THE RADIOLOGICAL ACCIDENT AT THE IRRADIATION FACILITY IN NESVIZH

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FOREWORD

Technologies that make use of radiation continue to spread around the world: millions of people are employed in radiation related occupations, and hundreds of millions of people benefit from these applications. Use of intense radiation sources for purposes such as sterilization of medical products requires special care in the design and operation of equipment to prevent radiation injury to workers.

More than 40 years of experience in radiation processing has shown that such technology is generally used safely, and steady improvement in the design of facilities and careful selection and training of operators have contributed to this good safety record. However, some cases of circumvention of safety systems have been registered and it is documented that the consequences of radiological accidents at industrial radiation facilities can be extremely serious.

The causes of accidents may have some points in common, but at the same time may be highly specific. A detailed study of these common and specific features seems to be of great importance for further improvements in safety systems.

One such event occurred on 26 October 1991 at an industrial sterilization facility in Nesvizh, Belarus, when the operator entered the irradiation chamber and was severely exposed to a lethal dose of radiation. The significant feature of this case was related to the medical management. It should be underlined that some circumstances of the accident only came to light during the post-accident review made by the IAEA. To document the causes and consequences of the accident and to define the lessons learned are of help to those people with responsibility for the safety of such facilities and to those medical authorities who might be involved in the management of a radiation event.

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CONTENTS

1. INTRODUCTION

1.1. BACKGROUND TO THE ACCIDENT

On 26 October 1991, a radiological accident occurred in an irradiation facility in the town of Nesvizh, about 120 km from Minsk, Belarus. A variety of agricultural and medical products are sterilized at the facility by means of an internal transport system that passes them, in a controlled manner, close to an intensely radioactive ^{60}Co source in a moveable rack. Following a jam in the product transport system, the operator entered the facility to clear the fault; at this point, the source is thought to have been in the safe position. However, on entering the facility the operator bypassed a number of safety features and left the controls in a position such that exposure was imminent.

At some stage, the source rack became exposed and the operator was irradiated for about 1 minute. He suddenly felt unwell and then noticed the source rack in the irradiation position. The accident was quickly reported to the authorities and the operator was taken into medical care, first in Nesvizh and Minsk, and then for specialized treatment in Moscow. It was estimated that he had received a whole body dose of 11 Gy, with localized areas of up to 20 Gy. Despite intensive medical treatment, he died 113 days later.

1.2. BACKGROUND TO THE IAEA POST-ACCIDENT REVIEW

Technologies that make use of radiation continue to spread around the world. Millions of people are employed in radiation related occupations and hundreds of millions of people benefit from these applications. Facilities using intense radiation sources for purposes such as radiotherapy, radiation processing of products, preservation of foodstuffs and gamma radiography require special care in the design and operation of equipment to prevent radiation injury to workers or to the public. Experience has shown that such technology is generally used safely, but on occasions controls have been circumvented and serious radiological accidents have ensued.

To the extent that reports on such accidents are incomplete or are unavailable to the scientific community, potentially valuable information is lost. Although the causes of accidents and the treatment of patients may be highly case specific, review of the circumstances in which they have arisen can yield generally applicable lessons that are of help in preventing further accidents or in improving the response to those accidents that do occur. This was the motivation for reviews by the IAEA of three fatal accidents: in Goiânia, Brazil, in 1987 [1]; in San Salvador, El Salvador, in 1989 [2]; and at the Sor-Van facility, Israel, in 1990 [3]; the last two of these accidents took place in irradiation facilities. Two other fatal accidents have occurred at irradiators: at the Stimos plant, Italy, in 1975 [4]; and in Kjeller, Norway, in 1982 [5]. It

is relevant to note that there have also been a number of accidents involving gamma and electron beam irradiators that have resulted in serious, but non-fatal, radiation injuries [6–8].

There are more than 600 industrial irradiation facilities of the gamma ray and electron beam type in use worldwide. Some of these are to be found in developing countries, where the radiation protection infrastructure may be less strong. However, as is evident from the above references, accidents are not confined to those irradiators that are in use in developing countries. The number of fatal accidents in irradiators has given further impetus to the IAEA programme in this area; one aspect of this work has been the post-accident review reported on here. Three other important features of the IAEA programme are:

(1) The publication of a Safety Guide [9] and an associated set of Practical Radiation Safety Manuals [10, 11];
(2) The organization of a series of regional training courses and the production of a training video tape [12];
(3) The holding of a Technical Committee Meeting for competent authorities and the designers and operators of irradiators [13].

