured persons. The Russian Federation also provided medical assistance.

The lessons learned from this accident, particularly in the medical management of radiation induced skin lesions, are invaluable. In fact, some of the techniques used to treat the injured Georgian patients are pioneering.

The IAEA and the WHO, co-sponsor of this publication, wish to express their gratitude to the Government of Georgia and its authorities for their co-operation in the conduct of the investigation.

The Scientific Secretaries responsible for the preparation of this publication were M. Oresegun, R. Cruz-Suarez and I. Turai of the Division of Radiation and Waste Safety.

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## EXECUTIVE SUMMARY

On 9 October 1997, the IAEA received a facsimile message from the Government of Georgia stating that nine servicemen of the Lilo Training Detachment of Frontier Troops had developed local radiation induced skin diseases on various parts of their bodies. It requested the IAEA to assist in the evaluation of the radiological situation at the Lilo Training Centre and in the examination and treatment of the patients. The IAEA officially informed the World Health Organization (WHO) of the accident and on the same day the Ministry of Health of Georgia requested assistance from the WHO under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency.

Prior to the request for assistance from the IAEA, recovery of the radiation sources and medical assessment of the exposed servicemen had begun in Georgia. Source recovery was accomplished by the Centre of Applied Research of the Institute of Physics, Tbilisi. Their investigation found a large number of radiation sources, namely 12  $^{137}\text{Cs}$  sources, one  $^{60}\text{Co}$  source and 200  $^{226}\text{Ra}$  sources. Immediately following the request for assistance, the IAEA fielded an expert mission, from 11 to 14 October 1997, to assist in source recovery, characterization of the sources and a radiological survey of the accident site.

Primary medical assessment of the patients by Georgian physicians revealed that all patients developed one or several erythemas in different parts of the body. For most patients, the prevailing general symptoms were nausea, vomiting, headache, loss of appetite and weakness. The hospitalization of the patients took place in different centres in Georgia. Treatment was complicated owing to the late diagnosis. General treatment included medications to improve microcirculation and blood rheology, antibacteriological therapy, immunostimulators and vitamins. In addition, all patients received psychotherapy. Later, two additional persons were found to have been overexposed. All eleven overexposed persons suffered from a cutaneous syndrome caused by radiation, with significant differences among the patients as to signs and symptoms.

After the official request for assistance from the WHO, the patients were treated at specialized hospitals of WHO collaborating centres within the Radiation Emergency Medical Preparedness and Assistance Network (REMPAN)<sup>1</sup> network in France, Germany and the Russian Federation.

In this particular accident, the exposure was very inhomogeneous and distributed over a relatively long period of time. Even if there is still a lack of detailed information about the chronology of the accidental exposure, it is known that the patients

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<sup>1</sup> A list of abbreviations is to be found on page 99.

developed skin reactions of different stages between April and August 1997, except for one patient who had already complained of symptoms in June 1996. It can be assumed that during this time the patients had been exposed to an 'ill defined' and/or 'protracted' ionizing irradiation, and that for these patients, the most likely time frame of accidental exposure in a radiation field may have been between 60 and 300 days.

The clinical consequences of radiation exposure observed in the patients fall into two major problem areas: local radiation injuries leading to a cutaneous syndrome, and general signs and symptoms due to total body exposure to ionizing radiation. On the admission of these patients to the specialized hospitals in France and Germany and in the weeks which followed, the cutaneous syndrome was the utmost priority in terms of diagnosis and further treatment. Several patients underwent repeated plastic surgery. However, the exposure of the skin to  $^{137}\text{Cs}$ , which is mainly a gamma emitter, was not limited to local skin injuries but undoubtedly also resulted in the exposure of internal organs and systems, including sensitive tissues such as the bone marrow and the reproductive system. To a large extent, the clinical picture of these patients was determined by the consequences of multiple local radiation lesions resulting in the cutaneous syndrome.

Non-invasive diagnostic techniques, such as high frequency ultrasound (20 MHz), magnetic resonance imaging (MRI) and especially thermography, proved to be helpful in assessing the extent of the disease and in the planning of surgical and non-surgical treatment.

At the time of writing (1998), all patients had been discharged from hospital. However, concerns remained about the development of radiation induced diseases which might appear in the future. These may include skin cancers, impaired testicular function, cataract formation, hepatitis, hypothyroidism and leukaemia. Ongoing medical surveillance is therefore likely to be necessary.

The review of the radiological accident in Lilo revealed that the major cause of the accident was the improper and unauthorized abandonment of the 12  $^{137}\text{Cs}$  radiation sources at the Lilo site.

The contributing factors leading to the accident were the following:

- (a) The sources were not subject to regulatory control (authorization, inspection and enforcement).
- (b) The inventory of sources was not transferred to the new owner of the site.
- (c) There was no accountability with respect to the sources; the physical inventory was not documented and maintained.
- (d) There was no proper conditioning or disposal of sources no longer in use.
- (e) There was an absence of clear labelling and radiation warning signs on the sources.
- (f) An appropriate emergency response plan did not exist.

Several of these contributing factors are not unique to this accident, and in this light the following lessons to be learned are presented in order that this will help reduce the likelihood of similar accidents occurring or, if they do occur, help to mitigate their consequences:

- (1) Regulations should specify the appropriate protection and safety requirements, *including administrative control of notification, authorization by registration or licensing, inspection and enforcement.*
- (2) Military sources should be included in this regulatory control.
- (3) Accurate and comprehensive records of the inventory of radioactive sources should be kept. These records should clearly indicate the current owner and location of sources, enabling any lost or missing sources to be quickly identified.
- (4) Transfer of ownership of sources or disposal of sources should only be authorized by the regulatory authority. This will ensure that all sources are under regulatory control.
- (5) Regulations should require that warning signs on sources clearly indicate danger.
- (6) All users of ionizing radiation should have an emergency response and preparedness plan, as well as up-to-date equipment, well trained personnel and financial resources to execute the plan.
- (7) General practitioners should be knowledgeable about basic radiation biology, associated clinical symptoms and the medical management of persons overexposed to ionizing radiation.





# 1. INTRODUCTION

## 1.1. BACKGROUND

On 9 October 1997, the IAEA received a facsimile message from the Minister of Health of Georgia stating that nine servicemen of the Lilo Training Detachment of Frontier Troops had developed local radiation induced skin diseases on various parts of their bodies. The message included details of the medical diagnoses of the nine victims, together with information on the radiation sources and dose rates which had caused the exposures. The Minister requested the IAEA to assist in the examination and treatment of the patients.

The IAEA officially informed the World Health Organization (WHO) of the accident and on the same day the Ministry of Health of Georgia requested assistance from the WHO under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency.

An investigation had revealed the presence of 12  $^{137}\text{Cs}$ , one  $^{60}\text{Co}$  and 200  $^{226}\text{Ra}$  radiation sources, and in some places high dose rates had been detected. The Government of Georgia requested the IAEA to send an emergency team to evaluate the radiological situation at the Lilo Training Centre. The purpose of the IAEA mission was to verify that dose rates at the Lilo Training Centre were at the level of natural background and that no surface contamination was detectable by field measurements or soil sample measurements. The mission was also charged with verifying that the radiation sources were safely stored and physically protected inside lead containers at the site and that dose rates at and around the storage room were acceptably low.

Prior to the request for assistance from the IAEA, medical assessment of the exposed persons had begun in Georgia. The first clinical manifestations which led patients to contact physicians were in most cases similar. All patients developed one or several transient erythemas in different parts of the body. For most patients, the prevailing general symptoms were nausea, vomiting, headache, loss of appetite and weakness. The hospitalization of the patients took place in different centres in Georgia. Treatment was complicated owing to the late diagnosis. General treatment included medications to improve microcirculation and blood rheology, antibacteriological therapy, immunostimulators and vitamins. In addition, all patients received psychotherapy.

Two additional persons were found to have been overexposed. All 11 overexposed persons suffered from a cutaneous syndrome caused by radiation, with significant differences among the patients as to signs and symptoms. The patients were later treated at specialized hospitals in France and Germany. Four of the injured were cared for at the Curie Institute and the Percy Hospital of the Armed Forces, both in Paris, France, and the other seven at the Dermatology Department of the University of Ulm at the Armed Forces Hospital in Ulm, Germany.

Subsequently, there was recurrence of some of the radiation induced skin ulcers in four patients treated in France and Germany; additional ulcers appeared at other anatomical sites. At the request of the Georgian health authority, these individuals were treated at the Medical Radiological Research Centre of the Academy of Medical Science of the Russian Federation, located in Obninsk. Further recurrences took place in three of the patients treated in Obninsk. Medical treatment in France, Germany and the Russian Federation was free of charge to the patients.

At the time of writing (1998), all patients had been discharged from hospital. However, concerns remained about the development of radiation induced diseases which might appear in the future. These may include skin cancers, impaired testicular function, cataract formation, hepatitis, hypothyroidism and leukaemia. It was therefore considered advisable, at the time of discharge from the hospitals in France and Germany, that the accident victims undergo follow-up visits twice a year, subject to adjustment on an individual basis. However, follow-up for the therapeutic regimens initiated in France and Germany could not be carried out in Georgia.

The IAEA has a statutory function to establish safety standards relating to radiation protection and safety and to assist in their application. The International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources (BSS) [1] provide the essential requirements for protection and safety; these are supported by more detailed safety standards and guidance documents. The BSS lay down obligations for users of radiation sources and presuppose that States have an adequate infrastructure within which they can be effectively applied. Guidance on the establishment of an appropriate infrastructure is provided in Ref. [2].

For a number of years the IAEA has provided support and assistance in the event of serious accidents involving radiation sources and has prepared several reports on this kind of accident, namely on those of El Salvador [3], Israel [4], Viet Nam [5], Estonia [6] and Brazil [7]. The findings of these reports have provided useful lessons on how safety improvements might be made in the future, and such is the principal aim of this report.

This report gives detailed information on the therapeutic approaches used in the specialized hospitals in France and Germany. Some of these were innovative and highly successful, and should therefore be of interest to those involved in the treatment of radiation injuries.

## 1.2. OBJECTIVES

The objectives of this report were to collect and report the facts about the accident. General lessons to be learned have been identified and it is hoped that the dissemination of this information will help reduce the likelihood of similar accidents

occurring or, if they do occur, help to mitigate their consequences. Extensive information was also collected about the medical effects of acute radiation exposure and the medical management of exposed persons.

### 1.3. SCOPE

This report describes the circumstances of the accident, the management of the accident and the medical management of the exposed persons until 1998. As with other accidents of this type, a number of uncertainties remain relating to the details of the events leading up to and following the accident. There may also be further developments, particularly relating to health consequences, for those substantially exposed. However, sufficient information is available at this stage to analyse the main causes and contributing factors of the accidents and the lessons to be learned.

*The information in this report is aimed at national authorities and regulatory organizations to enable them to take steps to minimize the likelihood of similar accidents occurring in the future, and to put in place arrangements to limit the consequences of such accidents if they do occur. This report also contains information relevant to licensees and operating organizations using radioactive sources.*

This report gives extensive coverage to pioneering techniques in the medical management of radiation induced injuries. This information should be of interest to the medical community.

### 1.4. STRUCTURE

Background information about the radiation protection infrastructure in Georgia and the management of the facility involved in the accident is provided in Section 2. A chronology is presented in Section 3, and the recovery of the sources is discussed in Section 4. International co-operation in connection with the accident and the IAEA's response are discussed in Sections 5 and 6, respectively. Section 7 addresses the results of the biological dosimetry. The medical management of persons exposed to radiation is discussed in Sections 8–14. Section 15 summarizes the lessons to be learned and the conclusions drawn on the basis of the accident review. Annex I deals with the status of the patients as of August 1999, and Annex II contains a list of the WHO collaborating centres and institutions within the Radiation Emergency Medical Preparedness and Assistance Network (REMPAN).

## 2. BACKGROUND INFORMATION

### 2.1. THE SITE

Georgia is in southwest Asia and lies along the Black Sea, between Turkey and the Russian Federation. Georgia's population stood at 5 725 972 in July 1995. The country includes two autonomous republics, Abkhasia and Ajaria. Tbilisi is the capital.

The Lilo Training Centre is located at a remote site about 25 km east of Tbilisi. The centre covers approximately 150 000 m<sup>2</sup>. A plan of the site is presented in Fig. 1. The black dots represent places where radiation sources were found.

In the past the centre was used by Soviet troops for civil defence training. The sources may have been used for calibration of survey equipment and for training in radiological monitoring to be carried out in the event of a nuclear accident or nuclear war. The site was transferred to the Georgian Army in 1992. There were three main areas: the management and living area, which included several buildings for soldiers and officers (centre part of Fig. 1); the living quarters, where some of the officers lived with their families (left side); and the empty buildings used for training (right side).

### 2.2. RELEVANT ORGANIZATIONS AND RADIOLOGICAL PROTECTION INFRASTRUCTURE IN GEORGIA

#### 2.2.1. Regulatory authority

The central inspectorate of the State Sanitary Supervision and Hygiene Standardization (SSSHS) at the Ministry of Health is the national body which authorizes practices involving ionizing radiation and carries out inspections of all radiation sources. In principle, this institution is responsible for the supervision of the protection of workers, patients and the public. The Chief Medical Inspector, as head of the Central Inspection Bureau of the SSSHs, reports directly to the Minister of Health. There is also a register of radiation sources. The SSSHs does not undertake any monitoring of workers or retain any dose records of measurements made by other institutes. The unit comprises 12 employees, 8 of whom are technicians.

Additionally, the Regional Sanitary Supervision Centres at Tbilisi, Batumi, Poti and Sujumi, with some ten workers altogether, carry out the inspection of the less significant radiation sources and some environmental measurements. They are under the purview of the Central Inspectorate of the SSSHs. Radiation sources in the regions of Abkhasia and Ajaria are currently not subject to much control.

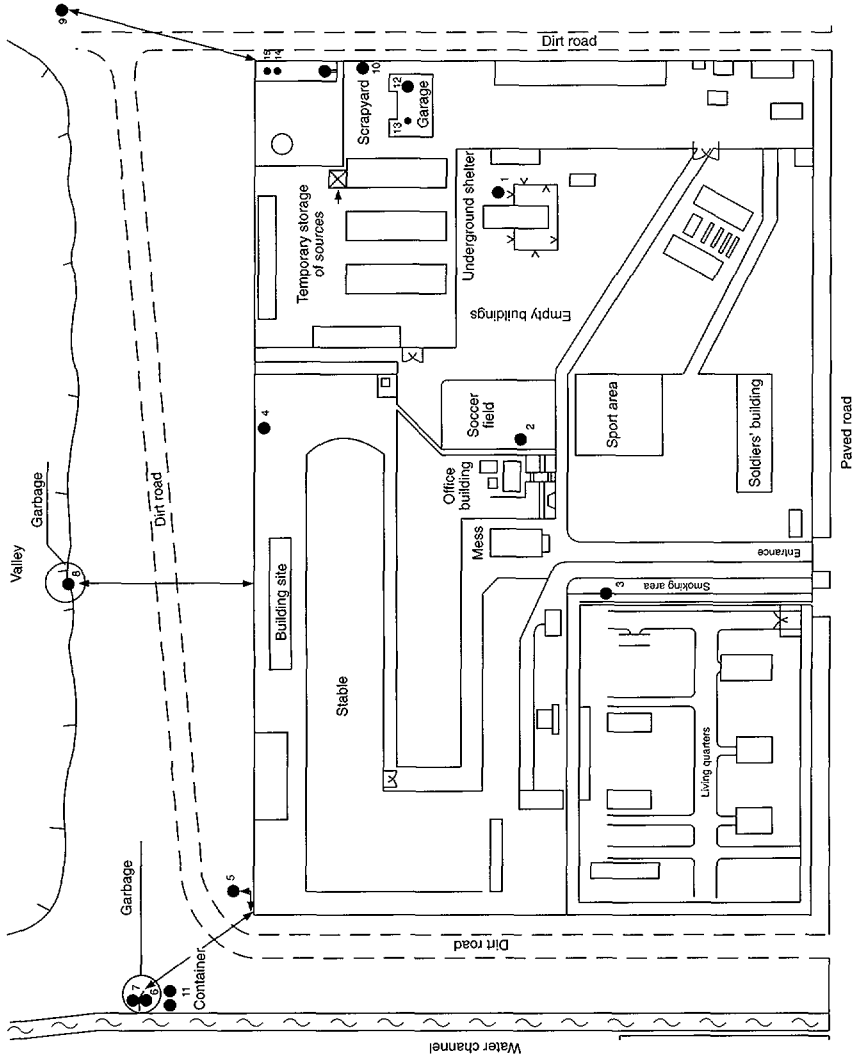


FIG. 1. Schematic diagram the Lilo Training Centre.

At the time of the accident, a proposal for an independent regulatory body, directly under the Government of Georgia, and a draft law on nuclear and radiation safety were under consideration. In October 1998 a Law on Nuclear and Radiation Safety was promulgated by the Georgian Parliament, and in February 1999 the Nuclear and Radiation Safety Service was established as the regulatory authority of Georgia within the Ministry for Protection of the Environment and Natural Resources.

## **2.2.2. Relevant organizations**

### *2.2.2.1. Institute of Physics*

The Institute of Physics, under the Georgian Academy of Sciences, was founded in 1950 and currently employs nearly 500 persons. The institute undertakes basic research in particle and plasma physics. It formerly had an operating light water pool research reactor, which was constructed in 1959 and was shut down in 1988. The main field of research was neutron damage of solids, primarily at very low temperatures. Closure in 1988 was precipitated by public concern following the Chernobyl accident and the need for expensive upgrading of safety systems. The fuel was 90% enriched uranium. In 1990, the main part of the fuel was removed and sent to the Russian Federation. About 900 g of irradiated fuel remain in the reactor. There were also 10 kg of unirradiated fuel on the site, 5 kg of which were sent to Tashkent in Uzbekistan in 1995 for use in a 10 MW research reactor. The remaining 5 kg were sent to the United Kingdom in 1998. The reactor will not be dismantled; rather the intention is to fill the 8 m deep tank with concrete to a depth of about 2.7 m. Following this, the institute plans to use the space above the concrete for a low power reactor, using low enriched fuel, for neutron activation analysis and training.

### *2.2.2.2. Georgian Cancer Research Centre*

There are some 700 diagnostic X ray facilities and nine gamma therapy facilities in Georgia. In all, close to 2000 employees are involved in the operation of these establishments. In particular, the Cancer Research Centre (CRC) runs three gamma therapy facilities using  $^{60}\text{Co}$  sources and two X ray therapy facilities. The CRC works closely with the SSSHS, providing authorizations for medical radiation facilities throughout the country and informing the SSSHS whenever any of its staff become aware of 'anomalies' in the facilities they inspect.

The dosimetry unit at the CRC formerly provided individual monitoring and calibration services to these facilities. Several years ago, during the war, the only car available for use in providing these services was stolen, and since then services outside Tbilisi have been stopped.

Individual monitoring was undertaken at the CRC using film badges which were replaced on a monthly basis and the doses of which were recorded in writing on sheets of paper. Films were not properly calibrated and there is doubt about the validity of the records. Eleven professionals were involved in dosimetry services and five others performed the calibration of the gamma therapy sources.

Nuclear medicine is currently not practised in the CRC. Some of the facilities (gamma cameras) were damaged during the war, and radionuclides are not available owing to the lack of funds. Only the Diagnostic Centre, a privately run hospital in Tbilisi, is operating nuclear medicine facilities. The Republican Hospital in Tbilisi also has a nuclear medicine facility which includes a gamma camera; at the time of the IAEA visit to the facility, the camera did not have any radionuclides.

#### 2.2.2.3. *Institute of Radiology*

The Institute of Radiology studies the movement of radionuclides in the environment and the effects of radiation on plants. It has two gamma irradiation facilities with  $^{137}\text{Cs}$  sources. The more active source originally had an activity of 130 TBq and is kept under water; the other source originally had an activity of 93 TBq and is housed in a heavily shielded container. The institute falls under the purview of the Ministry of Agriculture and is run by a staff of 80 persons, 50 of whom are scientists.

### 3. CHRONOLOGY OF THE ACCIDENT

*April–August 1997:* Soldiers from the Lilo Training Centre developed skin lesions on several parts of their bodies. Medical doctors from the Georgian Army were initially unable to determine the cause of the lesions, which resembled thermal burns, allergic contact dermatitis or vasculitis. In August, a haematologist and a dosimetrist from the Institute of Biophysics in Moscow confirmed the diagnosis first made by the Georgian physicians in June of ‘radiation burns of various degrees’. Judging by the clinical situation, the exposures had been fractionated and had occurred over the course of several months. No information was available on the time and circumstances of the beginning of the exposures. One of the affected soldiers (AN) had been recruited into the army in November 1995, one in March 1996 and nine in November 1996.

*26 August 1997:* A radiation hot spot was discovered at the Lilo Training Centre near the underground shelter (Location No. 1 in Fig. 1; Fig. 2). The dose rate was about 45 mGy/h. The measurement was carried out by officers from the Chemical, Radiological and Biological Protection Division of the Georgian Army.



FIG. 2. Entrance to the underground shelter.

*5 September 1997:* The same personnel and a representative of the SSSHS performed a second measurement to confirm the high radiation levels.

*10 September 1997:* The Georgian authorities contacted the Safety and Radiation Protection Department of the Centre of Applied Research of the Institute of Physics. A working group of physicists was established to assess the radiological situation at the site.

*13 September 1997:* The source that was removed from the pocket of a soldier's winter jacket on 13 September 1997 was a metal cylinder of about 6 mm diameter and roughly 12 mm height.

*Beginning of September 1997:* The health authority of Georgia requested the WHO/Radiation Emergency Medical Preparedness and Assistance Network (WHO/REMPAN) collaborating centre of the Institute of Biophysics, Moscow, to send specialists to Georgia to carry out medical examinations on nine patients suspected of having radiation injuries. Two medical doctors experienced in radiation pathology travelled to Georgia, examined the patients and provided the Georgian Ministry of Health with preliminary medical conclusions. They confirmed that all the patients had developed local radiation reactions and that some of them, in addition, had chronic radiation syndrome.

*9 October 1997:* The IAEA received a facsimile message from the Minister of Health of Georgia stating that nine servicemen of the Lilo Training Detachment of Frontier Troops had developed local radiation induced skin disease on various parts



of their bodies. Details were provided on the medical diagnoses of the nine victims, together with information on the radiation sources and dose rates that had caused the exposure. The Georgian Minister of Health requested the IAEA to assist in the examination and treatment of the patients.

The IAEA officially informed the WHO of the accident and on the same day the Ministry of Health of Georgia requested assistance from the WHO under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency. The WHO was further informed that there were two new patients, raising the total number of overexposed persons to 11.

*22 October 1997:* Two patients were admitted to the Curie Institute and two to the Percy Hospital of the Armed Forces, both in Paris. Both institutions are WHO/REMPAN collaborating centres in France.

*29 October 1997:* The remaining seven patients were hospitalized in the Dermatology Department of the University of Ulm at the Armed Forces Hospital in Ulm, Germany, also a WHO/REMPAN collaborating centre.

## 4. RECOVERY OF SOURCES

### 4.1. RADIOLOGICAL MONITORING AT THE LILO FACILITY

The working group of physicists started monitoring the area on 11 September 1997. The complete lack of information about the sources made their task more difficult. No information was available on the type of radionuclide, its chemical and physical form, its activity, etc.

The radiological survey equipment available at the Chemical, Radiological and Biological Protection Division of the Georgian Army and at the Safety and Radiation Protection Department of the Institute of Physics was made available to the working group. The main characteristics of the equipment are summarized in Table I.

### 4.2. RADIOLOGICAL SURVEY

The survey began close to the underground shelter (Location No. 1 in Fig. 1; Fig. 2). On 12 September 1997 the exact location of a source was determined, but owing to the high dose rate at the location and the lack of a lead container to store the source, no action was taken.

On 13 September a source was removed from the pocket of a soldier's winter jacket. In order to establish the type of radionuclide and the activity, the source was

TABLE I. RADIOLOGICAL SURVEY EQUIPMENT USED BY THE GEORGIAN WORKING GROUP

Monitor	Detector type	Radiation (energy range, MeV)	Measuring range	Uncertainty (%)	Comment
DP-5	GM tube	Photons (0.08–1.25)	0.5 $\mu\text{Gy/h}$ –2 Gy/h	$\pm 30$	
DKS-04	GM tube	Photons (0.05–3)	1 $\mu\text{Gy/h}$ –10 mGy/h	$\pm 20$	Designed for individual monitoring
SRP-68-01	NaI(Tl)	Photons (0.05–3)	0–26.2 $\mu\text{Gy/h}$	$\pm 30$	
RDM-2	GM tube	Photons (0.05–1.5)	0.1–9.9 $\mu\text{Sv/h}$	$\pm 30$	
MR meter 12 SA	GM tube	Photons (0.05–1.5)	0–30 $\mu\text{Gy/h}$	$\pm 30$	
Stephen 6000	GM tube	Photons (0.035–1)	0–999 mSv/h	$\pm 20$	Designed for individual monitoring
RUP-1	GM tube	Alpha (2–6) Beta (0.07–2.3) Photons (0.2–1.25)	$(0.5\text{--}2) \times 10^4 \text{ cm}^{-2} \cdot \text{min}^{-1}$ $(1.0\text{--}5) \times 10^4 \text{ cm}^{-2} \cdot \text{min}^{-1}$ 5 $\mu\text{Gy/h}$ –0.4 Gy/h	$\pm 20$	Surface contamination monitor

measured at different distances and was later placed inside lead shielding. Additional measurements showed that there was no radioactive contamination directly at Location No. 1.

A slight increase over the background level was determined near Location No. 1. Another source was found at the soccer field (Location No. 2 in Fig. 1) located 130 m from the underground shelter and a few metres from the office building. In this case the source was buried approximately 30 cm below the surface of the soil. On the same day elevated dose rates were discovered just a few metres from the smoking area (Location No. 3 in Fig. 1). The third source was found 10 cm below the ground surface.

At that stage the working group decided to survey the whole facility and its surroundings at 1 m above the surface of the ground. Detailed measurements were

TABLE II. DOSE RATES ASSOCIATED WITH SOME OF THE SOURCES (Cs-137) FOUND AT THE LILO TRAINING CENTRE<sup>a</sup>  
( $\Gamma = 79 \mu\text{Gy} \cdot \text{h}^{-1} \cdot \text{m}^{-2} \cdot \text{GBq}^{-1}$  for Cs-137)

Source number	Date found	Dose rate at ground surface (mGy/h)	Dose rate at 1 m from the source ( $\mu\text{Gy/h}$ )	Estimated activity (GBq)	Source location
1	1997-09-13	—	13 000	164	Coat pocket
2	1997-09-13	2	9 900	126	Soccer field
3	1997-09-13	0.15	30	0.37	Smoking area
5	1997-09-14	35	70	0.88	Outside facility
6, 7	1997-09-19	20	2	0.02	Outside facility
8	1997-09-19	10	50	0.63	Outside facility
9	1997-09-19	8	1.5	0.01	Outside facility
10	1997-09-20	—	2	0.02	Scrapyard

<sup>a</sup> Information provided by the Georgian authorities.

carried out in the ensuing days. A total area of 250 000 m<sup>2</sup> was monitored. The results of the monitoring are detailed in Table II (all location numbers refer to Fig. 1):

- Source 4 (Location No. 4) was found at the building site.
- Source 5 (Location No. 5) was found 5 m away from the fence (solid line around the perimeter of the facility in Fig. 1) in the area beyond the grounds of the facility and approximately 5 cm below the surface of the ground.
- Sources 6 and 7 (Locations Nos 6 and 7) were found 176 m from the fence in the refuse mound in the area beyond the grounds of the facility and close to the water channel. Two lead containers were found nearby, presumably the containers for these two sources.
- Source 8 (Location No. 8) was found 125 m away from the fence in the refuse mound beyond the grounds of the facility.
- Source 9 (Location No. 9) was found 270 m away from the fence in the area beyond the grounds of the facility and approximately 5 cm below the surface of the ground.
- Source 10 (Location No. 10; Fig. 3) was found in an old military transport scrapyard.
- Source 11 (Location No. 11) was found inside a lead container.
- Source 12 (Location No. 12) was found inside a lead container.
- Searches at locations 13, 14, 15 and 16 revealed some 200 discarded devices



*FIG. 3. Location where source No. 10 was found (scrapyard).*

which contained  $^{226}\text{Ra}$  sources earlier used by the army and affixed to machine-gun sights.

The dose rates given in Table II correspond to an average of several readings at a distance of 1 m after removal of the source from the ground. Two other  $^{137}\text{Cs}$  sources were found, but as they were stored in their lead containers, the dose rate at the surface of the container was very low. Some 200 discarded sighting devices for machine guns, which contained  $^{226}\text{Ra}$ , were also found in several places. A  $^{60}\text{Co}$  source with a very low dose rate was found at Location No. 4.

#### 4.3. DETERMINATION OF THE RADIONUCLIDE INVOLVED

In order to establish the type of radionuclide and the activity, the sources were measured at different distances. Since no field gamma spectrometer was available, a series of gamma absorption measurements were carried out using a lead screen. From these measurements the presence of  $^{137}\text{Cs}$  was determined. On 1 October 1997 a spectrometric measurement at the temporary storage facility confirmed the previous findings.



*FIG. 4. Temporary storage conditions.*



*FIG. 5. Containers with sources Nos 6, 7 and 8.*



FIG. 6. About 200 units of night shooting guides with  $^{226}\text{Ra}$  sources.

#### 4.4. STORAGE FACILITY

The sources were temporarily stored at the Lilo site next to the scrapyard (Fig. 1). The first six sources found were placed inside the lead shielding provided by the Institute of Physics. The rest of the sources were retained inside their lead containers found at the site. Figures 4 and 5 show the storage conditions at the Lilo facility. Figure 6 shows the gunsights in the wooden box. The room used for this temporary storage had brick walls with a thickness of 20 cm and no electrical or water installation. It was protected by metal doors.

#### 4.5. PHYSICAL PROTECTION OF THE SOURCES

Physical protection of the sources was assured by the Detachment of Frontier Troops. The storage room was locked and clearly identified, and security surveillance was maintained at all times.

## 5. CO-OPERATION BETWEEN THE WHO AND THE IAEA

At the beginning of September 1997, the WHO/REMPAN collaborating centre at the Institute of Biophysics in Moscow was requested by the health authority of Georgia to send specialists to Georgia to carry out medical examinations on nine patients suspected of having radiation injuries. Following this request, two medical doctors experienced in radiation pathology travelled to Georgia, examined the patients and provided the Georgian Ministry of Health with preliminary medical conclusions. They confirmed that all the patients had developed local radiation reactions and that some of them, in addition, had chronic radiation syndrome.

On 9 October 1997 the IAEA officially informed the WHO of the accident and on the same day the Ministry of Health of Georgia requested assistance from the WHO under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency. In addition, the WHO was informed about two new patients with the same pattern of injuries, thus raising the total number of overexposed persons to 11.

The IAEA fielded an expert mission from 11 to 14 October 1997 to assist in source recovery, characterization of the sources and a radiological survey of the accident site. On 28 October 1997 another mission by the IAEA was undertaken to reassess the situation, in particular the medical condition of the exposed persons.

The WHO/REMPAN co-ordinator contacted the IAEA and the Ministry of Health of Georgia and alerted the network of REMPAN collaborating centres.

On the next day, 10 October, the WHO/REMPAN collaborating centre at the University of Ulm, Germany, informed the WHO of the possibility of providing treatment for all patients in the hospital facilities of the university and that the centre was seeking financial support for this purpose from the German Government. The WHO established a communication link between the Ministry of Health of Georgia and the collaborating centre in Ulm.

In the following week, the WHO obtained additional offers of assistance from other WHO/REMPAN collaborating centres. The Curie Institute and the Institute for Protection and Nuclear Safety (IPSN), both in Paris, informed the WHO that they had negotiated with the Ministry of Health of Georgia to hospitalize two patients in the Radiotherapy and Radiopathology Department of the Curie Institute and two others in the Centre for the Treatment of Burns of the Percy Military Hospital in Paris. The cost for their treatment would be covered by the French authorities. The collaborating centre in Moscow (Institute of Biophysics) was ready to accept nine patients for treatment during a two month period if financial support (US \$60 000) could be provided by Georgia. In order to have free medical assistance from the Institute of Biophysics, an official request from the Ministry of Health of Georgia to the Ministry of Health of the

Russian Federation was required. Two WHO collaborating centres in the Russian Federation (the Ural Research Centre of Radiation Medicine in Chelyabinsk and the Medical Radiological Research Centre in Obninsk) offered to provide medical treatment for two or three patients in each of the centres from their own resources. Four WHO/REMPAN collaborating centres located in Australia, Brazil, India and the United States of America informed the WHO of their readiness to send experts to Georgia for evaluating the situation and providing possible medical assistance in situ. All this information was forwarded by the WHO to the Ministry of Health of Georgia for consideration. Further arrangements for the hospitalization of the patients, including the financial aspects, were undertaken by the Ministry of Health of Georgia in co-operation with the relevant WHO/REMPAN collaborating centres.

On 22 October, the Ministry of Health of Georgia decided to transport the two most severely injured patients to the WHO collaborating centre in France, the Department of Radiotherapy and Radiopathology at the Curie Institute, and two others to the Centre for the Treatment of Burns of the Percy Military Hospital.

On 27 October, a medical team headed by a specialist from the IPSN, Paris, and including specialists from the WHO/REMPAN collaborating centre in France, visited Georgia to examine the seven remaining patients. This team prepared a report providing general information on the accident and the radiation victims. On the same day the Ministry of Health of Georgia accepted a proposal from the WHO/REMPAN collaborating centre in Ulm, Germany, to hospitalize these patients in the Dermatology Department of the University of Ulm at the Hospital of the Armed Forces, after the Government of Germany had approved funding.

## **6. IAEA MISSION**

### **6.1. OBJECTIVES OF THE MISSION**

The IAEA expert mission took place from 11 to 14 October 1997. It had the following objectives:

- (1) To verify that the dose rates at the Lilo Training Centre were at the natural background level and that no surface contamination was detectable by field measurement or by soil sample measurement;
- (2) To verify that the radiation sources were safely and securely stored inside lead containers at the site and that dose rates around the storage room were at the natural background level;
- (3) To verify that the sources were physically protected.



TABLE III. RADIOLOGICAL SURVEY EQUIPMENT USED BY THE IAEA MISSION

Monitor	Detector type	Radiation (energy range, MeV)	Measuring range	Uncertainty (%)	Comment
FH40-F2	GM tube (ZP 1200)	Photons (0.045–1.3)	0.5 $\mu$ Sv/h–9.9 mSv/h	$\pm 24$	—
Telepole	GM tube (ZP 1301)	Photons (0.7–2)	5 $\mu$ Sv/h–10 Sv/h	$\pm 10$	—
Mini Con	GM tube (Type 7313)	Photons, beta	0.5–1000 cps $\cdot$ cm <sup>2</sup> $\cdot$ Bq <sup>-1</sup>	$\pm 20$	Surface contamination monitor

## 6.2. RADIOLOGICAL SURVEY EQUIPMENT

The equipment used to fulfil the mission is described in Table III. The sets of equipment used by the Georgian working group and the IAEA were intercompared and showed good agreement in the measurements taken.

## 6.3. RADIOLOGICAL SURVEY RESULTS

The IAEA team performed a radiological monitoring survey in the areas inside and around the Lilo Training Centre. All the open areas and various buildings were surveyed. The measurements were done at 1 m from the ground. The values presented in the following figures represent the average values of ten measurements at each location. Figure 7 shows the dose rate values at the different locations where sources had been found. The values obtained were less than 0.5 mSv/h and correspond to background levels. The surface contamination measurements show no detectable contamination at the site (Fig. 8).

The temporary storage room was carefully monitored. The dose rate values on the outside surface of the walls of the room were similar to natural background levels. All measurements on the containers were taken as close as possible to their outside surface; the dose rates obtained are presented in Fig. 9. The maximum value was 44  $\mu$ Sv/h, from source No. 11. The dose rates at different distances from the group of containers are presented in Fig. 10. At a distance of 3.5 m from the group of sources, the dose rate was at the natural background level.

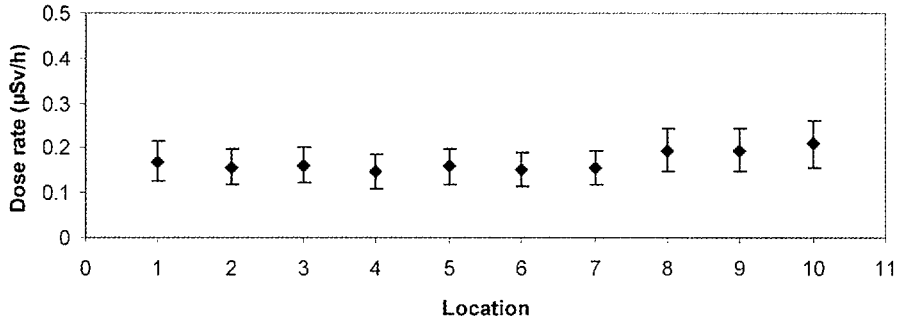


FIG. 7. Dose rate values at different locations measured with an FH40-F2 monitor.

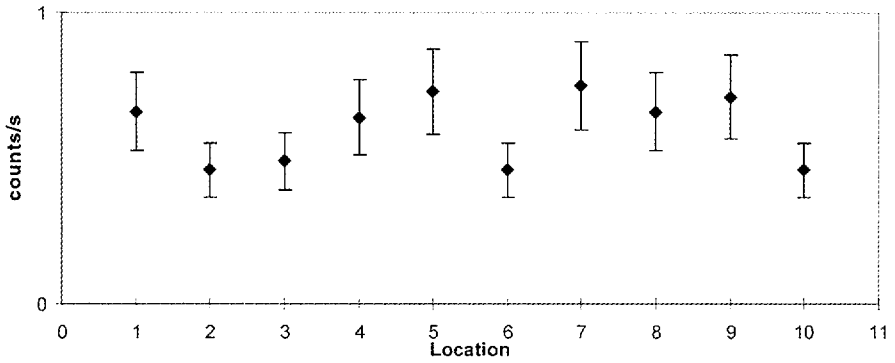


FIG. 8. Readings of the surface contamination monitor Mini Con at different locations.

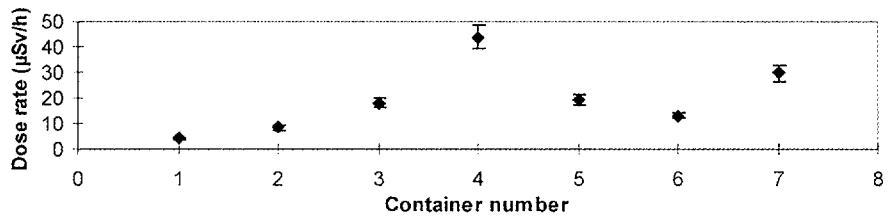


FIG. 9. Dose rate values measured with the Telepole monitor in the temporary storage facility.

The IAEA team made a dose rate measurement at the top of container No. 1 without the lead cover in place. The six sources stored in this container were situated at a distance of 10 cm from the top. The average dose rate value in this position was around 0.1 Sv/h.

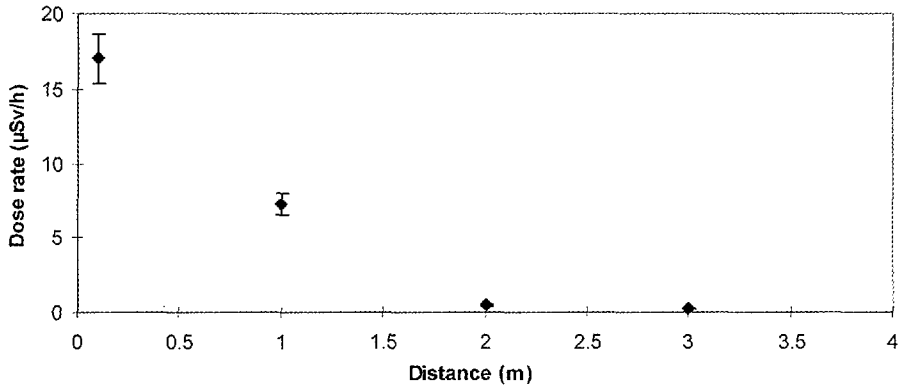


FIG. 10. Dose rate values at different distances from the group of containers.

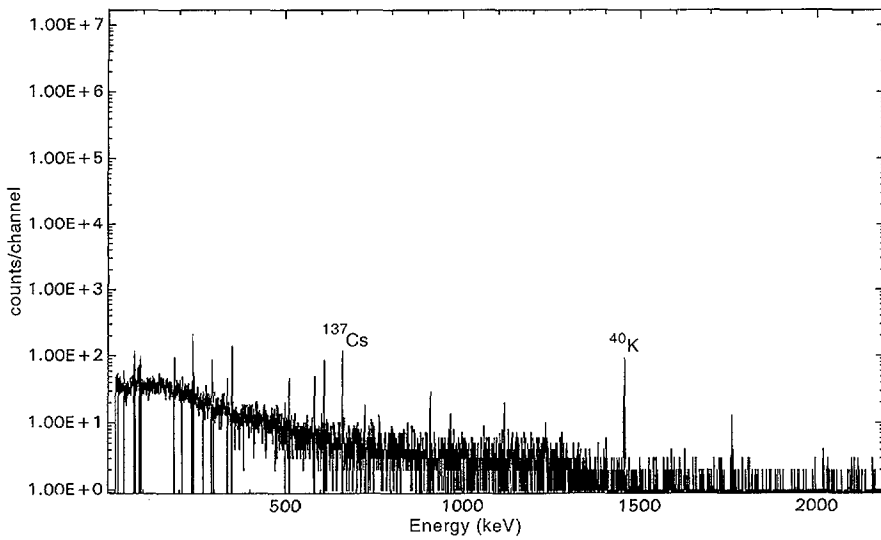


FIG. 11. Gamma spectrum of sample No. 10 measured with a germanium detector.

Estimates of internal doses for the patients were not necessary since radiological surveys made at the sites showed that none of the sources was damaged or leaking radioactive material and that the environment was free of radioactive contamination.

In addition, external dose estimates were not possible for this accident, since the information on the relevant parameters contributing to the irradiation of the

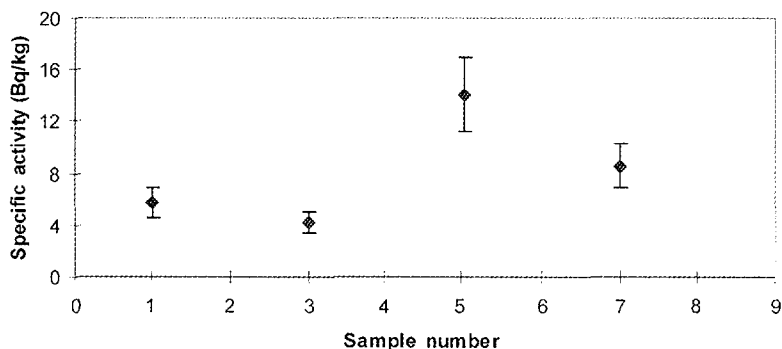


FIG. 12. Specific activity of soil samples analysed by gamma spectrometer.

persons involved was not sufficient to permit precise dose calculation. The dates and times of irradiation, the specific sources producing the irradiation and the exposure geometries were all unknown. Moreover, the patients were not willing to discuss the circumstances surrounding their exposure. An assessment of the external doses received was therefore not attempted.

#### 6.4. SOIL SAMPLE MEASUREMENTS

Soil samples were taken from the four locations where the buried sources had been found. The samples were analysed by gamma spectrometry in order to identify any possible soil contamination due to leakage from the sources. The measurements were carried out at the IAEA's Radiation Safety Services Section (RSSS, now called the Radiation Monitoring and Protection Services Section) facility. Figures 11 and 12 show the specific activity of each soil sample analysed. The specific activity in the samples ranged from 3 to 15 Bq/kg. These values are in line with the background levels in this area.

## 7. BIOLOGICAL DOSIMETRY

### 7.1. CYTOGENETIC INVESTIGATIONS

Biological estimation of the exposure doses was accomplished by scoring unstable chromosome aberrations (dicentric and centric rings) in peripheral blood lymphocytes.

TABLE IV. RESULTS OF CYTOGENETIC INVESTIGATION

Patient	Number of metaphases	Dicentrics	Centric rings	Dicentric + centric rings per cell	Hypothetical mean effective dose (Gy)	95% confidence interval	U test
1 AN	502	55	4	0.12	1.2	1.0–1.4	4.7
2 EP	518	80	4	0.16	1.6	1.3–1.9	3.6
3 CG	500	19	1	0.04	0.7	0.5–0.9	–0.6
4 TK	500	14	0	0.028	0.5	0.3–0.7	–0.4
5 GL	500	2	1	0.006	0.1	0–0.3	
6 BZ	500	4	4	0.016	0.3	0–0.5	
7 GG	500	7	8	0.03	0.5	0.3–0.7	
8 SO	500	8	1	0.018	0.3	0.1–0.5	
9 ID	500	46	4	0.11	1.2	1.0–1.4	
10 VZ	500	2	1	0.006	0.1	0–0.3	
11 SN	500	1	7	0.016	0.3	0.1–0.5	

Blood samples taken in the first week of November 1997 were prepared and analysed at the Laboratory of Multiparametric Biology, IPSN, Fontenay-aux-Roses, France, and in the Department of Medical Genetics of the University of Ulm.

The technique used by the two laboratories for the lymphocyte cultures was similar to that described in Ref. [8]. In brief, lymphocytes separated from peripheral blood are cultivated in an appropriate culture medium containing phytohaemagglutinin (PHA) and are then blocked to the stage of the metaphase by antimitotics. The fixed lymphocytes are spread out over microscopic blades and then coloured in such a way that the unstable chromosome aberrations are observed only in the first mitosis. Dicentrics, centric rings and excess acentrics are scored in each complete metaphase (consisting of 46 centromeres).

The results were obtained about one week after analysis of at least 500 metaphases, depending on the patient examined. The number and the frequency of the aberrations thus observed in patients are presented in Table IV according to type of aberration.