2. IRRADIATION FACILITY

2.1. HISTORY OF THE FACILITY AND REGULATORY CONTROL

The gamma irradiation facility at the Biochemical Plant of the Pharmindustry Corporation in Nesvizh, about 120 km from Minsk, Belarus, was designed in 1981 and commenced operation in 1984; subsequent refurbishment was completed in 1989. It was built by the All-Union Scientific Research Institute of Radiation Technology of the former USSR, and is of the 'Pepel' model type. Several such facilities are in use in the former USSR republics. The design and construction of the plant were carried out according to specifications laid down by the then regulatory authorities.

Under international classification [9] it is a category II gamma irradiator of dry storage design with an original capacity of 6.72 PBq (182 kCi), which was subsequently increased to 30 PBq (800 kCi) of ^{60}Co. It was originally designed for sterilizing peat to be used in fertilizers, but is capable of dealing with a wide range of products; at the time of the accident, the irradiator was being used to sterilize medical syringes and haemostatic sponges.

Since its commissioning, two important factors have altered the system of regulatory control. First, the Chernobyl accident had a significant impact on parts of Belarus and, although this focused attention on radiation protection problems, it

diverted resources from radiation protection in the industrial sector. Second, the breakup of the former USSR and the emergence of Belarus as a separate sovereign state produced some changes in organizations and their responsibilities.

At the time of the accident, two relevant organizations existed. The first was the State Committee on the Supervision of Operational Safety in Industrial and Atomic Power Engineering, which was responsible for the technical aspects of the design, construction and modifications of facilities. It licensed the facilities and was also responsible for the drawing up of the regulations that control plant operation. The second organization was the Radiation Protection Division of the Public Health Inspectorate within the Ministry of Health (Gossannadzor). It had specific responsibilities in terms of assessing the radiation doses to staff and the means of controlling these doses. Visits by provincial and district inspectorate staff took place approximately every 3 months.

2.2. DESCRIPTION OF THE FACILITY

Comprehensive documentation on the plant as-built, on its condition at the time of the accident and on subsequent alterations was not available to the post-accident review team, and the following description is based on the original specifications, together with the observations and data presented at the time of visiting the plant.

In the 'Pepel' design the source, when not in use, is stored in a shielded dry storage pit, from which it can be raised to the irradiation position. The product to be irradiated is rotated at a constant rate around the source in a transport container system suspended from an overhead rail. The irradiation chamber has massive concrete shielding, the primary barriers of the walls and ceiling being 1.8 m thick and designed to reduce accessible dose rates to below 14 μSv/h, a level that is specified in the regulations. The facility has a maze entrance and a variety of safety systems to prevent entry when the source rack is exposed. The source exposure and product transport systems are controlled from a control room in the product loading area. Figure 1 shows a plan view of the facility, with the location of safety devices.

2.3. RADIOACTIVE SOURCE

The basic source elements are of Russian origin and of the GIK-7-4 type. They are in the form of metallic rods, with a diameter of 11 mm and a length of 81 mm, each incorporating a nominal 70 TBq (1890 Ci) of ^{60}Co encapsulated in stainless steel. Up to 12 elements, together with spacers, are loaded into 64 stainless steel tubes placed in four sections of 16 source pencils each, with a 30 mm gap between each pencil. The sections are held together with stainless steel strips to form a planar source (2.2 m $\times$ 1.2 m), known as the source rack. At the time of the accident, the source activity was 28.1 PBq (760 kCi).