For the dose estimates a dose–effect relationship fitted from the chromosome aberrations scoring of in vitro irradiated blood lymphocytes was applied. Their irradiation was at a dose rate of 0.5 Gy/min of  $^{60}\text{Co}$ . The data were provided by the IPSN laboratory.

The accuracy of the measurement is related to the number of metaphases observed and to the background frequency, which is roughly 1 dicentric for 2000 metaphases. Table IV shows that significant dicentric levels were found in all patients. For these patients, the mean doses were calculated supposing a homogeneous whole body irradiation of between 0.1 and 1.6 Gy.

When aberrations are present, their distribution makes it possible to assess to a certain extent the heterogeneity of the irradiation. When irradiation is homogeneous, the distribution of chromosome aberrations follows Poisson's law, and the two most numerous classes of cells are those with 0 and 1 aberration per cell. For heterogeneous irradiation, the distribution moves towards the classes of cells containing several anomalies. Papworth's extended U test based upon the mean to variance ratio of the aberration distribution quantifies the deviation from Poisson's law. When the U test level exceeds 2, the radiation exposure may be considered heterogeneous. If this is applied to the results of Table IV, one can conclude that in patients 1 AN, 2 EP and 9 ID exposures were clearly heterogeneous. Without additional information, it could not be determined from the cytogenetic analysis whether the irradiation to which the other patients had been exposed had also been heterogeneous. Consideration was also given to the possibility of the exposures having been protracted.

The calibration curve usually used to define the absorbed dose as a function of the frequency of unstable chromosome aberrations is given by  $Y = \alpha D + \beta D^2$ , with  $Y$  being the frequency of dicentrics,  $D$  the whole body received dose and  $\alpha$  and  $\beta$  the coefficients of quadratic linear regression. For the sake of simplicity and by extension from the models of cell survival curves, the coefficient  $\alpha$  is often considered as representing lesions created by a single increment of ionizing radiation and the coefficient  $\beta$  as related to the lesions from two or more increments. In the case of a protracted irradiation, DNA repair and degradation can be considered as simultaneous, according to the fractionation of the exposure. This results in a number of chromosome aberrations below the number expected for an acute irradiation. To simulate this fact experimentally, a new coefficient,  $G$ , is added to the parameter  $\beta$ , reducing it to 0 when the repair time exceeds the irradiation time ( $\geq 6$  h). The dose-effect curve then becomes  $Y = \alpha D + (G)\beta D^2$ .

Table V presents the whole body integrated doses which were recomputed taking into account only the coefficient  $\alpha$  of the dose-effect relationship.

A significant number of unstable chromosome aberrations were observed in the blood of all patients. Two conclusions can be drawn:

- (1) The patients had unstable chromosome aberrations reflecting recent exposure to ionizing radiation.
- (2) This demonstrated that, if the calculated dose was close to or below 1 Gy, the U test was not informative.

TABLE V. CORRECTED DOSES BASED ON THE HYPOTHESIS OF A PROTRACTED IRRADIATION

Patient	Dicentrics + centric rings per cell	Hypothetical mean effective dose (Gy)	95% confidence interval	Corrected mean dose (Gy)
1 AN	0.12	1.2	1.0–1.4	4.2
2 EP	0.16	1.6	1.3–1.9	5.9
3 CG	0.04	0.7	0.5–0.9	1.5
4 TK	0.028	0.5	0.3–0.7	1.1
5 GL	0.006	0.1	0–0.3	0.2
6 BZ	0.016	0.3	0–0.5	0.6
7 GG	0.03	0.5	0.3–0.7	1.1
8 SO	0.018	0.3	0.1–0.5	0.7
9 ID	0.11	1.2	1.0–1.4	4.1
10 VZ	0.006	0.1	0–0.3	0.2
11 SN	0.016	0.3	0.1–0.5	0.6

Whereas the irradiation exposure was always heterogeneous, this heterogeneity was not reflected in the distribution of aberrations. There can be two essential reasons, not mutually exclusive, for this phenomenon: in some cases, the exposure was too localized to result in a significant number of aberrations; in other cases, lymphocyte renewal led to the disappearance of most of the irradiated metaphases. Even if a protracted irradiation had taken place, it would not have resulted in a proportional formation of the unstable chromosome aberrations. In this regard, the whole body dose estimations obtained by means of the  $G$  function must be considered a working hypothesis rather than a true estimate.

## 7.2. ELECTRON SPIN RESONANCE DOSIMETRY

Table VI presents results of the estimation of individual doses of external irradiation measured by electron spin resonance (ESR) dosimetry of patients' tooth enamel at the Institute of Biophysics, Moscow.

## 7.3. MONTE CARLO METHOD OF DOSE RECONSTRUCTION

The Lilo radiological accident is a special case since the date of the accident, the duration of the exposure and the activity of the sources are unknown.

TABLE VI. INDIVIDUAL PATIENT DOSES  
AS MEASURED BY ESR DOSIMETRY

Patient	Dose (Gy)
1 AN	No data
2 EP	$4.5 \pm 0.3$
3 CG	$1.4 \pm 0.4$
4 TK	$1.5 \pm 0.2$
5 GL	No data
6 BZ	$0.7 \pm 0.5$
7 GG	$1.3 \pm 0.6$
8 SO	0.1
9 ID	$0.4 \pm 0.3$
10 VZ	No data
11 SN	0.1

Nevertheless, a reconstruction of the irradiation process was carried out by linking the photon transport simulation with the clinical observations. The calibration of the dose calculation was made on the basis of the degree of the necrosis. It was assumed that the dose received was about 25 Gy. The dose reconstruction of the localized irradiation was performed for patient 4 TK with a sealed source assumed to be located in the anterolateral area of the right thigh 16 cm above the knee. Indeed, this patient had a circular necrotic lesion typical of a single source geometry and a static source position.

As the exact distance between the source and the skin was not known, different values were taken into account (3, 10 and 20 mm). The geometry of the source was a cylinder with a size of 6 mm  $\times$  12 mm.

Dose simulation involved calculation and computer aided design (CAD) software which is used to represent the source and the patient. The Monte Carlo dose reconstruction method uses a code which calculates how the particles emitted by the source are transported in a three dimensional (3-D) geometrical structure representing the patient. The way in which particles emitted by the source are transported was calculated by a 3-D transport code known as MORSE (Multigroup Oak Ridge Stochastic Experiment) using a Monte Carlo probabilistic method. CAD software was applied to represent the patient and the source. The CAD software package known as MGED (Multidevice Graphics Editor) allows the modelling of complex shapes such as skeleton and tissues by combinatorial geometry. The right leg and the abdomen of the patient were modelled using the thigh dimensions determined by magnetic resonance imaging (MRI). Owing to the drastic reduction of the patient's muscle around the lesion, the data for the contralateral thigh were used.



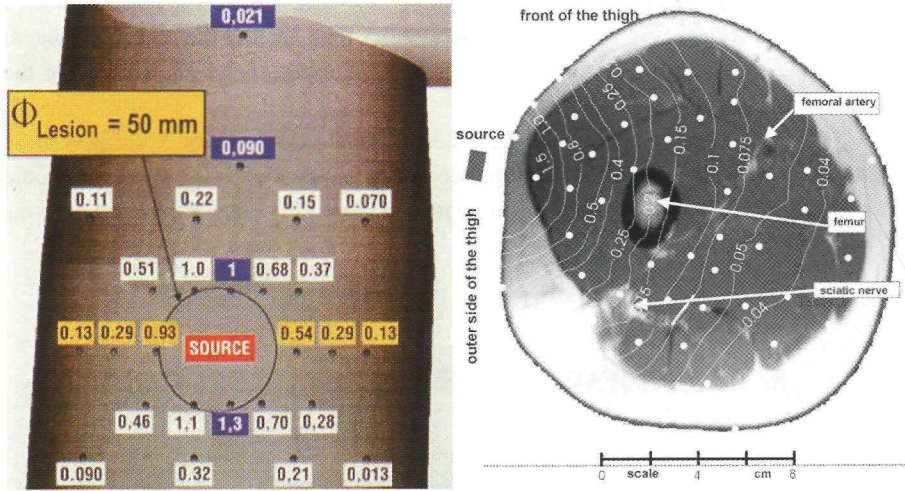


FIG. 13. (a) Distribution of the dose coefficient at the surface of the skin. (b) Dose distribution for a horizontal cross-section of the thigh.

After the morphological parameters were introduced, the distribution of the surface and internal doses was calculated. The absorbed dose was calculated at various points located in areas of interest. Data given in Figs 13(a) and (b) represent the dose coefficient normalized to 1 at the rim of the lesion. If the circumference of the lesion represents the necrosis limit for tissues, i.e. a dose of 25 Gy, the absorbed dose  $D$  at any given point is:

$$D = \text{dose coefficient} \times 25 \text{ Gy}$$

Generally speaking, the uncertainty of the results of the calculations is on the order of 20%.

Figure 13(a) shows the distribution of the dose coefficient at the surface of the skin for a lesion of 5 cm diameter and a source–skin distance of 10 mm. At the centre of the lesion, the dose was assessed at 150 Gy.

The dose profile along the horizontal axis was asymmetric in relation to the source because of the curvature of the thigh, which was not the same on both sides of the lesion. When the source was very close to the skin (less than 1 cm), the isodoses were ovoid owing to the cylindrical shape of the source.

Figure 13(b) shows the dose distribution for a horizontal cross-section of the thigh at the source level. The isodose curves were circular near the source and tended to flatten out deeper into the thigh because of the greater relative contribution of scattering.

This dose reconstruction by computational simulation shows that surface doses drastically decreased as a function of the distance of the source and the dose value at

7 cm from the source was a factor of 8–40 smaller than around the rim. The dose at the top of the femur was a factor of 1500 less than around the circumference of the lesion, i.e. 25 mGy.

The deep dose gradient was very steep and the deep doses decreased more rapidly than the surface doses. The bone dose was a factor of 7–20 smaller than the dose at the rim of the lesion, falling to approximately 4 Gy. The absorbed dose was around 2 Gy at the femoral artery.

## **8. OVERVIEW OF THE MEDICAL ASPECTS**

The medical assessment of the radiation accident at the Lilo Training Centre is presented in five parts, in Sections 9–13.

Section 9 provides information on the initial assessment of the patients by local physicians prior to hospitalization. Initially the attending physicians did not consider radiation exposure as an aetiological factor. The diagnostic and therapeutic approaches adopted during the patients' treatment in the hospitals in Georgia are described. In June 1997, the local Georgian physicians suggested that radiation exposure might have played a role in the development of the clinical signs and symptoms observed. However, the diagnosis of radiation injuries was not accepted by the medical council, and the patients were treated symptomatically. Later, in August 1997, the local physicians again reported their opinion that radiation might be an aetiological factor. As of that time the diagnosis was 'acute radiation syndrome, subacute phase, radiation burns'. In order to verify the diagnoses, consultants from the Institute of Biophysics in Moscow travelled to Georgia and examined the patients. They confirmed the role of radiation as an aetiological factor of the pathological conditions which had affected the patients, and the diagnosis was 'chronic radiation sickness' and 'radiation burns' of various degrees of severity.

Section 10 presents the results of the diagnostic examinations and treatment provided for the patients in the specialized hospitals in Ulm and Paris. Taking into account that local radiation injuries of the skin were the predominant signs in the clinical picture at that period, in this part of the report attention is mainly given to the description of cutaneous signs and symptoms which are included within the term 'cutaneous radiation syndrome'.

Section 11 deals with the pathophysiological considerations of the development of signs and symptoms. Taking into account the unusual type of radiation exposure (no fixed time for the beginning of the exposure or its duration, unknown character of the type of exposure — continuous or fractionated, etc.), the question arose as to whether the patients received a total body irradiation as well and to what extent.

Section 12 details the medical treatment provided in the Russian Federation, and Section 13 presents the conclusions drawn from the medical management of the patients. Section 14 presents recommendations that were made for the follow-up of the patients, and Section 15 presents conclusions and lessons to be learned.

## **9. PRIMARY MEDICAL ASSESSMENT OF THE PATIENTS BY LOCAL PHYSICIANS IN GEORGIA**

### **9.1. PERIOD PRIOR TO HOSPITALIZATION**

The first clinical manifestations which led patients to contact physicians were in most cases similar (see Table VII). All patients developed one or several erythemas in different parts of the body. Three patients (1 AN, 2 EP, 3 CG) complained of nausea, vomiting and a loss of appetite. In addition, patient 2 EP experienced headaches and patient 3 CG complained of headache and weakness. The prevailing general symptoms in other patients (with the exception of 11 SN) were nausea, headache, loss of appetite and weakness. Patient 11 SN did not report any general signs of the disease. On the basis of this clinical picture, the first physicians contacted did not provide any diagnosis and the patients were hospitalized in different local medical facilities for detailed examination, diagnosis and treatment.

### **9.2. DIAGNOSIS AND TREATMENT IN HOSPITALS IN GEORGIA**

#### **9.2.1. General clinical manifestations and management of patients**

The hospitalization of the patients in Georgia was characterized by the late diagnosis, which to a degree complicated the care of the patients and affected their treatment. The late diagnosis also resulted in the patients being sent to different hospitals in Georgia for treatment.

The first lesion was found on patient 1 AN, who was hospitalized in Dmanisi Hospital on 10 July 1996. On 17 July 1996, without preliminary diagnosis, he was transferred to the Russian Military Hospital in Tbilisi. There he was diagnosed with 'serum disease'. Owing to the worsening of his condition, he was transferred in August 1996 to the National Antiseptic Centre with a diagnosis of anaerobic phlegmona of both thighs and both hands. The patient was discharged from the centre in December 1996 with skin and soft tissue defects on both thighs and with contracture of the thumb, index finger and middle finger of both hands. Until May 1997, he was

TABLE VII. MEDICAL ASSESSMENT OF THE PATIENTS BY LOCAL MEDICAL STAFF IN GEORGIA

Patient	Age (a)	Probable period of contact with the source	Date and character of first clinical symptoms	Date and character of first local symptoms
1 AN	20	May–Jun. 1996	June 1996, nausea, vomiting, loss of appetite	June 1996, 1997-04-15, erythema
2 EP	23	Dec. 1996–Apr. 1997	April 1997, nausea, vomiting, loss of appetite, headache	April 1997, erythema
3 CG	21	Dec. 1996–Apr. 1997	April 1997, nausea, vomiting, loss of appetite, headache, weakness	April 1997, erythema
4 TK	22	Dec. 1996–Apr. 1997	April 1997, nausea, headache, weakness	April 1997, erythema
5 GL	19	Dec. 1996–Apr. 1997	1997-05-10, nausea, headache	1997-05-10, erythema
6 BZ	22	Dec. 1996–Apr. 1997	1997-05-25, nausea, loss of appetite, headache	1997-05-25, erythema
7 GG	23	Dec. 1996–Apr. 1997	May 1997, nausea, headache, weakness	May 1997, erythema
8 SO	22	Dec. 1996–Apr. 1997	May 1997, nausea, headache, weakness	May 1997, erythema
9 ID	18	Dec. 1996–Apr. 1997	May 1997, nausea, headache, weakness	May 1997, erythema

TABLE VII. (cont.)

Patient	Age (a)	Probable period of contact with the source	Date and character of first clinical symptoms	Date and character of first local symptoms
10 VZ	20	Dec. 1996–Apr. 1997	1997-09-18, nausea, headache, weakness	1997-09-18, erythema
11 SN	19	Dec. 1996–Apr. 1997	Patient did not report any symptoms	September 1997, erythema

monitored as an outpatient. On 13 May 1997 he was readmitted to the Russian Military Hospital for a skin graft. The operation was unsuccessful. The patient was discharged from the hospital on 21 August 1997 with a skin defect. By this time, Georgian physicians had made a suggestion that radiation exposure was an aetiological factor of the patient's disease. Therefore he was readmitted to the National Antiseptic Centre on 10 October 1997 with the diagnosis 'acute radiation syndrome, subacute phase, radiation burns of the fourth degree to both thighs'. On 22 October 1997 he was taken to France for further treatment.

Five patients (2 EP, 3 CG, 4 TK, 5 GL, 6 BZ) were admitted to a hospital of the Research Institute of Skin and Venereal Diseases, Tbilisi. They were examined for ten days for skin diseases. The patients were then transferred without any preliminary diagnosis to the Russian Military Hospital, where the diagnosis was given as a 'polyform exudative erythema'. Later the erythemas became sharply demarcated ulcers with central necrosis. Different symptomatic treatments were applied to the patients. Some of the defects epithelialized. The more severe defects deteriorated.

The patients 8 SO and 9 ID were hospitalized in June 1997 at Clinic 1 of the Tbilisi State Medical University. They were diagnosed as having 'toxic dermatitis' complicated by secondary infections. The patients were treated symptomatically. The defects healed and the patients were discharged from the clinic. However, on 18 August 1997 the patients were readmitted to the hospital owing to relapse.

Two patients, 7 GG and 10 VZ, did not seek professional medical help for their symptoms.

Patient 11 SN developed the first clinical symptoms on 18 October 1997 and was admitted to Clinic 1 of the Tbilisi State Medical University on 23 October 1997.

In summary, all the patients displayed general signs and symptoms compatible with the diagnosis of chronic radiation sickness combined with skin ulceration (cutaneous syndrome) caused by exposure to external non-uniform fractionated gamma radiation. This diagnosis was suggested by the medical team of the Institute of Biophysics, Moscow.

### 9.2.2. Cutaneous signs and symptoms

A description is given below of the local injuries in the nine patients who were examined on 9 October 1997 by the doctors from the Institute of Biophysics in Moscow.

#### *PATIENT 2 EP*

Starting on 3 April 1997 the patient noticed the appearance of the following symptoms: nausea, vomiting, weakness and an increase in temperature from 37.5 to 38.0°C. The primary skin reaction appeared in the period from 12 to 15 April 1997. At the time of examination the clinical signs were as follows: multiple (33) depigmented macules on the skin located in different parts of the body — abdomen, back, arms and legs, thorax and the area of the thyroid gland (Fig. 14). These lesions were round in shape, with hyperpigmentation and depigmentation on the perimeter. The surrounding skin was thin and without markings, and looked like paper, being smooth, shiny and dry. In some spots the skin was peeling and small haemorrhages

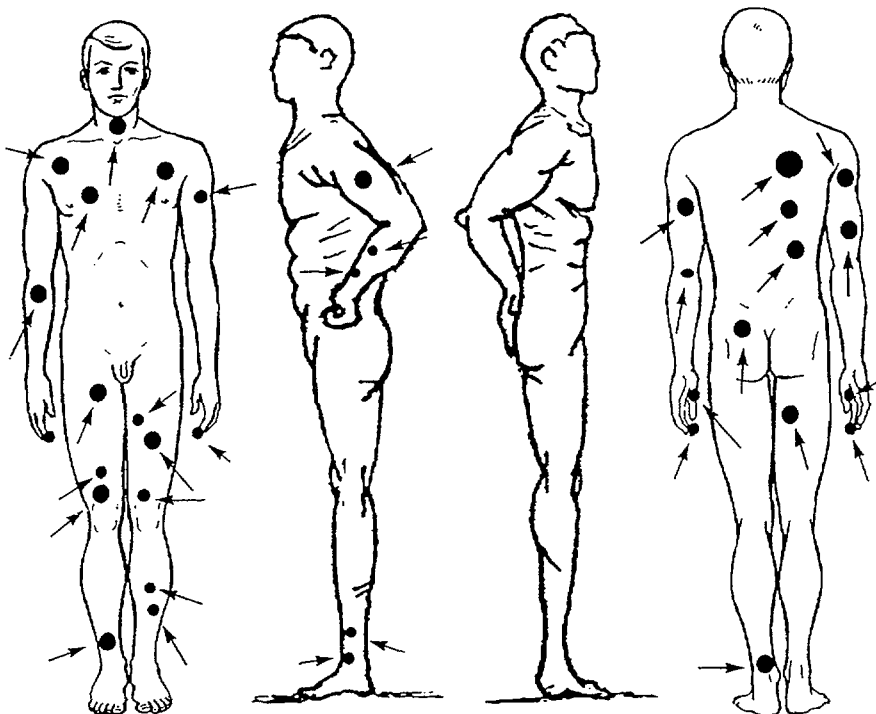


FIG. 14. Patient 2 EP: 33 depigmented macules.

could be seen. On the upper third of the right forearm, the back, the right buttock and the left calf there were non-recoverable primary erosions, round in shape and from 1.5 cm × 1.5 cm to 3 cm × 4 cm in size, the largest being on the back. The bottom of these erosions was covered with a greenish-yellow fibrin crust. These lesions were not mobile in relation to the surrounding tissue. The edges of the injury were regular and without excavation marks. On contact they bled. At the periphery of the defect there were small haemorrhages. Hair was absent from the area of the scars and around the radiation ulcers.

**Diagnosis:** Multiple local radiation injuries (altogether 33) ranging between the first and fourth degrees of severity in different parts of the body.

#### *PATIENT 3 CG*

Starting in the middle of April the patient noticed the following symptoms: nausea, vomiting, weakness and a temperature of from 37.6 to 38.2°C. At the time of examination, there was a radiation ulcer on the lateral surface on the upper third of the right thigh with a size of 18 cm × 10 cm which was spreading to the front surface. The ulcer had well defined swollen edges due to inflammation. At the bottom of the ulcer, necrosis of the anterior group of muscles of the thigh could be seen. The depth of the ulcer varied from 0.5 to 1.00 cm. The perimeter of this defect was covered by a fibrin crust of a greyish-yellow colour. On contact, the injured surface bled. At the edge of the defect there were punctuated haemorrhages. The fluid that exuded from the ulcer was serous and pus-like in character. Hair was absent from the area of the scars and the radiation ulcer. Two autologous skin grafts were performed on this patient. The results were unsatisfactory. After the operations the ulcer increased in size.

**Diagnosis:** Local radiation injuries of the fourth degree (extremely severe) to the skin and subcutaneous tissues of the right thigh with large areas of necrosis (18 cm × 10 cm) in the anterior group of thigh muscles.

#### *PATIENT 4 TK*

On the lateral surface of the middle third of the right thigh there was a radiation ulcer of 8 cm × 8 cm (Fig. 15). The edges of this defect were swollen and well defined, forming an inflammation barrier. At the bottom of the defect at a depth of 0.5 cm there was tissue necrosis. The ulcer perimeter was covered with a greyish-yellow fibrin crust. On contact, the ulcer bled, and punctuated haemorrhages were located on the periphery of the defect. There was a serous and pus leakage from the ulcer. Hair was absent from the area of the scar and the radiation lesion.

**Diagnosis:** Local radiation injury of the fourth degree of severity to the right thigh.



*FIG. 15. Patient 4 TK: large (8 cm × 8 cm), deep radiation ulcer, October 1997.*

#### *PATIENT 5 GL*

On the lateral surface of the lower third of the left calf there was a primary ulcer of an oval form with a size of 2.5 cm × 2 cm. The bottom of the defect was located at the skin level and at a depth of 0.5 cm it was covered with a greyish-brown fibrin crust. It was not mobile in relation to the surrounding tissue. At the bottom there were spots of scarce granulation. The lesion margins were regular, were not undermined and were clearly defined. On contact these margins bled, and on the periphery there were punctuated haemorrhages. On the left foot and in the lower third of the right calf there were round depigmented macules which appeared after recovery of the ulcers but were more superficial. The skin was paperlike, thin, smooth, shiny, dry and devoid of skin markings. In some spots the skin was peeling, with punctuated haemorrhages. There was no hair in the area of the skin scars and the radiation ulcers.

**Diagnosis:** Local radiation injury of the second and third degrees of severity to both calves.

#### *PATIENT 6 BZ*

In the middle third of the left calf and lower third of the right thigh there were primary radiation ulcers of 2 cm × 3 cm and 10 cm × 2 cm. Around these ulcers the skin was hyperpigmented, depigmented and hairless. The lesion edges were well





*FIG. 16. Patient 7 GG: right thigh, ulcer (2 cm × 3 cm, 0.5–2 cm deep), October 1997.*

defined, blistered and above the surface of the surrounding tissue. The bottom of the ulcer was covered by a fibrin layer. The surrounding skin was thin and without markings, and looked like paper, being smooth, shiny and dry. In some spots the skin was peeling, and punctuated haemorrhages could be seen. In the area of the scar there was no hair.

**Diagnosis:** Local radiation injury of the second and third degrees of severity to both calves.

#### *PATIENT 7 GG*

On the lateral surface of the lower third of the right thigh just on the border with the knee joint there was a primary ulcer 2 cm × 3 cm in size (Fig. 16). This ulcer was surrounded by hyperpigmented and depigmented skin without hair. The lesion edges were well defined and blistered, and were above the surface of the surrounding tissue. At the bottom of the ulcer a non-intensive granulation process could be seen. Exudation was moderate and serous in character. The surrounding skin was dry, shiny and without markings. The depth of the defect was 0.5–2 cm. Earlier this lesion had occupied more space but then had become smaller. There were also several spots of peeling skin and punctuated haemorrhages. This area was hairless.

**Diagnosis:** Local radiation injury of the third to fourth degrees of severity to the right thigh.

#### *PATIENT 8 SO*

On the front surface of the middle third of the left thigh there was a primary ulcer with a round shape and a size of 2.5 cm × 3.5 cm. The bottom of the lesion was located at a depth of 0.2 cm below the skin. The bottom was covered by a greyish-yellow fibrin crust and was not mobile in relation to the surrounding tissue. At the bottom, small spots of granulation could be seen. The lesion edges were regular and without excavation marks. There was no intensive serous/pus leakage. On contact, the margins of the lesion bled. On the periphery there were punctuated haemorrhages. On the front surface of the lower third of the right thigh, hypopigmented areas could be detected. The macules had a round shape and were hyperpigmented and depigmented. The skin in this area was thin and without markings, and looked like paper: smooth, shiny and dry. In some spots the skin was peeling, and punctuated haemorrhages could be seen. The area of the scars and the ulcer was hairless.

**Diagnosis:** Local radiation injury of the third to fourth degrees of severity to the left thigh.

#### *PATIENT 9 ID*

There were multiple (14) depigmented macules mainly on the upper part of the body. They were on the front part of the left shoulder, the left part of the thorax, the right part of the abdomen and the lower third of the back. Scars were round shaped with hyperpigmentation and depigmentation (Fig. 17). The skin around the lesions was thin, smooth, shiny and peeling, was without characteristic marks, and looked like paper. In some spots, punctuated haemorrhages could be seen. On the middle third of the left calf there was a non-recoverable primary erosion and in the midline at the level of thoracic vertebra 12 (D12) projection area a recurrence of the ulcer with a round shape (1.5 cm diameter). The ulcer bottom was covered with a greyish-yellow fibrin crust and the defect was not mobile in relation to the surrounding tissue. The edges of the lesion were regular and without excavation marks. The scar and ulcer areas were hairless.

**Diagnosis:** Local radiation injury of the third to fourth degrees of severity to the left calf.

#### *PATIENT 11 SN*

On the front surface of the lower third of the left thigh there was a primary ulcer of a round form and a size of 2 cm diameter. The bottom of the lesion was located at a depth of 0.2 cm below the skin and was covered by a greyish-yellow fibrin crust. The lesion's edges were regular and not excavated. Leakage was moderate and serous in character. On contact the lesion edges bled. On the periphery there were punctuated



FIG. 17. Patient 9 ID: five depigmented hairless macules, August 1997.

haemorrhages. At the centre of the lesion separate spots were covered by hairs which were hardened. There were hypopigmented margins of the skin at the periphery of the ulcers. The skin was hyperpigmented and depigmented. The surrounding skin was thin, without markings and with the appearance of cigarette paper, being smooth, shiny and dry. In some spots the skin was peeling and punctuated haemorrhages could be seen. This area was devoid of hair.

**Diagnosis:** Local radiation injury of the second to third degrees of severity to the left thigh.

### 9.2.3. Haematological indices

In October 1997, some abnormalities were found in the number of neutrophils and lymphocytes. Five patients (2 EP, 3 CG, 6 BZ, 8 SO, 9 ID) developed moderate leucopenia and six patients (1 AN, 2 EP, 3 CG, 6 BZ, 8 SO, 10 VZ) developed lymphocytopenia, with the number of lymphocytes at less than 50% of the normal value. Table VIII provides more detailed information on the blood count of each patient.

### 9.2.4. Chromosomal analysis

Different types of chromosome aberration in lymphocytes were identified in the patients who developed severe radiation induced skin injuries. The investigation was

TABLE VIII. PERIPHERAL BLOOD COUNT (2 OCTOBER 1997)

Patient		Leu- cocytes (10 <sup>9</sup> /L)	Button nucleus (%)	Segmented (%)	Eosinophils (%)	Lymphocytes (abs. number)	Lymphocytes (%)	Monocytes (%)
1	AN	4.1	1	75	3	492	12	9
2	EP	3.3	0	69	6	561	17	8
3	CG <sup>a</sup>	3.45	1	73	1	655	19	5
4	TK	3.85	4	77	1	589	13	5
5	GL	7.8	0	46	2	3120	40	12
6	BZ	3.15	0	69	0	661	21	10
7	GG	4.6	0	72	2	1150	25	1
8	SO	3.8	3	64	3	760	20	9
9	ID	3.2	1.5	69	6	464	14.5	9
10	VZ	4.1	0	68	3	820	20	9
11	SN	6.5	0	70	6	1400	22	2

<sup>a</sup> In this patient only 1% plasmatic cells were found.

performed in the haematological department of the State Hospital in Tbilisi on 13 October 1997.

*Patient 1 AN:* A high mitotic index in the bone marrow was observed with acentric fragments. In 20 metaphases scored, a centric ring was found but no dicentrics.

*Patient 2 EP:* 30 dicentric chromosomes were observed in 100 metaphases.

*Patient 3 CG:* In the culture of peripheral lymphocytes, 50 metaphases were observed. Acentric ring and dicentric chromosomes, polyploid metaphases and acentric fragments were found.

*Patient 4 TK:* In 60 metaphases observed, four dicentrics (6.5%), a polyploid metaphase and two excess fragments were found.

*Patient 5 GL:* In 100 metaphases scored, dicentrics and acentric fragments were observed.

*Patient 6 BZ:* In 100 metaphases scored, acentric chromosome aberrations (1.0 per cell) were found, but there were no dicentrics.

*Patient 7 GG:* 30 metaphases were analysed in two samples of peripheral lymphocytes; four were described as hypodiploid, but the majority were diploid. An acentric fragment and one dicentric were found.

*Patient 8 SO:* In the cultured bone marrow, a scarcity of cells was observed, only 3–4 metaphases on each slide. Chromosome fragments were found in six out of 20 metaphases, and in one metaphase, two dicentrics (without fragments) were observed.

TABLE IX. RESULTS OF MICROBIOLOGICAL INVESTIGATIONS

Patient	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>	<i>Proteus vulgaris</i>	<i>Candida</i> spp.
1 AN	+	+	—	—
2 EP	+	+	—	—
3 CG	+	+	—	—
4 TK	+	+	—	—
5 GL	—	+	—	—
6 BZ	+	+	—	—
7 GG	+	—	—	+
8 SO	—	+	—	+
9 ID	+	—	—	—
10 VZ	—	—	—	—
11 SN	—	—	+	+

*Patient 9 ID:* In 60 metaphases investigated, seven dicentrics and three ring chromosomes were found. In five metaphases, multiple aberrations were described with numerous fragments.

*Patient 10 VZ:* In 20 counted metaphases, two dicentrics were detected.

*Patient 11 SN:* Four dicentrics were detected in 50 metaphases.

### 9.2.5. Immunological status

The following immunological indicators were studied in all patients: CD3, CD4, CD8, CD4/CD8, B lymphocytes, NK cells, IgG, IgE, IgM and circulating immunocomplexes. There were no abnormalities in these indices.

### 9.2.6. Results of microbiological investigations

As can be seen from Table IX, *Staphylococcus aureus* and *Pseudomonas aeruginosa* were detected in seven patients. In one patient (11 SN) *Proteus vulgaris* was found. In three patients (7 GG, 8 SO, 11 SN) candida infections were identified. All infections detected were resistant to the following antibiotics: ampicillin, doxycycline, erythromycin, gentamicin, Cotrimoxazol, cefotaxime, Nitrofuranzin, licomycin, ciprofloxacin, rifamycin and penicillin.

### 9.2.7. Functional status of physiological systems

Apart from hepatomegaly in three cases (6 BZ, 7 GG, 8 SO) none of the patients showed any abnormalities in the examination of the cardiovascular system,

respiratory system, renal function and gastrointestinal system. Serological tests for hepatitis A, B and C were negative. No HIV infections or venereal diseases were detected.

### **9.2.8. Treatment provided in Georgia**

The patients were treated according to the following procedures: treatment of the local lesions included application of antiseptic and enzyme creams (10% sintomycin, solcoseryl gel and iruxsol), a traumatic wound covering and local infiltration of Novocain in case of pain. General treatment included medications to improve microcirculation and blood rheology, antibacteriological therapy, immunostimulators and vitamins. In addition, all patients underwent psychotherapy.

## **10. DIAGNOSIS AND TREATMENT IN SPECIALIZED HOSPITALS IN FRANCE AND GERMANY**

### **10.1. OVERVIEW**

After the official request for assistance from the WHO under the terms of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency, the treatment of the 11 overexposed persons was performed at the Curie Institute and the Percy Hospital of the Armed Forces, both in Paris, and in the Dermatology Department of the University of Ulm at the Armed Forces Hospital in Ulm, Germany. On 22 October 1997, two patients were admitted to the Curie Institute (1 AN, 2 EP) and two to the Percy Hospital of the Armed Forces (3 CG, 4 TK). The remaining seven patients (5 GL, 6 BZ, 7 GG, 8 SO, 9 ID, 10 VZ, 11 SN) were hospitalized in the Dermatology Department of the University of Ulm at the Armed Forces Hospital on 29 October 1997.

At the time of reporting (June 1998), it was apparent that all 11 patients injured as a result of this accident suffered from a cutaneous syndrome which was caused by radiation and which differed significantly from patient to patient in its signs and symptoms.

On the other hand, on the basis of the quality of the radiation sources causing the accident, there must have been a total body exposure which most likely extended over several weeks, if not months, again differing from patient to patient. Therefore it had to be expected that haematopoiesis was affected at least during the time of the patients' contact with the radiation sources. At the time of admission to the hospitals in Paris and Ulm, at least 8–20 weeks had elapsed since the last contact with the

radiation field, and the haematological findings have to be reviewed with this scenario in mind.

Furthermore, the total body exposure by hard gamma rays was also expected to cause effects in the reproductive organs. Therefore the study of the reproductive system was specifically considered and the findings are presented in Section 10.4.

Finally, in the present report detailed information is given on the therapeutic approaches used in the specialized hospitals in France and Germany. These therapeutic findings are of special interest, because this type of accident has never been described before in the scientific literature.

## 10.2. CUTANEOUS SYNDROME

All patients were examined directly after their admission to the hospitals in France and Germany. The results, which mainly relate to the status of the patients before any treatment had been given in the specialized hospitals, are summarized in the subsections below which deal with the initial medical check-up, the results of the cutaneous examinations and the findings of different diagnostic examination methods performed following the admission of the patients to the hospitals, such as MRI, telethermography, ultrasound, X ray and bacteriological investigations. Owing to the fact that patients were treated in specialized hospitals in different countries, not all of the examination results were available for each patient.

On the basis of the main cutaneous symptoms and the different examinations, the overall diagnosis for the patients was cutaneous syndrome (of different stages) caused by radiation. Thus the diagnoses made by the Georgian and Russian doctors were confirmed after the examination of the patients in the specialized hospitals in France and Germany in October 1997. The term cutaneous syndrome describes a complex of pathophysiological reactions and resulting clinical symptoms of the skin and its appendages which occur in a characteristic time sequence. This allows a clear identification of the pattern of evolution of the different cutaneous lesions induced by radiation exposure in a given patient [9–12].

In order to assess the general health detriment to each patient, an exact knowledge of the involvement of other organ systems was essential. This varied for each patient according to the individual exposure situation.

### 10.2.1. Initial medical check-up

For all patients, the initial clinical examinations were performed on the day of their admission to the treatment centres.

The age of the patients was between 18 and 23. From the weight and the height of the patients, which were average in all cases, the body surface area in square metres

TABLE X. RESULTS OF THE INITIAL MEDICAL CHECK-UP

Patient	Age (a)	Weight (kg)	Height (m)	Body surface (m <sup>2</sup> )	Blood pressure (mmHg)	Temperature (°C)	General symptoms	Pain
1 AN	20	61	1.85	1.81	100/60	(normal)	None	Yes
2 EP	23	90	1.78	2.03	130/90	37–38	None	Yes
3 CG	21	68	1.75	1.82	150/80	37.3	None	Yes
4 TK	22	70.5	1.57	1.71	140/80	36.6	None	Yes
5 GL	19	82.5	1.75	1.8	110/70	36.8	None	Yes
6 BZ	22	73.0	1.82	1.93	115/80	36.6	None	Yes
7 GG	23	90.5	1.78	2.03	115/80	36.4	None	Yes
8 SO	22	65.0	1.73	1.77	120/75	36.6	None	Yes
9 ID	18	73.0	1.70	1.84	145/90	36.2	None	Yes
10 VZ	20	72.0	1.75	1.87	120/80	36.2	None	Yes
11 SN	19	70.0	1.68	1.79	120/80	36.4	None	Yes

was based on the method of Dubois and Dubois. For all patients, the initial systolic and diastolic blood pressure values were within the normal ranges. This was also true for their temperature, except for patient 2 EP, whose temperature was subfebrile. None of the patients complained any longer about general signs and symptoms, as they had at the time when their skin changes primarily developed (see Section 9, Table VII). However, all of them complained about pain localized in the area around the radiation induced cutaneous lesions at the time of their admission to hospital.

Most of the patients were in a good nutritional and general condition. However, the general condition of patient 1 AN was poor and that of patient 2 EP was moderately good. Patient 8 SO suffered from local pain in the left thigh and patient 7 GG was in pain and experienced a motility disturbance in his right knee joint. Detailed patient results are provided in Table X.

### 10.2.2. Cutaneous signs and symptoms

In all patients the skin lesions first described by the Georgian and Russian physicians (see Section 9) were confirmed by the physicians in the specialized hospitals in France and Germany. The quality of the lesions differed from patient to patient as to diameter, depth and state of evolution. In some patients multiple lesions were disseminated all over the body. For example, 33 different lesions were observed in patient 2 EP and 17 in patient 6 BZ.

As shown in Table X, all patients suffered from pain localized mainly in the area around the radiation induced skin lesions. Owing to the particular localization of the lesions, their extent and/or the subsequent secondary defects, the following patients complained of severe pain: 1 AN from lesions on the hand, the left thigh, the



right thigh and the lower part of the thorax; and 3 CG from the flexion deformity of the hip.

A more detailed description of the lesions for each patient is given in Table XI. The percentage of the body surface involved was estimated and did not exceed 15% for any patient.

### **10.2.3. MRI results**

MRI is a relatively new diagnostic approach for the examination of the musculoskeletal system. Morphological changes and tissue reactions due to oedema, inflammatory reactions and necrosis can be seen with an appropriate examination technique and/or the application of a contrast medium such as gadolinium DTPA. Furthermore, changes in the bone marrow can be described by detection of abnormal signal intensity.

MRI was performed on all patients for the most severely injured parts of the body. Cutaneous and subcutaneous involvement was found in all patients, in some of them with necrosis. In 7 of the 11 patients the muscles and muscular fascia showed signs of impairment. In one patient (10 VZ) signs of signal intensity changes in the bone marrow were observed. A detailed description of the MRI results is provided in Table XII.

### **10.2.4. Telethermography results**

Only patients 1 AN and 2 EP underwent telethermography. The results are presented in Table XIII.

### **10.2.5. 20 MHz ultrasound results**

High frequency, 20 MHz sonography is a well established, non-invasive procedure, which renders an exact determination of the skin thickness and densitometry. B scan sonography with 20 MHz frequency allows the measurement of skin ulcers, atrophy and cutaneous radiation fibrosis up to 10 mm in depth [13, 14]. The different results of this examination performed on patients 5–11 are given in Table XIV.

### **10.2.6. X ray results**

Conventional local X ray examination was performed on two patients to exclude bone involvement, which was thought possible because of the depth of the ulcers. In patient 6 BZ the X ray examination of the right knee joint showed a normal aspect of the bone. The X ray of the top of the right arm for patient 10 VZ also showed a normal bone.

TABLE XI. DETAILED DESCRIPTION OF CUTANEOUS LESIONS

Patient	Results of cutaneous examination
1 AN	<p>Numerous skin lesions were disseminated on the fingers and were characterized by thinness of the skin, telangiectasias, aponeurotic retractions, fingers blocked in flexion and loss of the index nail. The most severe lesions were radionecrosis of the last phalanx of the right thumb, the pulp of the left thumb and the left middle finger. On the left thigh a 10 cm × 6 cm necrotic lesion was found, surrounded by fibrous tissue, profoundly modified by previous surgery. On the right thigh an 8 cm × 3 cm lesion with a superficial zone of necrosis was found. The front side of the lower part of the thorax presented a zone of fibrosis (6 cm × 4 cm) with depigmentation and telangiectasia.</p>
2 EP	<p>Three cutaneous–subcutaneous ‘punched-out’ round lesions of radionecrosis (3–4 cm in diameter) were found on the right musculus triceps brachii as well as on the middle part of the right side of the back and on the right musculus quadriceps femoris, just above the kneecap. Multiple, more or less bleached scars were visible on the whole body (total number 33).</p>
3 CG	<p>The principal lesion was on the anterolateral aspect of the middle third of the right thigh. Several necrectomies had already been performed without it being possible to cover the wound. An extensive loss of substance was found; the lesion was atonic, superinfected, with necrotic tissue on the surface and a fibrous muscle deep down. It was surrounded by a halo of inflammation but no lymphadenopathy was found. There was severe muscular wasting and a flexion deformity of the hip. The morphological and functional picture seemed poor. The lateral necrosis area was found to be 12 cm in diameter and the other one at the anterior surface was 2 cm × 3 cm. Additionally, retractions due to fibrosis were found in the thumb, index and middle finger of the right hand.</p>
4 TK	<p>Radiation injury was found on the outer aspect of the right thigh, situated at the junction of the middle third and the lower third of the thigh. This lesion presented as a necrosis of 5 cm diameter, sharply demarcated and punched out. The adjacent tissues and muscles of the whole thigh were oedematous and tense, indicating that major local/regional extension might occur, with a major inflammatory reaction.</p>
5 GL	<p>At the lower extremity of the left leg, above the lateral malleolus, a 3 cm × 2 cm ulcer was found. It was sharply contoured, with a reddish basis; it had a yellow coating and was surrounded by an erythema.</p>

TABLE XI. (cont.)

Patient	Results of cutaneous examination
5 GL (cont.)	<p>At the front of the left foot, a white macule was observed of 1.5 cm diameter, irregularly contoured and surrounded by a brown border of 5 mm. In the middle of the white spot several dark brown macules of some 2 mm diameter could be seen.</p> <p>At the right medial malleolus a 3 cm × 1.5 cm white discoloration with palpable induration was found.</p> <p>Onychodystrophy was noted on the left great toe.</p>
6 BZ	<p>A 7 cm × 2 cm ulcer was found on the right thigh above the knee joint. It was sharply but irregularly contoured with a yellow coating at the basis. An erythema surrounded the ulcer.</p> <p>At the lower extremity of the right leg a sharply contoured white macule of 1.2 cm × 5 cm was found.</p> <p>There was an ulcer of 1 cm × 0.8 cm covered by a central haemorrhagic scab in the lower extremity of the left leg.</p>
7 GG	<p>A 5 cm × 6 cm sharply contoured ulcer with a yellow coating was found on the right thigh. An erythema surrounded the ulcer.</p> <p>In the region of the breastbone, a sharply contoured red spot (macule) of 1.2 cm × 1.4 cm was observed.</p>
8 SO	<p>A sharply and irregularly contoured ulcer of 3.5 cm × 4 cm, with a yellow coating in the centre and surrounded by an erythema, was found on the left thigh.</p> <p>A sharply contoured white macule of 2 cm diameter was found on the right thigh.</p>
9 ID	<p>In the region of the lower thoracic vertebrae a 2.2 cm × 2 cm ulcer was found; it had a yellow coating and was surrounded by an erythema.</p> <p>Eleven white macules of up to 2.5 cm diameter were observed in the region of the chest, abdomen and back.</p> <p>A white macule of 2 cm × 2 cm with palpable induration was found on the left shoulder.</p> <p>In the right gluteal region an ulcer with a diameter of 0.5 cm was noted.</p>
10 VZ	<p>In the upper area of the right arm, a sharply contoured and deep ulcer of 1.5 cm × 1 cm was observed. It was surrounded by an erythema and induration.</p> <p>Additional diagnosis: pityriasis versicolor.</p>
11 SN	<p>An ulcer of 1.8 cm was found on the left thigh; it was sharply contoured, flushed, flat and surrounded by an erythema.</p>

TABLE XII. RESULTS OF MRI IMAGING

Patient	MRI results
1 AN	A necrotic aspect of the whole left quadriceps, especially the lower third, and of a limited part of the vastus lateralis of the right thigh was found (27 October 1997). The MRI of the hands was non-contributive, while the radiographies revealed a demineralization of both thumb phalanges.
2 EP	A large extension of a necrotic-like aspect at depth in the triceps, with signs of inflammation, was found, while the back lesion, despite its dramatic aspect, was clearly more superficial, sparing the parietal muscles and ribs. The right thigh lesion also appeared relatively superficial, consisting of skin thickening (5 mm thickness, 8 cm length) with moderate inflammation of the subcutaneous fat and a hyperintensity signal of the anterior part of the musculus vastus internus (24 October 1997).
3 CG	Zones of necrosis were noted in the external anterior aspect of the right thigh, associated with anomalous hypersignals from the cutaneous and subcutaneous tissues around the lesion, and in the muscular structures of the anterolateral compartment throughout its height. All the muscles, those of the posterior compartment included, were atrophied, more so than the clinical examination had indicated, because there was an increase in the adipose layer, especially on the posterior aspect. Examination showed a strong signal from these vessel walls (T2 fat saturated) with no signs of circulatory disturbance after injection of gadolinium. There was inguinal lymphadenopathy. The bone was not affected.
4 TK	There was evidence of a zone of necrosis and an anomalous signal in the cutaneous and subcutaneous tissues around the lesion, and in the muscular structures of the underlying anterolateral compartment.
5 GL	An ulcer at the lower part of the left leg reached the subcutis and muscular system, with oedema in the muscles. The bone had a normal appearance.
6 BZ	An ulcer at the distal part of the thigh to the side of the kneecap on the right knee joint was found (31 October 1997). The ulcer reached the subcutaneous tissue. Muscle and fascia did not seem directly affected, but lateral intrafascial muscular changes and a bone marrow oedema could be seen. No fluid was found in the knee.
7 GG	A deep ulcer on the right thigh, laterodistal and reaching the subcutaneous tissue, was found. A raised signal in the region of the quadriceps femoris and signs of fibrosis next to signs of oedema were observed. The bone had a normal appearance.