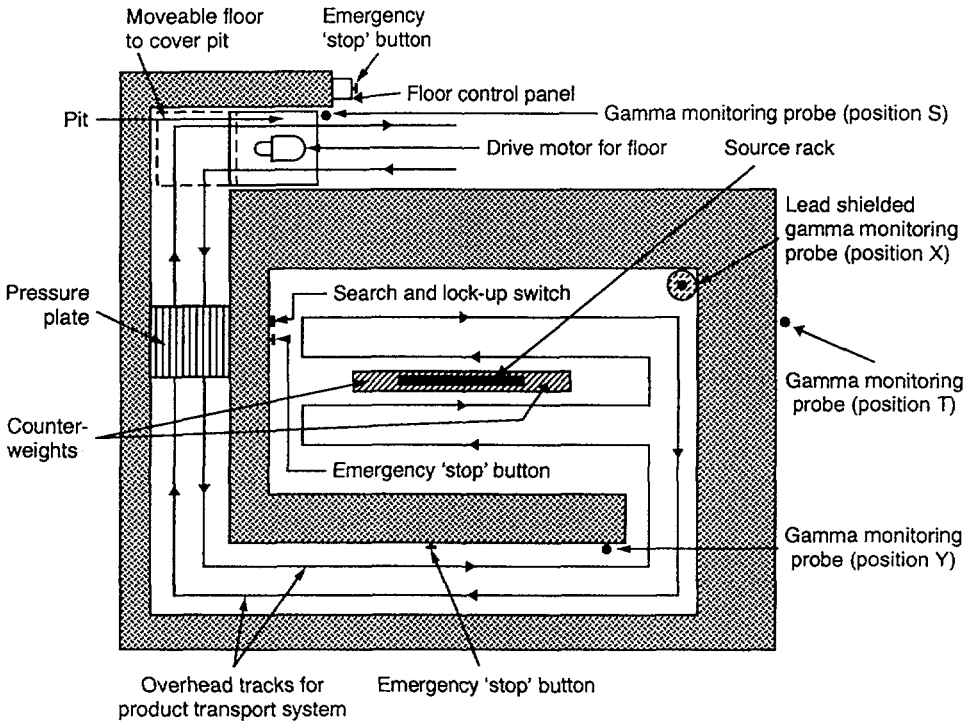


FIG. 1. Plan view of the facility, with the location of safety devices (for explanation of the gamma monitoring probe positions, see Section 2.5.2).

The source rack is connected by stainless steel cables to two counterweights. The source rack and counterweights run in vertical stainless steel guides, as shown in Fig. 2 and photographs 1 and 2. In addition, the source rack is protected against interference from the product boxes by a metal grid. The source is raised and lowered by an electric motor driven by gears, a hydraulic damper and two traction chains attached to the source rack. During 'source up' and 'source down' movements it is possible to stop the drive motor and to hold the source rack in an intermediate position. In an emergency, the clutch disengages from the motor and the source rack returns to the safe position under gravity.

In the source pit, water cooled heat exchangers remove the radiogenic heat. In the irradiation chamber, forced ventilation removes the radiogenic heat, ozone (O_3) and oxides of nitrogen produced by radiolysis.

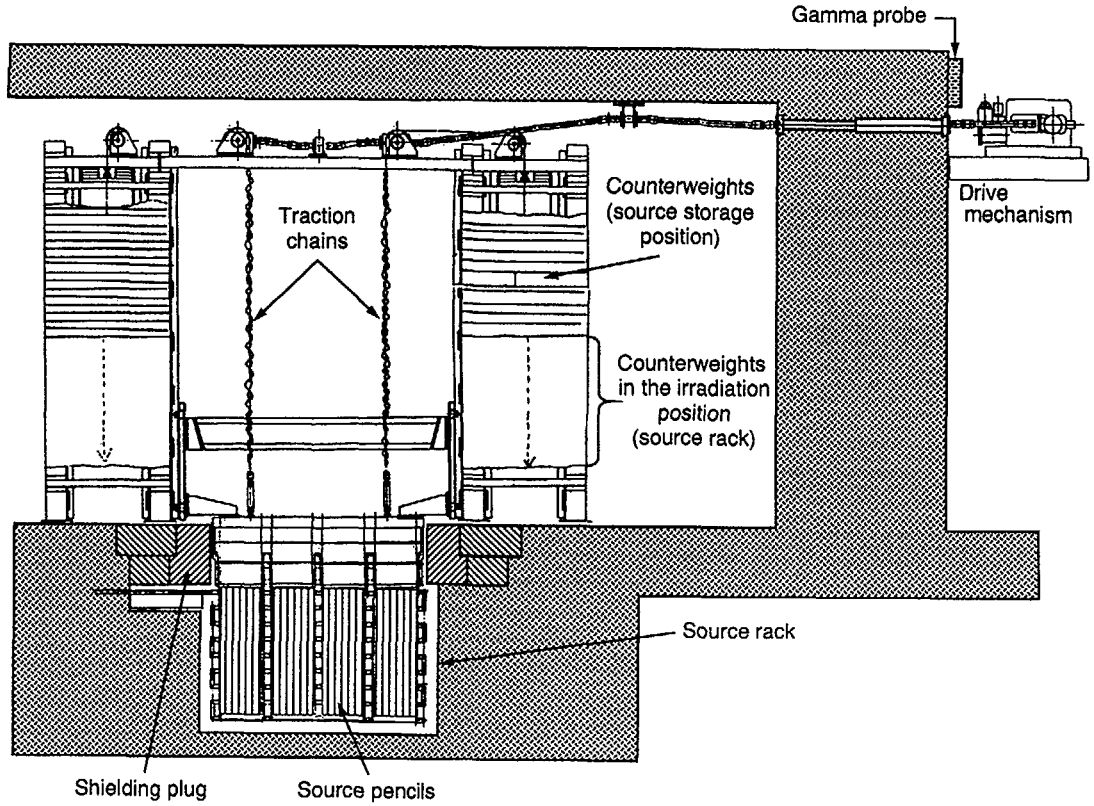


FIG. 2. Source rack, counterweights and drive mechanism.

2.4. PRODUCT TRANSPORT SYSTEM

The product to be irradiated is transported around the facility in carriages suspended from an overhead track. Each carriage has a cradle supporting two stainless steel boxes, each 500 mm × 560 mm × 800 mm. The cradle can be rotated in a vertical plane orthogonal to the direction of travel so that the top box is moved to the bottom and vice versa (photographs 3 and 4). There are 24 irradiation positions around the transport track, and the product rotates around each position twice. For the second pass, the cradle is turned upside down. The time spent in each irradiation position can be adjusted from the control panel to ensure that the product dose is 25 kGy (±40%).

Attached to the top of each carriage are linkage arms (photograph 5(a)) that couple the carriages to one another for movement around the facility. Problems can occur with linkage at bends in the overhead track. If loading of the boxes is unbalanced, movement of the carriage can result in decoupling of the linkage (photograph 5(b)) and the product transport system jams. This can occur up to three times a day and necessitates the operator entering the irradiation chamber, first to lever the jammed couplings back into place with a metal rod (photograph 6), and then to recouple the units.

2.5. SAFETY AND CONTROL SYSTEMS

In the control room there are three adjacent control panels: the product transport control panel; the gamma monitoring probe system; and the source movement and safety mechanisms. These are described in Sections 2.5.1 to 2.5.3, and their location in the facility is identified in Fig. 3.

2.5.1. Product transport control panel

The system was originally designed with a microswitch at each irradiation position to sense the presence of a carriage and to give a confirmatory illuminated signal for each position at the control panel. However, since decouplings have taken place at bends, only the sensors at each end of the four irradiation rows (i.e. eight sensors in total) are now used. A transport jam is signalled when one of the microswitches is *not* illuminated on the control panel. There is no audible alarm to indicate such an event, the only indication being the change in the sound of the drive motor when it is unable to move the product transport system. To protect the motor there is a thermal cut-out mechanism, which only operates after some time and which is indicated on the control panel. The noise of the drive motor cannot readily be heard in the control room, thus vigilance over the visible signals (from a product dose viewpoint) is important. Figure 4 shows the product transport control panel.

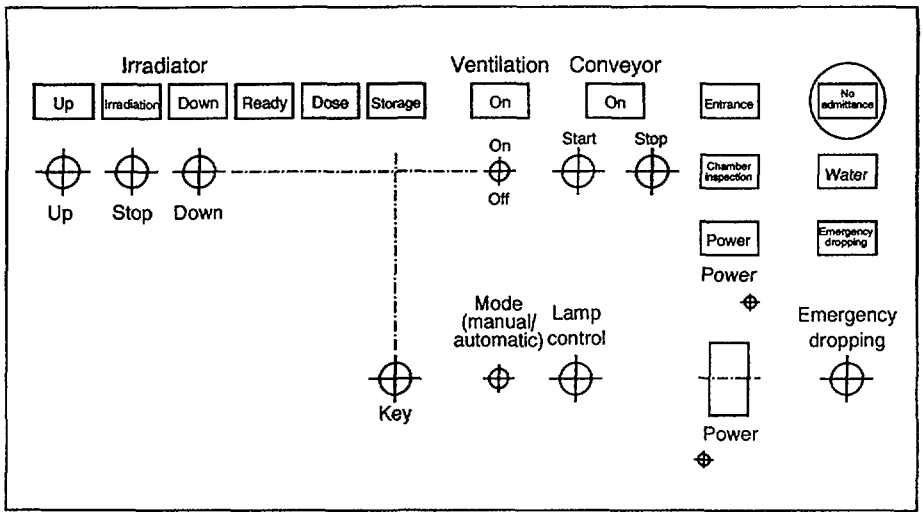


FIG. 3. Source control panel.