TABLE XII. (cont.)

Patient	MRI results
8 SO	There was an ulcer ventrodiscal on the left thigh with oedema in the region of the vastus intermedius, vastus medialis and vastus lateralis. There was thickening of the fasciae.
9 ID	There was an ulcer at the back parasagittal 1 cm in diameter. In the region of the subcutaneous tissue, there was an enhancement of the contrast medium in an area of 4 cm × 6 cm.
10 VZ	At the upper right part of the arm, a cutaneous ulcer was found over the triceps brachii muscle. Neither the muscle nor the fascia was affected. There was extensive infiltration of the subcutaneous tissue, and a local inflammatory reaction of the muscles and the bone marrow was found.
11 SN	On the left thigh a cutaneous–subcutaneous lesion was noted which did not reach the muscle fascia.

Local X ray examination was not performed on the other patients because there was no suspicion of bone involvement or because this possibility had been ruled out by MRI.

#### 10.2.7. Bacteriological results

Because in all patients ulcerations of different ages and extensions were observed which were partially covered with yellowish coatings that suggested secondary infection, bacteriological examinations were also conducted. On the basis of knowledge of the microorganisms involved, the most effective antibiotic treatment available was selected for each individual patient. The detailed results and the medications applied for each patient are given in Table XV.

#### 10.2.8. Treatment of the cutaneous syndrome

The 11 patients presented cutaneous lesions differing significantly with respect to extent and severity and thus required individualized diagnostic and therapeutic approaches.

Extensive diagnostics of the local cutaneous radiation damage were performed on all patients admitted to the Ulm hospital. It was also necessary to examine the involvement of the haematological system, reproductive system, internal organs and eyes. Therefore, a thorough set of examinations were performed on the seven patients

TABLE XIII. RESULTS OF TELETHERMOGRAPHY

Patient	Telethermography results
1 AN	23 October 1997: The thoracic lesion was slightly inflammatory. The left thigh exhibited three hypothermic zones ( $\Delta = -4^{\circ}\text{C}$ ) in a diffuse inflammatory zone. This was probably due to a rather extended necrosis.
2 EP	23 October 1997: The punched out lesions located at the tip of the scapula were moderately hypothermic, suggesting that the necrosis was limited in depth, and surrounded by extended inflammatory zones. Many hypothermic rings, enclosing a colder central zone, were disseminated on the inferior limbs. A large hypothermic inflammatory reaction was present in the front of the neck. Hypothermia was found in fingers D1/ D2 of the right hand.

TABLE XIV. RESULTS OF 20 MHZ ULTRASOUND EXAMINATION

Patient	20 MHz ultrasound results
5 GL	White discoloration at the right medial malleolus: skin thickness 2.3 mm, compared with 1.4 mm of the contralateral healthy ankle. Diagnosis: dermal fibrosis.
6 BZ	White discoloration at the lower part of the right leg: no indications of dermal fibrosis. No differences in skin thickness in comparison with the contralateral healthy skin.
7 GG	Right thigh: enlarged entry echo. Echo lucent skin and corium; bottom of ulcer cannot be visualized.
8 SO	White discoloration on the right thigh: no indications of dermal fibrosis. Ulcer on the left thigh: ulcer reaches the subcutaneous tissue.
9 ID	No indications of cutaneous fibrosis in the regions of discoloration on the right scapula, the chest and the back.
10 VZ	Ulcer at the top of the right arm 3 mm deep. At the border, increase of skin thickness due to radiation induced fibrosis.
11 SN	Left thigh: in the region of the ulcer, decrease in the density of the corium. No changes in the subcutaneous tissue. Ulcer localized in the corium only.

TABLE XV. RESULTS OF BACTERIOLOGICAL INVESTIGATIONS

Patient	Localization	Result	Sensitive to
1 AN	Lesions on the fingers, thighs and thorax	<i>Pseudomonas aeruginosa</i> (Type 5)	Imipenem and ciprofloxacin
2 EP	Lesions on the arm and right thigh	<i>Pseudomonas aeruginosa</i> (Type 2)	Imipenem and ciprofloxacin
3 CG	Lesion on the right thigh	<i>Pseudomonas aeruginosa</i> (Type 3), <i>Enterobacter cloacae</i>	Imipenem and ciprofloxacin
4 TK	Lesion on the right thigh	<i>Pseudomonas aeruginosa</i> (Type 2), <i>Staphylococcus methi</i> S	Imipenem and ciprofloxacin
5 GL	Ulcer on bottom of left leg	<i>Pseudomonas aeruginosa</i>	Tazobactam and imipenem
6 BZ	Ulcer on the right thigh  Control on 4 December 1997	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Enterobacter cloacae</i> , <i>Corynebacterium</i> species <i>Pseudomonas aeruginosa</i> , <i>Corynebacterium</i> species	Tazobactam and imipenem, less sensitive to meropenem and ciprofloxacin Tazobactam, imipenem, netilmicin, amikacin
7 GG	Ulcer on the right thigh  Control on 1 December 1997	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Enterococci</i> <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Corynebacterium</i> species	Tazobactam, imipenem, netilmicin, amikacin Tazobactam, imipenem, netilmicin, amikacin
8 SO	Ulcer on the left thigh	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	Imipenem
9 ID	Ulcer on the back	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	Imipenem, less sensitive to ofloxacin
10 VZ	Ulcer on the upper part of the right arm	<i>Pseudomonas aeruginosa</i>	Ofloxacin
11 SN	Ulcer on the left thigh	<i>Staphylococcus aureus</i>	Cefuroxime

TABLE XVI. DESCRIPTION OF LOCAL TREATMENT

Patient	Local treatment
1 AN	Cleaning and aseptic agents (chlorhexidine or polyvidone iodine) on the lesions
2 EP	Cleaning and aseptic agents (chlorhexidine or polyvidone iodine) on the lesions
3 CG	Administration of silver nitrate to the right thigh; 5 November 1997: application of artificial dermis (Integra)
4 TK	5 November 1997: application of artificial dermis (Integra)
5 GL	Epigard, hydrocolloids
6 BZ	Local thrombokinin therapy, enzymatic fibrolytic cream for the ulcers, betamethasone dipropionate for the surrounding areas
7 GG	Local thrombokinin therapy
8 SO	Enzymatic fibrolytic cream for the ulcers, betamethasone dipropionate for the surrounding areas
9 ID	Enzymatic fibrolytic cream for the ulcers, betamethasone dipropionate for the surrounding areas
10 VZ	Ulcer: alginates and hydrocolloids (Cutinova foam)
11 SN	Enzymatic fibrolytic cream for the ulcers, zinc paste for the surrounding areas

treated at Ulm. On the basis of these results, both conservative treatment and surgery were planned and conducted.

The same approach was taken in France. Tables XVI–XVIII highlight the therapeutic recommendations and surgical procedures for each patient.

#### 10.2.9. Outcome of the treatment

After successful treatment, patients 5 GL, 7 GG, 8 SO, 9 ID, 10 VZ and 11 SN were able to return to Georgia before the end of 1997. However, owing to severe radiation induced lesions, extensive plastic surgery or secondary complications, the following patients were treated for a longer period in the specialized hospitals.



TABLE XVII. DESCRIPTION OF SYSTEMIC TREATMENT

Patient	Medication (oral, intravenous or subcutaneous)
1 AN	Perioperative antibiotic prophylaxis; analgesics; tranquilizers
2 EP	Perioperative antibiotic prophylaxis; morphine on request
3 CG	Perioperative antibiotic prophylaxis; morphine and anxiolytics in the beginning; low dose of heparin after surgery
4 TK	Perioperative antibiotic prophylaxis; morphine in the beginning
5 GL	Gamma interferon (Imukin): $2 \times 100$ mg subcutaneous per week; antibiotic therapy after surgery; low dose of heparin after surgery
6 BZ	Treatment of dermal and muscular vasculitis with corticosteroids (60 mg methylprednisolone orally daily); low dose of heparin after surgery; post-operative antibiotic therapy; low dose of heparin after first and second surgeries
7 GG	Low dose of heparin after surgery; perioperative antibiotic prophylaxis
8 SO	Low dose of heparin after surgery; treatment of dermal and muscular vasculitis with corticosteroids (60 mg methylprednisolone orally daily); perioperative antibiotic prophylaxis
9 ID	Antibiotic therapy before and after surgery
10 VZ	Antibiotic therapy after surgery (initially intravenous, after three days oral); treatment of dermal and muscular vasculitis with corticosteroids (60 mg methylprednisolone orally daily)
11 SN	Low dose of heparin after surgery; perioperative antibiotic prophylaxis

Patient 6 BZ stayed longer in the hospital owing to radiation induced synovitis of the right knee joint and associated complications. Complete joint synovectomy and multiple extensive plastic operations were necessary. Hyperbaric oxygenation was used to support wound healing and to prevent joint infection. On the patient's discharge from the hospital on 6 June 1998, functional recuperation was complete.

Patient 2 EP was sent home in January 1998 after successful treatment and no sequelae. Figures 18–21 show the progressive healing of his injuries.

Patient 4 TK was completely healed but remained for rehabilitation as an outpatient in Paris.

TABLE XVIII. DESCRIPTION OF SURGICAL PROCEDURES

Patient	Surgery
1 AN	<p>12 November 1997: excision of the necrotic tissue of the left thigh and application of a cutaneous expander, inguinal flap to reconstruct the right thumb.</p> <p>3 December 1997: curettage and inflation of the expander; release of inguinal flap for the left thumb and middle finger.</p> <p>23 December 1997: release of the left flap.</p> <p>16 January 1998: skin graft on the left thigh.</p>
2 EP	<p>29 October 1997: extensive removal of the necrotic part of the musculus triceps brachii; skin grafting and removal of the necrotic tissues down to the aponeurosis of the musculus quadriceps femoris, covering with flap.</p> <p>19 November 1997: extensive removal of the necrotic part of the dorsal lesion.</p> <p>11 December 1997: reintervention due to suture rupturing because of untimely muscular efforts.</p>
3 CG	<p>28 October 1997: skin and muscle excision on the right thigh; xenograft.</p> <p>21 November 1997: amplified skin autograft from the left thigh.</p> <p>20 January 1998: amplified skin autograft from the right thigh.</p>
4 TK	<p>28 October 1997: skin and muscle excision on the right thigh; xenograft.</p> <p>24 November 1997: non-amplified skin autograft from the left thigh.</p>
5 GL	<p>11 November 1997: debridement of the ulcer of the left lateral malleolus.</p> <p>29 November 1997: mesh graft from the right thigh.</p>
6 BZ	<p>5 November 1997: debridement of the ulcer on the right thigh under general anaesthesia, and excision of the ulcer on the lower part of the left leg.</p> <p>12 November 1997: second debridement of the ulcer on the right thigh under general anaesthesia.</p> <p>21 November 1997: third debridement under short anaesthesia.</p> <p>Further therapy in the orthopaedic department with synovectomy and muscle plastic surgery (translocation of musculus vastus lateralis).</p> <p>28 April 1998: final wound closure by a muscular rotation flap (musculus gracilis), with split skin graft under general anaesthesia.</p>
7 GG	<p>10 November 1997: excision of the ulcer on the right thigh under general anaesthesia.</p> <p>3 December 1997: covering of wound with mesh graft from the right thigh.</p> <p>No complications after surgery.</p>

TABLE XVIII. (cont.)

Patient	Surgery
8 SO	10 November 1997: excision of the ulcer on the left thigh under general anaesthesia. 12 November 1997: covering of wound with a rotation flap.
9 ID	5 November 1997: excision of the ulcer on the back and application of a rotation flap under local anaesthesia. 6 November 1997: excision of the gluteal ulcer and the keratosis on the forehead under local anaesthesia.
10 VZ	4 November 1997: fusiform excision of the ulcer on the top of the right arm under local anaesthesia. No complications after surgery.
11 SN	4 November 1997: excision of the ulcer on the left thigh under local anaesthesia and muscle plastic surgery.



FIG. 18. Patient 2 EP: legs, initial state, 23 October 1997.



FIG. 19. Patient 2 EP: right leg after surgery, 1 December 1997.



*FIG. 20. Patient 2 EP: back and right arm, initial state, 23 October 1997.*



*FIG. 21. Patient 2 EP: right arm after surgery, 10 December 1997.*

Patients 1 AN and 3 CG were still under treatment in 1998 at the time of writing.

The medical status of the patients as of August 1999 is reported in Annex I.

### 10.3. HAEMATOLOGICAL DATA

On admission to the hospitals in Paris and Ulm, a complete haematological assessment was made for each patient. Table XIX shows the average blood values of the patients treated in Paris and Ulm in comparison with the normal range.

TABLE XIX. PERIPHERAL BLOOD COUNT FOR PATIENTS TREATED IN FRANCE AND GERMANY (MEDIAN AND NORMAL VALUES)

	Patients 1-4, treated in Paris		Patients 5-11, treated in Ulm	
	Median (range)	Normal range	Median (range)	Normal range
Leucocytes ( $10^9/L$ )	5.2 (4.2-7.1)	4-10	5.9 (4.2-8.0)	4.8-10.0
Neutrophils ( $10^9/L$ )	3.4 (2.4-5.2)	2-7.5	3.8 (2.7-6.1)	2.0-6.8
Eosinophils ( $10^9/L$ )	0.1 (0.005-0.2)	0-0.7	0.2 (0.1-0.3)	0-0.2
Monocytes ( $10^9/L$ )	0.4 (0.3-0.5)	0.2-1	0.3 (0.2-0.4)	0.1-0.8
Lymphocytes ( $10^9/L$ )	1.4 (1.0-1.9)	1-4	1.5 (1.0-2.1)	1.0-4.2
Erythrocytes ( $10^{12}/L$ )	4.3 (4.2-4.58)	4.5-6.1	4.95 (4.41-6.03)	4.2-5.4
Haemoglobin (g/dL)	13.1 (12.3-13.8)	13-18	15.1 (13.5-18.0)	12.0-18.0
Haematocrit (%)	39.4 (36-42.3)	40-53	44.4 (39.3-52.2)	37-47
Mean corpuscular volume ( $10^{-15} L$ )	90.8 (84.4-99)	82-95	89.5 (79.9-94.8)	82-97
Platelets ( $10^9/L$ )	252 (172-297)	150-400	235 (163-289)	150-450

Table XX shows the blood cell counts in the peripheral blood for each patient. These findings indicate that at the time of admission to the specialized hospitals, the haematopoietic systems showed an essentially normal function.

Table XXI illustrates the results of the cytological assessment of the bone marrow aspirate smears for patients 3 CG, 4 TK, 5 GL, 6 BZ, 7 GG, 8 SO, 9 ID, 10 VZ and 11 SN. For patients 3 CG and 4 TK, the bone marrow aspiration was performed during surgery, so that the results from the right and the left side of the spina iliaca anterior were available. For patients 1 AN and 2 EP, only the bone marrow histology was available. In summary, these findings indicated an adequate cell production and maturation of all cell lineages. The erythropoiesis was qualitatively essentially normal, as was the myelocytogenesis. There was no evidence of gross abnormalities. However, a thorough examination of the cytological appearance of precursor cells revealed evidence of dyshaematopoietic cell proliferation and maturation activities characteristic of a state of haematopoietic recovery. This is expressed in mitotically connected abnormalities (nuclear/cytoplasm maturation dissociation, micronuclei, cytoplasmic fusion, etc.). This type of abnormality has been seen in bone marrow in the state of regeneration after exposure to ionizing radiation. This is in agreement with the histological examination of bone marrow biopsy material confirming active haematopoiesis but showing an unequal distribution of haematopoietic regeneration (Figs 22-24).

Thus the blood and bone marrow findings of all patients examined indicated a sufficient haematopoietic function at the time of examination but also confirmed the view that their haematopoietic systems were still in the process of recovery. The basic immunological status for patients 3-11 (Table XXII) was essentially normal and no significant alterations could be detected.

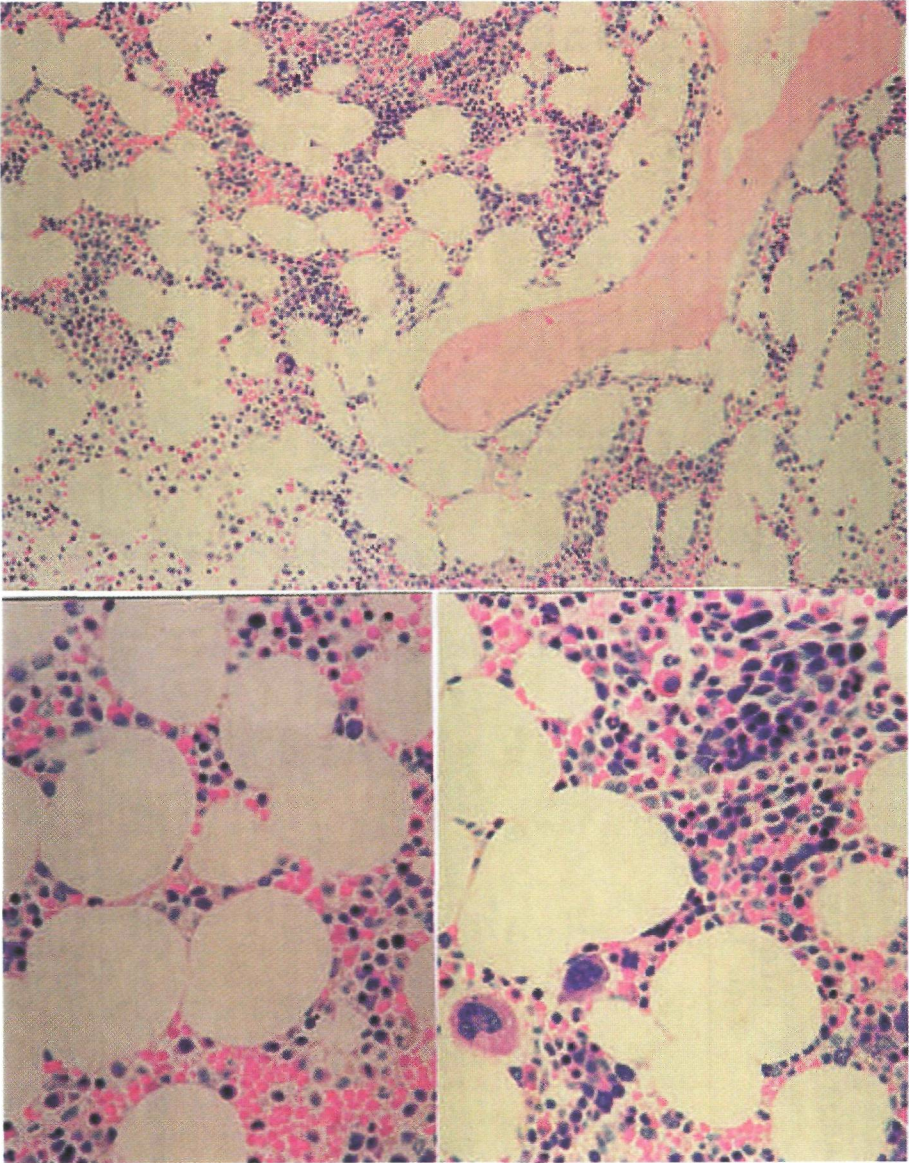
TABLE XX. PERIPHERAL BLOOD COUNT FOR PATIENTS AT TIME OF FIRST EXAMINATION AFTER ADMISSION TO THE HOSPITAL

	1 AN	2 EP	3 CG	4 TK	5 GL	6 BZ	7 GG	8 SO	9 ID	10 VZ	11 SN
Leucocytes ( $10^9/L$ )	4.3	5.2	4.2	7.1	5.9	4.6	6.6	5.9	4.2	6.6	8.0
Neutrophils ( $10^9/L$ )	2.4	2.7	3.2	5.2	3.8	3.1	4.6	3.9	2.7	3.8	6.1
Eosinophils ( $10^9/L$ )	0.1	0.2	0.05	0.1	0.1	0.1	0.1	0.2	0.3	0.3	0.2
Monocytes ( $10^9/L$ )	0.3	0.4	0.5	0.5	0.3	0.2	0.3	0.3	0.2	0.4	0.3
Lymphocytes ( $10^9/L$ )	1.5	1.9	1.0	1.3	1.7	1.2	1.5	1.5	1.0	2.1	1.4
Erythrocytes ( $10^{12}/L$ )	4.58	4.26	4.2	4.32	6.03	4.41	4.95	4.63	4.96	5.50	4.69
Haemoglobin (g/dL)	13.8	13.7	12.3	12.7	16.0	13.5	15.1	15.1	15.5	18.0	14.1
Haematocrit (%)	41	42.3	36	38.4	48	39	44	42	45	52	42
Mean corpuscular volume ( $10^{-15}$ L)	89	99	84.4	88.9	79.9	88.9	89.5	90.0	89.9	94.8	89.2
Platelets ( $10^9/L$ )	172	297	263	277	235	196	283	261	163	224	289

TABLE XXI. BONE MARROW DIFFERENTIAL (% OF 500 CELLS COUNTED)

	3 CG <sup>a</sup>		4 TK <sup>a</sup>		5 GL	6 BZ	7 GG	8 SO	9 ID	10 VZ	11 SN
	Right	Left	Right	Left							
Erythroblasts	23	18	14	21.5	27.6	25.2	22	19	39.2	30.2	31.6
Mitotic figures											
within erythropoiesis	—	—	—	—	1	1.2	1.2	1	0.4	1.8	2.6
Myeloblasts	3.5	2.5	2	2	1.6	1.8	2.8	2.2	1.6	3.2	2.8
Promyelocytes	2	2	2	0.5	4.4	8.4	4.4	3.4	5.4	4.6	5.2
Myelocytes	10	10	18	12.5	8.8	15.4	20.4	20.6	18.8	17	26.2
Metamyelocytes, band and segmented	53.5	59.5	52	48	38.6	25	36.6	31.4	16.7	24	19.2
Mitotic figures											
within granulopoiesis	—	—	—	—	1.4	—	0.2	0.4	0.2	0.4	—
Granulopoiesis	69	74.5	74	63	56.8	52.2	65.2	62	44.4	51.4	55.2
Lymphocytes	6	4	11	12.5	8.4	12	7	7.8	7.5	4.8	2.8
Eosinophils/basophils	—	—	—	—	5.2	3.8	2.2	6.4	3.8	4.2	4.8
Monocytes/macrophages	1	3	0.5	2	1.8	4.4	2.2	4.6	2.8	5.8	3.6
Others (plasma cells, megakaryocytes, mast cells, etc.)	1	0.5	0.5	1	2.4	4	2.2	4.2	4.4	4	3.8

<sup>a</sup> Punction site: spina iliaca right and left site.

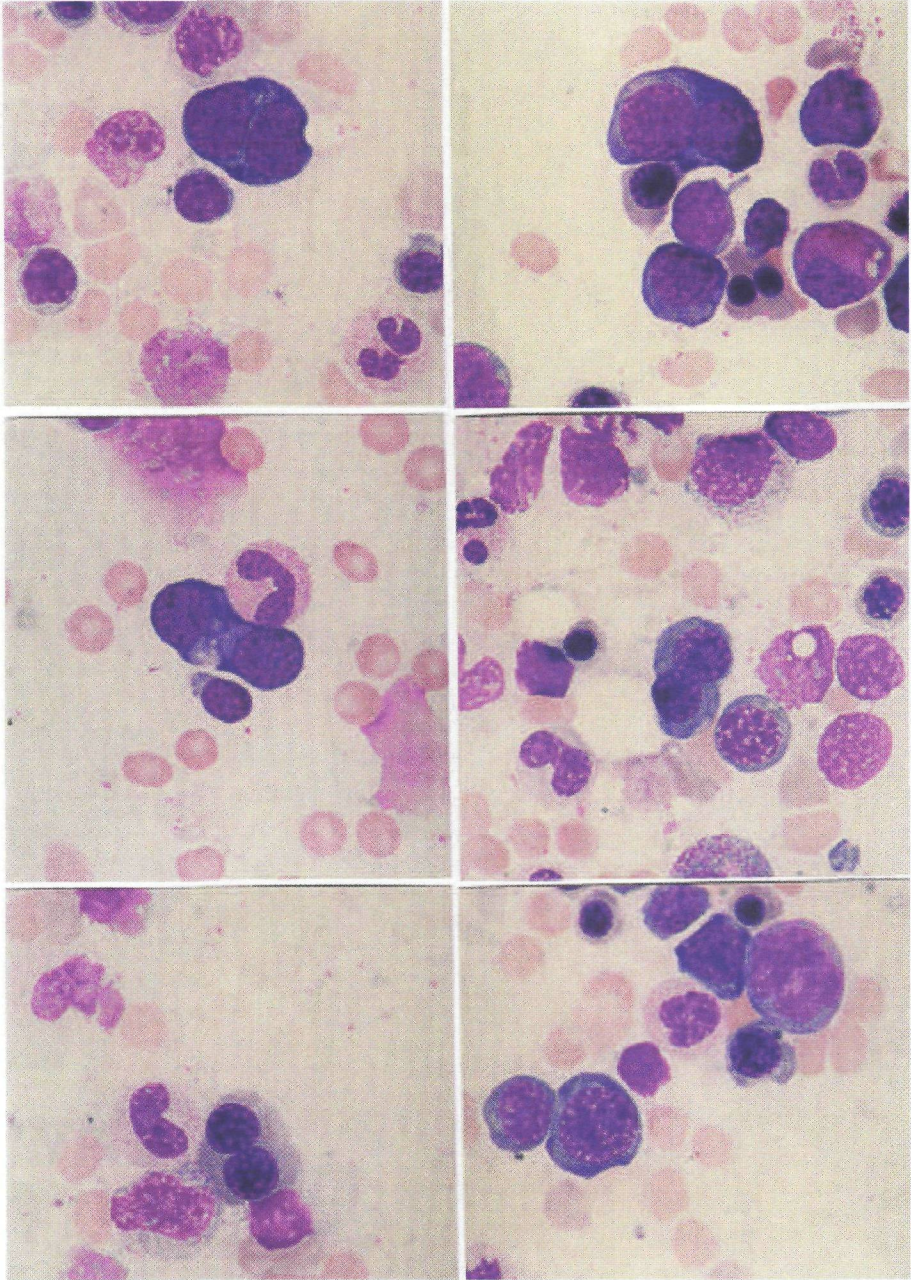


*FIG. 22. Bone marrow trephine biopsy of patient 6 BZ.*

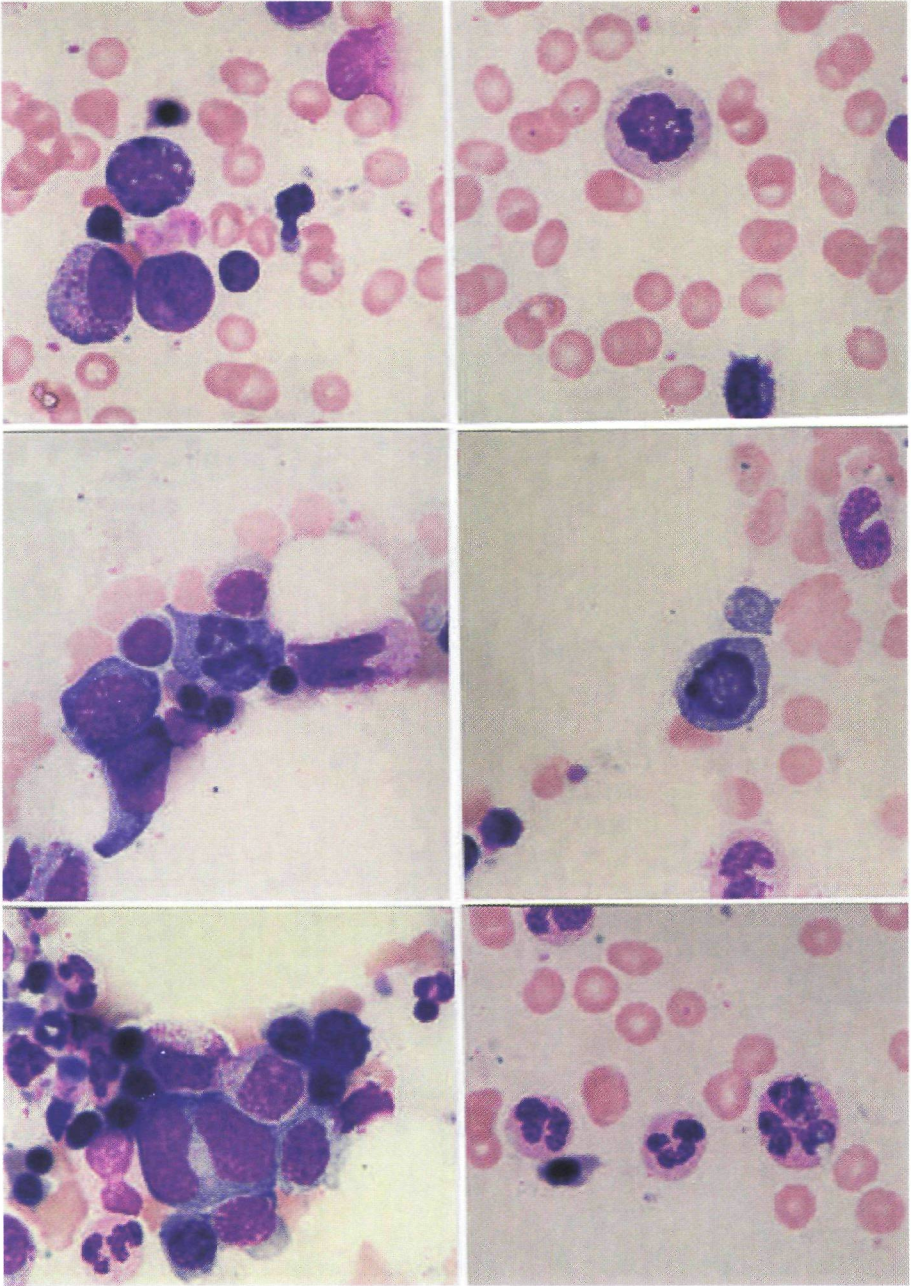
#### 10.4. REPRODUCTIVE SYSTEM

The results of the spermograms with azoospermia in seven cases, the laboratory measurements with increased levels of follicle stimulating hormone (FSH) in seven patients and the results of bone marrow examinations were in conformity with





*FIG. 23. Mitotically connected abnormalities in bone marrow smears of patients 7 GG and 6 BZ. The slides show different stages of maturity of erythropoietic precursor cells indicating incomplete mitoses resulting in premature cell death. The lower left hand slide shows a polychromatic erythroblast with a cariomere and a binucleated early myelocytic precursor cell.*



*FIG. 24. The upper four slides show abnormal mitotic figures with chromosomal clumping resulting in premature cell death. The lower slides represent myelocytic cells with mitotically connected abnormalities. The right lower slide represents a 'giant neutrophil' resulting from the maturation of binucleated precursor cells.*

TABLE XXII. IMMUNOPHENOTYPING OF PERIPHERAL BLOOD LYMPHOCYTES, ABSOLUTE COUNT (cells/ $\mu$ L)

	3 CG	4 TK	5 GL	6 BZ	7 GG	8 SO	9 ID	10 VZ	11 SN
T lymphocytes (CD3+)	924	1278	1229	966	942	1128	655	1528	1055
T helper cells (CD3+ CD4+)	401	520	772	476	617	613	364	804	538
T suppressor cells (CD3+ CD8+)	284	451	358	398	253	338	262	560	384
B lymphocytes (CD19+)	3.55% <sup>a</sup>	6.48% <sup>a</sup>	232	85	126	242	150	141	207
NK cells (CD16+ CD56+)	12.3% <sup>a</sup>	13.7% <sup>a</sup>	104	103	165	78	100	186	65

<sup>a</sup> Not available in absolute numbers.

TABLE XXIII. RESULTS OF EXAMINATIONS OF THE REPRODUCTIVE SYSTEM

Patient	Spermiogram	LH <sup>a</sup> (mU/mL)	FSH <sup>a</sup> (mU/mL)	Prolactin (mU/L)	Testosterone	Cortisol	ACTH <sup>a</sup>	STH <sup>a</sup>
1 AN	—	—	13.9 $\uparrow$	Normal	Normal	Normal	Normal	Normal
2 EP	Azoospermia	—	10.2 $\uparrow$	—	Normal	Normal	—	—
3 CG	Azoospermia	7.9	15.6 $\uparrow$	655 $\uparrow$	Normal	—	—	—
4 TK	Azoospermia	—	—	—	Normal	—	—	—
5 GL	Oligozoospermia	6.95	13.53 $\uparrow$	Normal	Normal	Normal	Normal	Normal
6 BZ	Azoospermia	7.81	12.78 $\uparrow$	Normal	Normal	Normal	Normal	Normal
7 GG	Azoospermia	6.75	16.25 $\uparrow$	Normal	Normal	Normal	Normal	Normal
8 SO	Azoospermia	4.04	6.75	Normal	Normal	Normal	Normal	Normal
9 ID	Azoospermia	9.27	24.07 $\uparrow$	Normal	Normal	Normal	Normal	Normal
10 VZ	Polyzoospermia	3.84	3.16	Normal	Normal	Normal	Normal	Normal
11 SN	Normospermia	5.08	3.91	Normal	Normal	Normal	Normal	Normal

<sup>a</sup> LH: luteinizing hormone; FSH: follicle stimulating hormone; ACTH: adrenocorticotrophic hormone; STH: somatotrophic hormone. Arrows indicate values above normal.

the assumption that in addition to severe local exposure, whole body radiation exposure had also taken place (Table XXIII).

In patient 1 AN a spermatogram could not be performed. The increased FSH suggested irreversible testicular damage. On the other hand, the low FSH in patient 8 SO may have accounted for the reversibility of the patient's azoospermia.

The oligozoospermia observed in patient 5 GL was probably additionally influenced by bilateral maldescensus testis and concomitant infection of the sperm ducts with *Pseudomonas aeruginosa*.

## 10.5. OTHER ORGANS AND ORGAN SYSTEMS

Albeit not directly affected, other organs and organ systems were examined mainly to detect abnormalities and to provide a complete view of the status of the patients, keeping in mind that further examinations would be necessary to evaluate the development of late effects.

### 10.5.1. Cardiovascular system

For the examination of the cardiovascular system, chest X ray, electrocardiogram and heart ultrasound examinations were conducted on all patients. None of these examinations brought any abnormalities to light, except for minimal mitral incompetence without clinical consequences detected with the aid of two heart ultrasound examinations in patient 6 BZ.

### 10.5.2. Liver

For the examination of the liver, an abdominal ultrasound examination was performed on patients 5–11. These showed no pathological abnormalities.

Similarly, biochemical investigations failed to show abnormalities in the patients. Only serological examinations were able to detect the status after hepatitis A in patients 5 GL, 6 BZ, 7 GG and 8 SO. The status after hepatitis B was detected in patients 3 CG, 4 TK, 5 GL, 8 SO and 9 ID, and hepatitis C was detected in patient 1 AN.

### 10.5.3. Respiratory system

For the examination of the respiratory system, chest X rays and pulmonary function tests were undertaken. The chest X rays showed no evidence of pneumonitis or pulmonary fibrosis in any patient. Likewise, the general pulmonary function test produced no pathological findings.

### 10.5.4. Thyroid

Owing to a scar in front of the thyroid gland in patient 2 EP, a control was made with a scintiscanner. The gland was normal except for a discrete heterogeneity of the right upper lobe.

Ultrasound examinations of the thyroid gland were performed on patients 2 and 5–11 along with laboratory hormone tests such as FT<sub>4</sub>, FT<sub>3</sub> and thyroid stimulating hormone (TSH). All the laboratory tests were found to be normal. In the ultrasound examination, a goiter I° and a goiter II° were found in patients 10 VZ and 11 SN, respectively.

### 10.5.5. Additional examinations by specialists

Additional examinations carried out by specialists such as an ophthalmologist, an otorhinolaryngologist, a dentist and a neurologist were performed on patients 5–11. Only an acute pharyngitis was observed in patient 9 ID and caries were detected in patients 6 BZ, 8 SO and 10 VZ.

An ophthalmological examination was performed on patients 2 EP, 3 CG and 4 TK and did not result in any pathological findings.

In patient 8 SO, an abnormal electroencephalogram (EEG) with slow waves was found. In addition, the laboratory parameter S 100 was found to be high both initially and in the controls. The MRI conducted in order to rule out any brain abnormalities showed no pathological results. Until now these findings have not been satisfactorily interpreted.

### 10.6. SPECIAL CASE HISTORIES

Owing to their special features, the medical treatments of four patients — 1 AN, 3 CG, 6 BZ and 10 VZ — are recounted chronologically in more detail below.

#### **Patient 1 AN, treated at the Curie Institute, Paris**

Patient 1 AN, 20 years old, was in poor general condition, was tired and suffered from pain. His weight was 61 kg and his height 1.85 m (he reported a weight loss of 15 kg within a few months). He was apyrexial, with a blood pressure of 100/60 mmHg.

Numerous skin lesions with different stages of cutaneous syndrome were disseminated on his fingers, thighs and thorax. The lesions of the hands were characterized by thinness of the skin, telangiectasias, aponeurotic retraction, fingers blocked in flexion and loss of index nails. The most severe lesions were necrosis of the last phalanx of the right thumb, the pulp of the left thumb and the left middle finger. All these lesions were extremely painful.

The lesion of the anterior left thigh, significantly modified by several previous surgical procedures, appeared rather necrotic (10 cm × 6 cm) and was surrounded by indurated tissue. On the external part of the right thigh there was a superficial zone of necrosis (8 cm × 3 cm) which was less painful.

The lesions were infected with *Pseudomonas aeruginosa* P<sub>5</sub>. The front side of the lower part of the thorax presented a moderately painful zone of induration (6 cm × 4 cm) with depigmentation and telangiectasia adhering to the chest wall.

On 23 October 1997, the patient underwent a telethermographic examination which showed a hypothermic thoracic lesion, probably inflammatory. The left thigh

exhibited three hypothermic zones ( $d = -4^{\circ}\text{C}$ ) in a diffuse inflammatory area, indicating a rather extended necrosis.

On 27 October 1997, MRI showed a necrotic aspect of the whole left quadriceps, especially the lower third, and a limited part of the right vastus lateralis. X ray examination revealed a demineralization of both thumb phalanges which had not been detected by MRI.

From 22 October 1997 to 10 November 1997, in parallel with antiseptic cleansing of the lesions, the patient was treated with analgesics, antibiotics and tranquillizers.

On 10 November 1997, the patient was transferred to the Boucicaut hospital for specialized hand surgery, performed in three steps:

- (i) On 12 November 1997: surgical excision of the necrotic tissues of the anterior part of the left thigh and application of a  $500\text{ cm}^3$  hemicylindrical cutaneous expander, placed on the inner side of the thigh, followed by a pediculated inguinal flap to reconstruct the right thumb.
- (ii) On 3 December 1997: release of the inguinal flap (right thumb); placement of the left pediculated inguinal flap on the left thumb and middle finger; debridement of the left thigh and inflation of the expander.
- (iii) On 23 December 1997: release of the flap on the left thumb and middle finger.

On 26 December 1997, the patient was transferred back to the Curie Institute. Additionally, on 16 January 1998, the left thigh was covered with a skin graft.

The clinical check-up performed on 2 February 1998 showed that the general condition of the patient had improved and that he had gained 10 kg in weight. The epidermization of the lesion on the left thigh was not yet complete. However, the prognosis was anticipated to be favourable. The cutaneous expander was maintained for a secondary flap to be placed after a few months. Secondary reconstruction was planned for the left thumb and middle finger.

The patient underwent a functional rehabilitation programme at the Curie Institute.

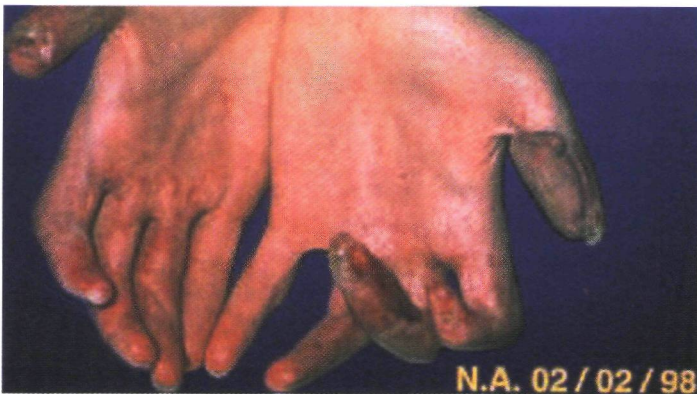
At the clinical check-up on 9 April 1998, the patient was found to be in good general condition. Epidermization of the lesion on the left thigh was complete. However, the inflation of the expander was at that time considered to be insufficient to allow a skin flap to cover the lesion on the anterior left thigh. The therapeutic result for the right thumb was considered to be good. Further reconstruction of the left thumb and middle finger was planned (Figs 25–27).



*FIG. 25. Patient 1 AN: right thumb, initial state, 23 October 1997.*



*FIG. 26. Patient 1 AN: left hand, initial state, 23 October 1997.*



*FIG. 27. Patient 1 AN: hands after surgery, 2 February 1998.*

### Patient 3 CG, treated at the Percy Hospital of the Armed Forces, Paris

Patient 3 CG, aged 21 and weighing 68 kg, was in good general condition. He had a blood pressure of 150/80 and was afebrile.

The location of this patient's principal lesion was on the anterolateral aspect of the middle third of the right thigh. Before admission to the hospital, several necrectomies had already been performed. Nevertheless, the wound was open. On 22 October 1997 the lesion presented as an extensive substance defect. Without signs of regeneration the wound was superinfected, with necrotic tissue on the surface and fibrotic muscle deep down. The lesion was surrounded by a halo of inflammation but no lymphadenopathy of the inguinal region was found. There was severe muscular wasting and an antalgic flexure position of the hip.

The results of the MRI for this patient detailed in Table XII show zones of necrosis involving cutaneous and subcutaneous tissue as well as atrophic muscles.

On 28 October 1997, surgery was carried out under antibiotic prophylaxis (imipenem–cilastatin and ciprofloxacin) adjusted to the multiply resistant strains found on the lesions (*Pseudomonas aeruginosa* P<sub>3</sub>, *Enterobacter cloacae*). An initial exploration showed that the local aspect was less threatening than MRI had previously indicated. The conservative alternative of covering the wound with a graft after wide necrectomy was chosen. The excision was wide, extending to the healthy cutaneous zone. The whole of the musculus rectus anterior and a part of the musculus vastus lateralis were resected. The surgically excised tissue weighed 280 g. The surgical scar of 750 cm<sup>2</sup> was covered by a porcine skin xenograft. This allowed the evolution of the granulation bud to be followed. During surgery, samples were taken for examination: bone marrow biopsies, myelograms, skin appendage samples for ESR examination and samples of the surgical area for histological analysis.

On 5 November 1997, ablation of the xenograft showed the granulation bud was of good quality. In a second stage, the bud was covered with a synthetic dermal matrix (Integra). This matrix was composed of a double layer with a sheet of collagen, treated to increase the colonization by cells from the underlying viable tissues. The upper surface was made of a silicone layer. This silicone layer was completely transparent and allowed survey of the underlying foundation.

On 21 November 1997, the silicone sheet was taken off, showing a complete integration of the artificial matrix. Nonetheless, a new lesion appeared on the antero-medial aspect of the thigh at the junction of the upper and the middle third. This lesion, some 4 cm in diameter, was brown, poorly demarcated and suspected of being necrotic. This was confirmed by biopsy. A thin skin graft of 0.2 mm was taken from the left thigh, meshed twofold and then grafted on the integrated dermal base. The initial evolution was favourable, with complete epidermization of the grafted wound. However, the lesion progressively developed into a typical eschar and had to be excised during dressing.



Subsequently, a secondary lesion developed on the middle third of the right thigh. The area was around 50 cm<sup>2</sup>, had an irregular shape and showed local signs of superinfection. At that time, local irrigations with silver nitrate solution (0.5%) were begun.

On 20 January 1998, the residual lesion was cleaned, and a new skin autograft was performed. In spite of antibiotic coverage with imipenem, ciprofloxacin and local cleansing with silver nitrate, a colonization of the wound with *Pseudomonas aeruginosa* persisted, showing progression to sustained infection. The patient was afebrile during the whole period (with the exception of a febrile peak of 39°C immediately after surgery on 21 November 1997). Blood and catheter samples remained sterile in culture. The leucocyte count, around  $11 \times 10^9/L$  on arrival, stabilized at around  $5 \times 10^9/L$  from 2 November 1997.

On admission and after surgery, high doses of morphine sulphate (>100 mg/d) were needed to relieve pain. The severity of the pain following the second intervention required additional administration of clonidine. Treatment with analgesics was reduced very quickly after each surgical procedure. In addition, the patient complained of moderate but persistent pelvic and genital pain, without any functional impairment or abnormalities on clinical examination.

Rehabilitation was begun after mid-November in order to preserve the integration phases of the dermis. An MRI carried out on 3 December 1997 showed a persisting hypersignal at the level of the neurovascular bundle and the muscles of the anterolateral compartment extending over the long head of the musculus biceps and the musculus semitendinosus in the posterior compartment of the thigh. This was associated with severe atrophy of all of the musculature of the posterior compartment.



FIG. 28. Patient 3 CG: right thigh, necrosis after cleaning, 27 October 1997.

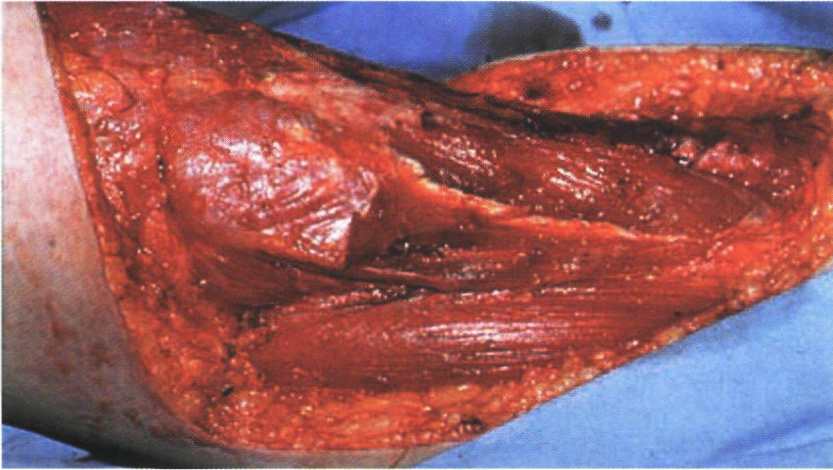


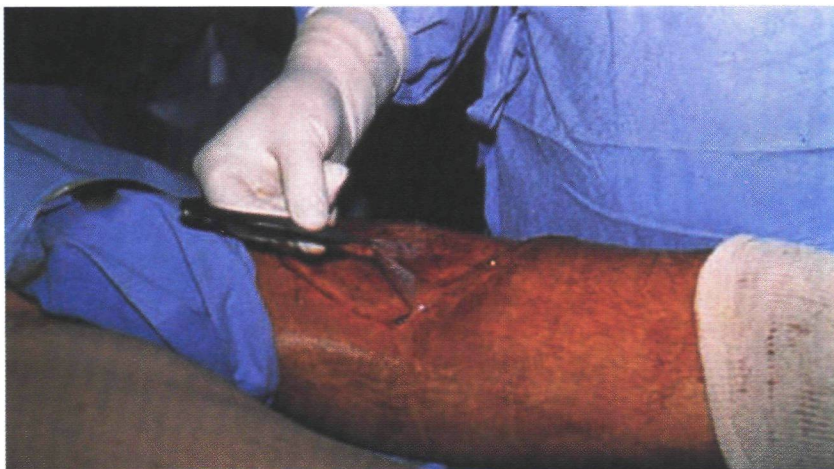
FIG. 29. Patient 3 CG: right thigh, skin and muscle excision, 28 October 1997.



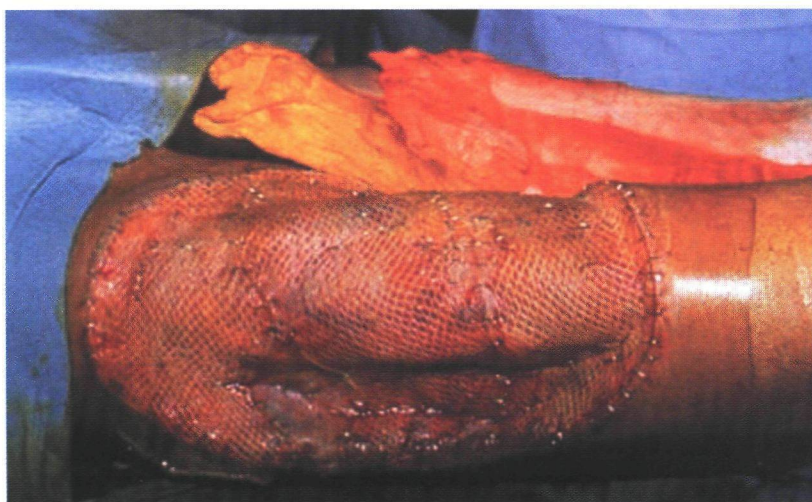
FIG. 30. Patient 3 CG: right thigh, Integra covering, 5 November 1997.

On 5 June 1998, five months after the first surgical procedure, the initial wound was found to be fully healed. Functionally, the motility of the right leg was completely restored.

However, necrosis appeared and progressed at the medial and lateral side of the distal phalanges of the right middle finger in an area which had been noted to be painful since the end of February 1998. A surgical excision was performed, followed by grafting on 17 June 1998. Figures 28–33 show the successive phases of the artificial skin graft on patient 3 CG.



*FIG. 31. Patient 3 CG: right thigh, Integra 'peeling', 21 November 1997.*



*FIG. 32. Patient 3 CG: right thigh, amplified skin autograft, 21 November 1997.*

**Patient 6 BZ, treated in the Dermatology Department of the University of Ulm  
at the Federal Armed Forces Hospital, Ulm**

The patient was admitted to the Department of Dermatology on 29 October 1997. He presented with a sharply demarcated, deep ulcer on the outer side of the right thigh above the knee. The ulcer was of a size of 70 mm × 20 mm and was coated with yellow fibrin clots. The surrounding area was erythematous. In addition, the

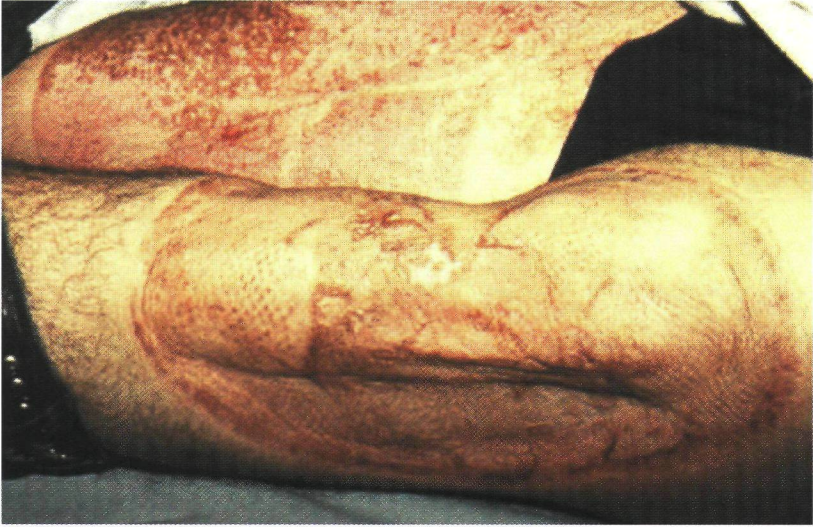


FIG. 33. Patient 3 CG: right thigh, July 1998.

patient had a second ulcer of 10 mm × 8 mm on the outer side of the lower part of the left leg and a white atrophic discoloration on the lower part of the right leg. MRI showed the ulcer reaching to the subcutis, and an increase of signal intensity of the muscle and the patellae. The joint was clinically swollen, but there was no water on the knee, as determined by MRI. Histology showed an ulceration, a dermal and muscular vasculitis and necroses. On the patient's admission to the hospital the ulcer was contaminated with a multiresistant *Pseudomonas aeruginosa*. On the basis of the clinical findings and the diagnostic results, the diagnosis established was a subacute stage of a cutaneous syndrome with ulceration on the outer side of the right thigh above the knee and on the outer side of the lower extremity of the left leg.

The ulcer above the knee was excised under general anaesthesia but was too large for primary closure. In the post-operative period the patient received local therapy with autologous thrombocytic growth factors to improve the granulation. A systemic therapy with oral steroids was performed: 60 mg of methylprednisolone per day initially for one week, with subsequent reduction of the dose. Steroids reduced the dermal and muscular vasculitis as demonstrated by MRI. In addition, the patient received perioperative intravenous antibiotic therapy.

Granulation was moderately rapid starting from the ulcer margins but was impeded by strong central exudation due to concomitant abacterial arthritis and synovitis of the right knee. The patient was transferred to the Orthopaedic Department in the Federal Armed Forces Hospital in Ulm. He was treated with three antibiotics and a drainage of the joint. Because of the loss of proteins his general status had deteriorated, and joint mobility was limited. An arthroscopy with arthrotomy and

synovectomy of the right knee combined with a transposition flap of the musculus vastus lateralis was performed on *21 January 1998*. This procedure resulted in a marked reduction in pain and swelling of the right knee and a rapid improvement of the patient's general condition.

Owing to insufficient granulation and development of new necrotic areas in the muscle of the upper part of the leg in the subsequent weeks, further surgery was carried out on *28 April 1998*. No further complications occurred, and functional recuperation was complete. Hyperbaric oxygen therapy was applied in order to increase granulation and prevent joint infection. Final wound closure was carried out with a musculus gracilis transposition flap and a subsequent split skin graft. Healing took place rapidly. Another ulcer on the lower extremity of the left leg was excised under full anaesthesia with primary suture and healing without complications.

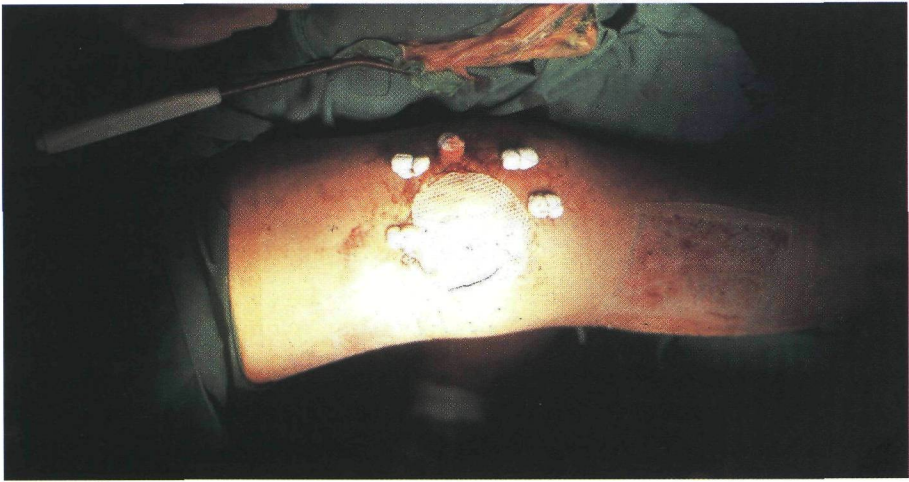
In addition, an examination of the internal organs was performed. The semen analysis showed azoospermia. The serum levels of gonadotrophic hormones (luteinizing hormone (LH), FSH) were elevated. No abnormalities of the eyes, mouth, throat, brain, lung or heart were detected. The bone marrow biopsy showed a minor dysplasia of erythropoiesis. The patient was discharged on *6 June 1998*, with the recommendation to continue the local treatment of the donor site of the graft with daily applications of dexpathenol cream. A follow-up of the patient was to be performed within six months. Figures 34–37 show the successive healing stages of the injuries.



*FIG. 34. Patient 6 BZ: right thigh before treatment, October 1997.*



*FIG. 35. Patient 6 BZ: right thigh before surgery, November 1997.*



*FIG. 36. Patient 6 BZ: right thigh during treatment, May 1998.*

**Patient 10 VZ, treated in the Dermatology Department of the University of Ulm at the Federal Armed Forces Hospital, Ulm**

The patient was admitted to the Department of Dermatology of the Federal Armed Forces Hospital in Ulm on 29 *October* 1997. He presented with a sharply demarcated, deep ulcer coated with yellow fibrin clots in the middle of the right arm. The ulcer was of a size of 15 mm × 10 mm with indurated surroundings and was very painful. The 20 MHz sonography showed an ulcer of a depth of 3 mm with a fibrotic



FIG. 37. Patient 6 BZ: right thigh showing healing, June 1998.

surrounding. MRI detected an increased signal intensity of the dermis and the muscle due to vasculitis. The forearm bone also showed increased signal intensity. Histology demonstrated an ulceration with dermal and muscular vasculitis. On the basis of the clinical findings and the diagnostic results, the diagnosis established was a subacute stage of a cutaneous radiation syndrome with ulceration in the middle of the right arm.

On admission of the patient to hospital the ulcer was contaminated with a multiresistant *Pseudomonas aeruginosa*. The ulcer was excised under local anaesthesia and primarily closed. The patient was treated with ofloxacin intravenously for the first five days and orally thereafter. The patient was also given oral steroids to treat the muscular vasculitis: 60 mg of methylprednisolone per day initially for one week, followed by a reduction of the dose. Steroids reduced the dermal and muscular vasculitis, as seen from MRI. No effect was observed on the bone. After this therapy the patient was free from pain. No post-operative complications occurred.

An examination of the internal organs was performed. The semen analysis showed polyzoospermia with normal serum levels of gonadotrophic hormones. There was no involvement of eyes, mouth, throat, brain, lung or heart. The bone marrow biopsy taken from the iliac spine showed a minor dysplasia of erythropoiesis but no malignancies. The patient was discharged on 11 December 1997. No further treatment was necessary at the time of the patient's release. It was recommended that a follow-up of the patient be performed at regular intervals, optimally every six months.

## 11. PATHOPHYSIOLOGICAL CONSIDERATIONS REGARDING THE DEVELOPMENT OF CLINICAL SIGNS AND SYMPTOMS

The clinical consequences of radiation exposure observed in the patients involved in the radiological accident at the Lilo Training Centre fall into two major problem areas: local radiation injuries leading to a cutaneous syndrome, and general signs and symptoms due to total body exposure to ionizing radiation.

On admission of these patients to the specialized hospitals in France and Germany, and in the weeks that followed, the cutaneous syndrome was the utmost priority in terms of the diagnosis and further treatment. However, the exposure of the skin to  $^{137}\text{Cs}$ , which is mainly a gamma emitter, was not limited to local skin injuries but undoubtedly also resulted in the exposure of internal organs and systems, including sensitive tissues such as the bone marrow and the reproductive system. Therefore, apart from the analysis of the effects of local radiation exposure, an analysis of the whole body radiation exposure of these organ systems is of interest and importance.

In this particular accident, the exposure was very inhomogeneous and distributed over a relatively long period of time. Even if there is still a lack of detailed information about the chronology of the accidental exposure (Fig. 38), it is known that the patients developed skin reactions of different stages between April and August 1997, except for patient 1 AN, who had already complained of symptoms in June 1996. Most of the affected patients had been in the army since November 1996, except for 1 AN, who had been recruited in November 1995. It can be assumed that during this time the patients had been exposed to an ill defined and/or protracted ionizing irradiation, and that for these patients, the most likely time frame of accidental exposure in a radiation field may have been between 60 and 300 days. The patients apparently were in this radiation field intermittently and therefore absorbed some gamma irradiation distributed over an unknown period of time and at an unknown exposure rate to the entire body.

The medical assessment of the patients in Georgia (Tables VII and VIII) indicated — on the basis of the general signs and symptoms such as nausea, vomiting, headache, loss of appetite and weakness — that these patients had been suffering for some time not only from local cutaneous injuries but also from a general radiation syndrome. However, the results of the haematological counts prior to 2 October 1997, which had been quite normal (no lymphocytopenia), had to be taken into account.

The changes in clinical signs and symptoms observed over time point to the possible pathophysiological mechanisms involved. Haematopoiesis and spermatogenesis are two major indicators which can be used to retrospectively assess the development of the general radiation syndrome.

As mentioned above, all patients developed transient skin erythema between April and May 1997, except for patient 1 AN, who developed first symptoms in June



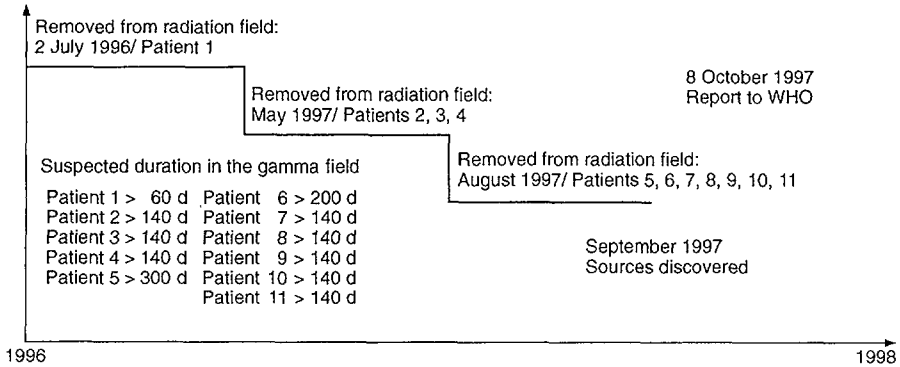


FIG. 38. Possible time sequence of accidental exposure.

1996. At the time the skin symptoms occurred, the patients additionally complained of general signs and symptoms. While these general symptoms disappeared without therapy, the skin symptoms became more severe, reaching a critical point in October 1997. Only after specialized treatment in November and December 1997 did most of the cutaneous lesions heal.

After admission of the patients to hospitals in France and Germany, some 60 to 420 days after the end of their exposure in the radiation field, the signs and symptoms characteristic of a general radiation syndrome had disappeared. The picture of mitotically connected cytological abnormalities observed in the bone marrow was indicative of a regenerating haematopoiesis after whole body exposure. Further indicators of whole body exposure — azoospermia and/or elevated FSH — were found in 8 out of 11 patients, proving severe impairment of the reproductive system.

The different localizations of the skin defects provided a distinct picture of the proximity of the sources to the blood-forming cells in the adult bone marrow. This was corroborated by MRI, which showed a signal intensity of the bone marrow localized in the humerus directly under the ulcer (patient 10 VZ). Therefore, in accordance with the clinical signs and symptoms and the physical characteristics of the source, the haematological findings for the patients can be formulated as follows: impaired haematopoiesis due to protracted, intermittent, inhomogeneous radiation exposure to the haematopoietic system.

The development of clinical signs and symptoms in this accident is similar to that observed in the accident in Mexico in 1962 [15], the accident in Algeria in 1978 [16] and the accident in Estonia in 1994 [6]. The patients involved in those accidents were also exposed to protracted, intermittent, inhomogeneous irradiation, from a  $^{60}\text{Co}$ , an  $^{192}\text{Ir}$  and a  $^{137}\text{Cs}$  source, respectively.

It is of interest to compare, in connection with such protracted exposure, the clinical consequences for the only surviving patient of the Mexican accident with

those for the Georgian patients. Without developing manifest clinical signs and symptoms, the Mexican patient was intermittently in the radiation field for 120 days. From the physical dose reconstruction, the daily dose was estimated to be a maximum of 143 mSv. When the patient was examined at the time of the end of his exposure in the radiation field, he showed signs of a bone marrow impairment with low lymphocyte values (about  $(0.1-0.2) \times 10^3/\mu\text{L}$ ), low granulocyte values (close to  $(1-2) \times 10^3/\mu\text{L}$ ) and low but still normal thrombocyte counts. The patient was treated with antibiotics only and haematopoiesis showed complete and spontaneous recovery 6–8 weeks after the end of his exposure in the radiation field.

This course is similar to that of the Georgian patients. They also showed signs of having had haematopoietic impairment at the end of their exposure in the radiation field. After they were admitted to the specialized hospitals in France and Germany, the intensive haematological diagnostic analysis indicated a strongly regenerating haematopoiesis.

From experiments on dogs that were continuously exposed during their life span to radiation from  $^{60}\text{Co}$ , it is known that the threshold at which haematological effects disappear but neoplastic late effects increasingly appear is about 75 mSv/d [17]. Two different patterns of effects have been observed: (1) with daily doses above 75 mSv, the animals died owing to various causes, including aplasia, septicaemia and myeloproliferative disorders; (2) with doses below 75 mSv/d, the early development of malignancies without acute symptoms was observed.

The pathophysiological basis of such a development must be seen in terms of the structure, function and regulation of haematopoiesis as well as other cell renewal systems. Depending on the daily dose rate, these systems can compensate for the increased cell loss from the dividing and maturing cell compartments by increasing the cell production rate. Owing to the high radiation sensitivity of the stem cell compartment, there is at the same time a decrease in the number of remaining stem cells of sufficient quality for replication. This is true not only for the haemopoietic–lymphopoietic system but also for the gastrointestinal system and to a certain degree for the skin [18]. The radiation exposure of the slowly proliferating cell systems such as the epithelium and connecting tissue cells will show up as late effects, which are to be expected within 10–30 years after exposure. Therefore, from a pathophysiological perspective, regular follow-up examinations are essential to investigate unrepaired injuries that may otherwise result in non-neoplastic or neoplastic late effects [19].

The medical observation over a period of several months of the patients radiologically exposed in the accident at Lilo would seem to confirm the following: There is evidence that even for exposure conditions in which the daily dose exceeds 100 mSv over an extended length of time, disorders of the haematopoietic system without concurrent clinical signs and symptoms can be detected by laboratory or other means. Therefore there is good reason to believe that a daily dose of 100 mSv

or so can be tolerated and compensated by increased cell production in the stem cell compartment of the haematopoietic tissue.

In this connection, a more in-depth comparison of the biological response patterns of the patients affected by the Lilo accident with those of individuals affected by other radiological accidents constitutes a challenge which specialists will no doubt want to take up. This will allow the development of ways and means of improving the diagnostic and therapeutic potentials for dealing with accidental radiation overdosage by analysing the responsible pathophysiological mechanisms [20]. To do this, it will be necessary to use the knowledge and experience gained from earlier radiation accidents.

Up until 1990, there had been no systematic international collection of individual case histories of radiation overexposure that included all the clinical signs and symptoms as a function of time. In 1990, in response to this need, the WHO collaborating centre within the REMPAN framework at the University of Ulm — in close co-operation with the radiation medical research centres in Moscow, Kiev and Chelyabinsk — designed and implemented a relational database.

This database is now being extended to a System for Evaluation and Archiving of Radiation Accidents Based on Case Histories, called SEARCH. The SEARCH database contains more than 800 case histories from 71 accidents in 17 countries between 1945 and 1994 and for two accidents includes follow-up of some 100 cases for up to 10–40 years. In order to be prepared for future radiation emergency situations as well as to provide information about the most likely late effects in the affected patients, it is necessary to collect and analyse as many data and patient records associated with radiation accidents as possible using appropriate pathophysiological models.

## **12. TREATMENT OF FOUR PATIENTS WITH RECURRENT SKIN ULCERS IN A SPECIALIZED HOSPITAL IN THE RUSSIAN FEDERATION**

There was recurrence of the radiation skin ulcers in four patients treated in France and Germany, owing to which the Georgian health authority requested the assistance of the Medical Radiological Research Centre of the Academy of Medical Science of the Russian Federation. This centre is located in Obninsk and has extensive experience in the treatment of local radiation injuries [21]. All four patients were admitted to the Department of Treatment of Local Radiation Injuries.

**Patient 2 EP.** A new radiation ulcer located on the frontal surface of the right thigh above the former lesion treated at the Curie Institute developed a few months



*FIG. 39. Patient 2 EP: reconstructive surgery of the new thigh lesion, June 1998.*

after the patient was released from the institute. The patient was hospitalized in the Medical Radiological Research Centre on 24 April 1998. Medical examination at the time of admission found an ulcer located in an area of hyperaemia near the skin graft left from the previous surgical operation. The ulcer had a diameter of 2 cm and was 2.3–3.0 cm deep. Before surgical treatment, the patient was treated with medication and hyperbaric oxygenation. On 13 April 1998, plastic surgery was performed. The tissue defect was covered with a skin–fascial graft. The histological conclusion for the examined removed tissues was ‘a chronic skin ulcer’. After recovery of the surgical wound by primary tension (Fig. 39), the patient was discharged from the hospital on 27 June 1998.

**Patient 5 GL.** There was recurrence of a radiation ulcer located on the lower third of the left calf after plastic surgery treatment at the Armed Forces Hospital in Ulm. Administration of gamma interferon had been started in Ulm for the treatment of radiation fibrosis and prevention of reactivation of the transplanted ulcer on the lower leg, but this was discontinued in Georgia, perhaps owing to lack of funds.

The patient was hospitalized in the Medical Radiological Research Centre on 16 April 1998. Medical examination at the time of admission found an ulcer of 4 cm diameter and with a depth of 2–3 cm, with a dense scar on the periphery of a width of 1.5–2 cm. At the bottom there were spots of scarce granulation with seropurulent liquid. After the usual perioperative preparation, the patient was treated surgically. The ulcer was removed from within the healthy tissue. The surgical tissue defect was covered by a skin–fascial graft and sewn up. The histological diagnosis was

'a chronic skin ulcer'. After recovery of the surgical wound by primary tension, the patient was discharged from the hospital on 27 June 1998.

**Patient 7 GG.** There was recurrence of a radiation ulcer after a surgical operation at the Armed Forces Hospital in Ulm, with fibrosis of the skin graft. The patient was hospitalized (16 April 1998) for continuation of the treatment in the Medical Radiological Research Centre. On primary examination there appeared to be a round ulcer with a diameter of 2 cm on the lateral surface of the lower third of the right thigh. The lesion edges were of high density. At the bottom of the ulcer a non-intensive granulation process was seen. The general health status of the patient was satisfactory. Clinical and laboratory examinations did not show any deviations from the normal condition. The medical team decided to perform additional surgical treatment. However, before this the patient underwent treatment with medication aimed at stimulating the healing processes and improving microcirculation and blood rheology. On 30 April 1998, the patient underwent surgery. The ulcer and its dense edges were removed.

The skin defect after these procedures was about 5 cm in diameter and it was covered by a splitting skin graft of a depth of 0.5 mm taken from the left thigh using an electrodermatome. Histological study of the removed tissues showed a chronic ulcer with significantly developed fibrosis in the hypoderm.

The graft took root by primary tension on 95% of the surgical wound and after additional medication treatment the patient recovered; he was discharged from the hospital on 25 May 1998. Subsequently, a new ulcer appeared on the other leg at the same height, in skin that had seemed uninvolved up to that point.

**Patient 9 ID.** A new radiation ulcer appeared on the frontal lateral surface of the right thigh. When this patient was admitted to the Armed Forces Hospital in Ulm, there was no ulcer on the right side of the thigh although the patient had suffered from fibrosis in this area. Most probably owing to a lack of follow-up of the medical treatment with interferon, an ulcer appeared.

The patient was hospitalized in the Medical Radiological Research Centre on 16 April 1998. At the time of the patient's admission, the ulcer had a diameter of 3 cm with fibrosis on the edges. After treatment with medication during a perioperative period, the ulcer, together with surrounding tissues, was removed on 29 April 1998. The skin defect was covered by an autodermic graft taken from the groin area. The histological diagnosis: a chronic skin ulcer with a significant fibrosis of the hypoderm. There was recovery of the surgical wound by primary tension and the patient was discharged.

Later new ulcerations appeared in those patients who had been hospitalized in Obninsk and these were treated (see Annex I).

### 13. CONCLUSIONS DRAWN FROM THE MEDICAL MANAGEMENT OF THE PATIENTS

In this accident the exposure conditions were special in respect of the homogeneity of radiation quality, primarily gamma radiation from  $^{137}\text{Cs}$ ; the highly inhomogeneous dose distribution over the whole body; and the protracted exposure pattern.

The clinical outcome of the patients was mainly determined by the tolerance levels of the rapid cell renewal systems such as the skin, haematopoietic system, reproductive system and gastrointestinal tract. In these patients the clinical picture was largely determined by the consequences of multiple local radiation lesions resulting in the cutaneous syndrome. However, beyond the lesions and the cutaneous syndrome, attention had to be given to the general reaction of the patients to the radiation exposure.

Non-invasive diagnostic techniques, such as high frequency ultrasound (20 MHz), MRI and especially thermography, proved to be helpful in assessing the extent of the disease and in the planning of non-surgical and/or surgical treatment.

Additionally, laboratory and consultant examinations provided further information on the patients' health impairment. For example, azoospermia and/or elevated FSH levels were diagnosed in 8 out of the 11 patients. This demonstrates the potentially severe impact on reproductive function in patients accidentally exposed to ionizing radiation. The same is true for the bone marrow, which in the patients was compatible in its expression with a strongly regenerating haematopoiesis. Typical mitotically connected cytological abnormalities of regeneration after total body exposure were found. Cytogenetic findings (e.g. dicentrics, ring chromosomes and others) were compatible with the levels of radiation exposure and might indicate the possibility of developing leukaemia or other stochastic effects at a later date. Therefore, cryopreservation of blood derived stem cells may be considered as a means of successfully treating such late consequences.

Although there was no evidence for cataract formation at the time of writing, examination for cataracts should be included in future follow-ups.

Given the complexity of dose distribution and clinical response, an individualized diagnostic and therapeutic approach was essential.

Newly developed non-surgical approaches (e.g. growth factors, hydrocolloid dressings, interferon) and surgical methods (e.g. coverage with artificial dermis) proved successful in the treatment of local radiation injuries. In specific conditions, anti-inflammatory therapy (e.g. corticosteroids) may obviate the necessity of surgery.

It is of paramount importance to state that, in view of the complexity of the problems encountered in such a radiation accident, close international and multidisciplinary co-operation is highly desirable. In this particular accident the concerted

action initiated at the international level by the network of WHO/REMPAN collaborating centres to examine and treat the affected patients proved successful. In addition, in the measures taken in response to this accident, the close co-operation between the IAEA and the WHO facilitated the evaluation of the radiological and medical effects of the accident and was useful to local authorities in alleviating the accident consequences. International funds for emergency treatment and initial follow-up should be secured and made available when required.

#### **14. RECOMMENDATIONS ON THE FOLLOW-UP OF THE PATIENTS**

The victims of the radiological accident at Lilo should be subject to ongoing medical surveillance, based on individual need. Consideration should be given to the following procedures during the course of any examinations.

- (a) Clinical assessment of the local radiation injuries should be performed, including high frequency ultrasound, thermography and, if necessary, histopathological evaluation and MRI. Additionally, total body examination should be performed to detect radiation induced skin cancers such as basal and squamous cell carcinomas or angiosarcomas, which can be expected between 10 and 30 years after overexposure to radiation.
- (b) In the event of ulceration, secondary skin malignancies should be ruled out. Treatment must be adapted to the results of the most recent diagnostic procedures. If systemic antibiotic treatment is considered, it should be carried out according to the results of an antibiogram.
- (c) Examination of peripheral blood is required (including differential blood analysis).
- (d) Bone marrow aspiration, bone marrow histology and cytogenetic examinations should be performed on a yearly basis for early detection of haematopoietic disorders.
- (e) To assess the regenerative capacity of the testicular function, spermatograms and determination of FSH should be carried out.
- (f) Ophthalmologic examination is necessary for early diagnosis of cataract formation.
- (g) In the course of the follow-up examination, other diseases that were detected, such as hepatitis and hypothyroidism, should be monitored.

- (h) To avoid additional damage to the skin increasing the risk of secondary malignancies, preventive measures are necessary, such as lifelong prescription of maximally effective sunscreens and strict avoidance of sunburn. Wearing sunglasses is recommended to reduce the risk of cataract development.
- (i) The generation and storage of autologous stem cells, allowing autologous transplantation in the event of future leukaemia development, should be seriously considered.

## **15. CONCLUSIONS AND LESSONS TO BE LEARNED**

### **15.1. CONCLUSIONS**

The review of radiological accidents is a mechanism for feeding back operational experience to reduce the likelihood of similar accidents in the future and to mitigate their consequences should they occur. Such reviews add to the store of knowledge and illustrate principles and criteria used or which should have been considered in policy and decision making.

The review of the radiological accident in Lilo revealed that the major cause of the accident was the improper and unauthorized abandonment of 12  $^{137}\text{Cs}$  radiation sources at the Lilo site. The lack of documentation relating to the plant suggested that there had been only limited contact between the former owners of the sources and the current operating organization. This was possibly due to changes in organizations and their responsibilities in the republics of the former USSR. The analysis of the main cause and the contributing factors leads to the following conclusions:

#### **A. Operating organizations**

The major cause of the accident was the improper and unauthorized abandonment of 12  $^{137}\text{Cs}$  radiation sources at the Lilo Training Centre. The inventory of sources was not transferred from the previous military owners to the new owners of the site, as no such physical inventory had been documented and maintained. Accountability of sources did not exist. The previous military owners had not properly conditioned or disposed of the sources when they had no further use for them.

#### **B. National authority**

Sources were not subject to administrative control, hence it was possible for the sources to be abandoned by the previous owners, unbeknown to both the new owners



and the regulatory authority. There was no authorization for transfer and no inspection at the Lilo site to monitor compliance with regulations and carry out enforcement as necessary. The absence of clear labelling and radiation warning signs on the sources prevented the soldiers from recognizing the potential health hazards they faced if they manipulated these objects.

Although the necessary actions were promptly taken following the identification of the radiation emergency, this was dependent on the collective experience of the staff as there was no national emergency response plan to cope with the situation. The non-existence of an appropriate emergency response plan, unavailability of up-to-date equipment, lack of financial resources and inadequate training of staff made it very difficult to manage the consequences of the accident. This, however, is not unique to Georgia. Many countries have limited resources for dealing with radiological emergencies, from both the medical response and the radiation protection points of view.

### **C. International organizations**

Accidents involving high activity sources that have subsequently resulted in severe deterministic effects have been reported previously by the IAEA [3–7], and the Lilo accident is yet another such instance. The similarity of the sequence of events leading to these accidents is a cause for concern, as is the potential for other sources to reach the public domain.

International co-operation has significantly facilitated both the treatment of persons injured and the management of accidents. In this case, the IAEA's Emergency Response Centre, the WHO and its REMPAN collaborating centres responded quickly and effectively.

The arrangements for responding to major radiation accidents often focus on the nuclear sector. Consequently, there are well established national and international protocols, guidance, training programmes and workshops for dealing with such events. Large non-nuclear radiation accidents have received much less support, even though such accidents have occurred more frequently.

### **D. Security of radiation sources**

There were no clear warning labels or radiation signs on the sources that conveyed the potential radiation hazard to persons. In addition, questions have been raised as to whether these notices would have been effective in warning the public of the serious potential hazard.

### **E. Medical community**

The lack of appropriate medical experience in the area of radiation induced

effects led to a long delay between the appearance of the initial clinical symptoms and the final diagnosis and hospitalization of the victims. The symptoms of the persons exposed were not initially diagnosed as being caused by radiation exposure by the physicians who first attended to them. This situation has occurred in many other reported accidents. Early diagnosis, and hence treatment, can be crucial and in some cases life-saving.

The victims of this accident were not willing to discuss the circumstances surrounding their exposures. The dates and times of irradiation, the specific sources producing the irradiation and the exposure geometries were all unknown. The medical team's perception of the exposure environment based on clinical symptoms differed somewhat from the actual accident scenario. This situation is not unique to this accident. As in the case of other accidents, medical decisions were primarily based on clinical and biological indicators. Nevertheless, physical and biological dosimetry estimates provided useful contributions.

## 15.2. LESSONS TO BE LEARNED

On the basis of the above findings, the lessons to be learned and recommendations which follow are given in order that the likelihood of similar accidents occurring will be reduced or, if accidents do occur, these lessons and recommendations will be of use in mitigating their consequences.

### **A. Operating organizations**

The Basic Safety Standards (BSS) establish basic requirements for protection against ionizing radiation and for the safety of radiation sources. The implementation of these standards is the prime responsibility of the 'legal person', in this case the management of the Lilo Training Centre and the previous military owners. One of these requirements is that transfer of ownership of sources or disposal of sources should be authorized by the regulatory authority in order to ensure that all sources are under regulatory control. The basic requirements also provide that accurate and comprehensive records of the inventory of radioactive sources must be kept. These records should clearly indicate the current owner and the location of sources, enabling any lost or missing sources to be quickly identified.

### **B. National authorities**

The BSS can only be implemented through an effective radiation safety infrastructure that includes adequate laws and regulations, an efficient regulatory system, supporting experts and services, and a safety culture shared by all those with

responsibilities for radiation protection, including workers and regulators. The regulatory infrastructure should comprise a regulatory body with adequate resources in terms of both personnel and finance, and regulations specifying the appropriate protection and safety requirements and covering administrative control of notification, authorization by registration or licensing, inspection and enforcement. Military sources are not to be excluded from this regulatory control.

National regulations should require that users of radioactive sources maintain comprehensive records of all sources in their possession and that an inventory of all sources be conducted at appropriate intervals to confirm that the sources are in their assigned locations and are secure. Regulations should also require that control of a source should not be relinquished without compliance with all relevant requirements specified in the registration/licence and that the regulatory authority should be notified of any decontrolled, lost, stolen or missing source. Regulations should also require that warning signs on sources clearly indicate danger, that sources be physically secured at sites and that only authorized personnel who have been trained have access to the sources.

Interim and permanent repositories for the storage of radioactive wastes, including spent sources, should be established in accordance with internationally agreed rules and practices, and possibly involving international co-operation. Sources no longer in use should be securely stored in an approved storage area, or conditioned as waste.

Guidance is provided in Ref. [2] for the establishment or improvement of a national radiation protection infrastructure. This document also contains model regulations consistent with the BSS. National authorities are invited to make use of this model when considering the implementation of the provisions of the BSS. Such authorities might also find it useful to consider whether their own regulatory system is sufficiently robust to prevent a sequence of events similar to those described in this report and other IAEA accident reports.

The need for a system of emergency response and preparedness plans established by regulations at licensee and national levels is evident. These emergency plans should consist of a clear allocation of responsibilities, detailing the actions to be taken, when they should be taken and who is responsible for them. This is imperative for the national emergency plan, which would include many organizations in addition to the regulatory authority, such as medical institutions, civil defence, police and fire brigades.

Personnel who may be required to use monitoring instruments should be trained in the use of a wide range of equipment, in deciding on their suitability for different scenarios, *in calibration and in the interpretation of measurements.*

To ensure efficiency and effectiveness in the implementation of the plan, particularly for off-site emergencies or contingencies involving the general public, it is necessary to conduct practice exercises involving all responsible parties. Equally

essential to the successful implementation of the plan is the availability of emergency funding; the source of funding should be provided by law and should be readily available.

For many years, the IAEA has been providing assistance, upon request, to Member States related to radiation emergency situations in the framework of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency. The assistance provided includes, inter alia: (a) technical advice on emergency planning, preparedness and response; (b) radiological survey; (c) source retrieval; (d) in situ verification of the radiological conditions and technical advice; (e) medical advice for the treatment of overexposed persons.

The governments of all countries where major radiation sources are used should therefore consider subscribing to the Convention on Early Notification of a Nuclear Accident and the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency.

### **C. International organizations**

In the framework of the Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency, the IAEA is currently establishing an Emergency Response Team Network (ERNET). The ERNET is a mechanism which provides a broad worldwide emergency assistance coverage to address situations demanding a rapid response in order to mitigate the consequences of a nuclear accident or radiological emergency. The ERNET focuses primarily on evaluation of the radiological consequences of an accident, evaluation of possible health effects and the provision in situ of the initial medical care to overexposed persons. The in-depth diagnosis, treatment, rehabilitation and follow-up of overexposed persons are to be carried out by the WHO/REMPAN centres.

The BSS require that information on both normal and abnormal operations significant to protection or safety be disseminated to all relevant parties. This information should cover, inter alia, doses associated with given activities, maintenance data, description of events and corrective actions, so that the lessons learned can be disseminated and help prevent similar accidents from occurring or mitigate the consequences when they do occur. The publication of accident reports will no doubt contribute to raising awareness in Member States. However, international organizations may wish to consider additional ways of assisting in the prevention, management or mitigation of the consequences of accidents. These may include:

- Organization of seminars and conferences on the subject.
- Maintenance and provision of radiological emergency equipment to be sent on short notice to an emergency site where equipment of this kind is not readily available. This should include field equipment capable of detecting and

- measuring a wide range of radiation types and levels as well as withstanding harsh environmental conditions such as high humidity and extreme temperatures, unstable environmental conditions and altitude variations, as appropriate.
- Establishment of additional regional centres for emergency preparedness and response on every continent.

Consideration should be given to establishing a suitable forum for the exchange of information and experience about preparing for and dealing with large non-nuclear radiation accidents. Guidance documents and training programmes should also be considered.

#### **D. Security of radiation sources**

The labelling and warning markings on radioactive sources should be regulated to a unified standard and should be in harmony with international standards such as ISO 361 of the International Organization for Standardization. Warning notices need to be in a language (or languages) easily understood by the persons who may encounter the source, especially members of the public. Consideration should be given to the question of whether the trefoil symbol is sufficient to warn of the significant danger associated with high activity sources. For sources readily capable of causing deterministic effects, it may be appropriate to provide additional wording and symbols on containers that more clearly indicate to the untrained eye that the contents are dangerous. More generally, there may be a need to review the purpose of the trefoil symbol, whether it is intended to act as a warning sign or simply to inform of the presence of radiation.

#### **E. Medical community**

There is a need for nationwide dissemination of information to general practitioners on basic radiation biology, associated clinical symptoms and the medical management of persons overexposed to ionizing radiation. This could be accomplished in the form of national training workshops. It will be also necessary to include these topics in the syllabus of the national medical curricula for doctors. A roster of doctors specializing in radiation induced injuries should be kept by general practitioners and regulatory authorities for referral. These specializations would include treatment of radiation burns, acute radiation syndrome, etc.

At least one well equipped medical team with trained staff should be designated by the national emergency plan for prompt reaction in the event of a radiological emergency. In order to obtain the most useful information from biological dosimetry, it is necessary to perform as early as possible biological sampling for standard blood counts, bone marrow aspirates for smears and histological sections.

Provision of photographs or videotape footage of the site of an accident can be helpful for the medical team's understanding of the reasons for the accident or prediction of the effects. It may be useful for both medical and physics staff to be involved at an early stage of accident reconstruction. It is always useful to use a multidisciplinary team in accident reconstruction.

It is extremely important that physicians obtain rapid and reliable information from the patient on the circumstances of the accident and on the initial symptoms. This point underlines the importance of the education and training of all radiation workers in radiation protection, including potential health effects and symptoms.

An adequate system of social and psychological support should be provided following a radiological accident which has caused serious overexposure, as in the present case. Psychological support should be provided to those individuals directly and indirectly affected as well as to the personnel working in response to the emergency. Psychologists should be available to provide counselling and be part of the accident management team in order to provide advice on the possible stress to the casualties and the public.

## Annex I

### STATUS OF THE GEORGIAN PATIENTS IN AUGUST 1999

- 1 AN Three additional operations (with 17 surgical steps) were necessary between October 1998 and January 1999 to treat new necrotic lesions of the left inguinal area and of several fingers. Pending surgery on the right anterior chest. Psychological status: normal.
- 2 EP Surgical treatment of a new radiation ulcer on the right thigh at the Medical Radiological Research Centre in Obninsk in July 1998. A second new ulcer developed on the right shoulder; surgical treatment is necessary. Psychological status: depression.
- 3 CG Amputation of fingers D I and D III of the right hand in Tbilisi in September 1998. A new radiation ulcer developed on finger D II of the right hand; amputation of the terminal phalanx of D II may be necessary. Psychological status: depression.
- 4 TK A new radiation ulcer developed in the former grafted area on the right thigh. Surgical treatment at the Medical Radiological Research Centre in Obninsk in April 1999. Psychological status: normal.
- 5 GL A second surgical treatment of the radiation ulcer on the left lateral malleolus at the Medical Radiological Research Centre in Obninsk in July 1998. Another new ulcer developed on the right lateral malleolus. Further surgical treatment may be necessary. The patient continues to be seen until now (August 1999) at the Medical Radiological Research Centre. Psychological status: depression.
- 6 BZ Good condition of the skin, no new ulcers. Intermittent pain attacks during walking. Psychological status: normal.
- 7 GG A surgical treatment of the recurrent radiation ulcer on the right thigh was performed at the Medical Radiological Research Centre in Obninsk in July 1998. After this treatment another recurrence of the ulcer developed. This ulcer healed during conservative treatment. Psychological status: normal.
- 8 SO Good condition of the skin, no new ulcers. Psychological status: normal.
- 9 ID Surgical treatment of a recurrent radiation ulcer on the left shoulder (originally treated in Georgia in a conservative way) at the Medical Radiological Research Centre in Obninsk in July 1998. General condition is satisfactory. Psychological status: normal.

- 10 VZ Good condition of the skin, no new ulcers. Occasional intermittent dizziness. Psychological status: normal.
- 11 SN Good condition of the skin, no new ulcers. Appendectomy in early 1999. Psychological status: normal.



## Annex II

### WHO COLLABORATING CENTRES AND LIAISON INSTITUTIONS WITHIN REMPAN

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## ABBREVIATIONS

abs.	Absolute
ACTH	Adrenocorticotrophic hormone
CD	Cluster determinants (mainly on the surface of leucocytes)
D 12	Level of thoracic vertebra 12
DNA	Deoxyribonucleic acid
EEG	Electroencephalogram
ESR	Electron spin resonance
FSH	Follicle stimulating hormone
ft3	Serum free triiodothyronine
ft4	Serum free thyroxine
Gd DTPA	Gadolinium diethylenetriamine pentaacetic acid
Ig	Immunoglobulin
i.v.	Intravenous
LH	Luteinizing hormone
MCV	Mean corpuscular volume
MGED	Multidevice graphics editor
MORSE	Multigroup Oak Ridge Stochastic Experiment
MRI	Magnetic resonance imaging
NK cells	Natural killer cells
PHA	Phytohaemagglutinin
REMPAN	Radiation Emergency Medical Preparedness and Assistance Network
S 100	Neuroectodermal tumour marker protein (still soluble at 100°C)
SEARCH	System for Evaluation and Archiving of Radiation Accidents Based on Case Histories
STH	Somatotrophic hormone
T2 fat saturated	T2 weighted sequences (relaxation time in MRI)
TSH	Thyroid stimulating hormone

*Results of spermatogram (according to WHO classification of sperm density)*

Azoospermia: no sperm	Normozoospermia: $>20 \times 10^6/\text{mL}$
Cryptozoospermia: $<10^6/\text{mL}$	Polyzoospermia: $>250 \times 10^6/\text{mL}$
Oligozoospermia: $(1-20) \times 10^6/\text{mL}$	





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