There is no interlock between the product transport system and the source control system, therefore in the event of a jam 'source down' movement has to be manually selected at the control console.

2.5.2. Gamma monitoring probe system

Two pairs of fixed gamma monitoring probes are installed at the facility; their location is shown in Fig. 1:

(1) The first pair of probes focuses on the inside of the facility and comprises a probe in a lead shield (photograph 7), position X, inside the irradiation chamber, and an unshielded probe, position Y, on the inner leg of the maze entrance;

(2) The second pair of probes focuses on the dose rates outside the facility and comprises a probe, position S, at the beginning of the maze entrance, and a probe, position T, by the drive motor near to where the source movement system enters the exposure chamber.

Each pair of probes has a single ratemeter (i.e. two in total) on a panel in the control room and the operator can choose which probe signal is to be displayed (photograph 8). However, it is not immediately clear which readings are being displayed, hence misinterpretation of the signals can easily occur.

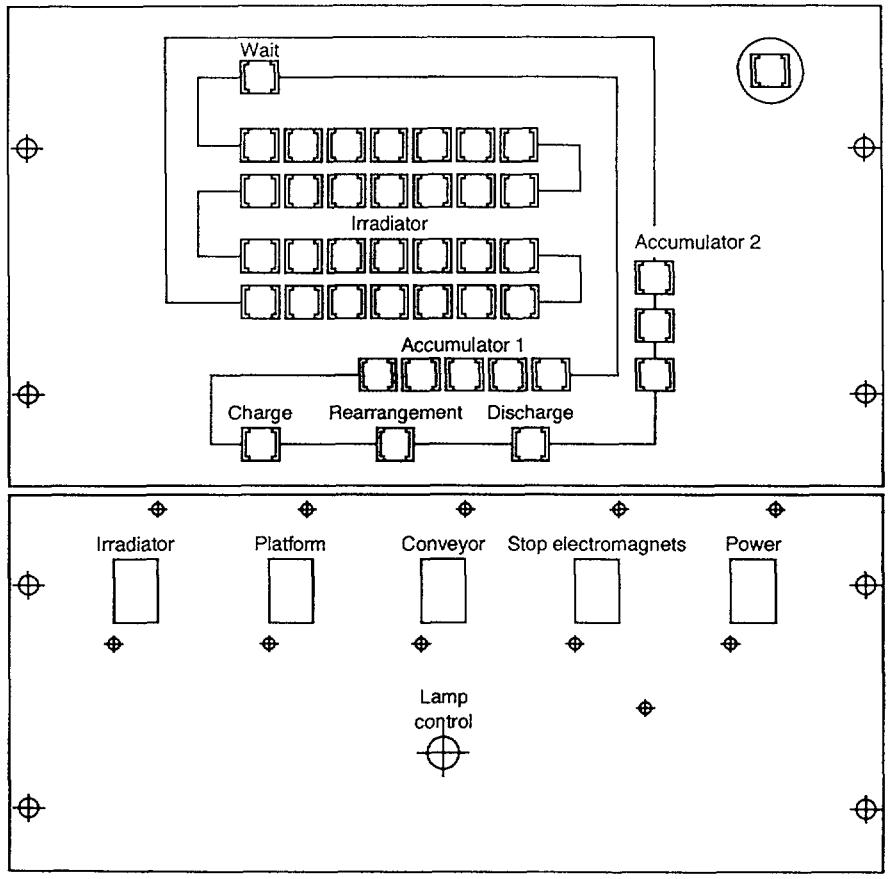


FIG. 4. Product transport control panel.

An interlock arrangement exists that activates the emergency source return sequence if the dose rate from probes S or T exceeds 14 μSv/h. However, the X and Y gamma monitoring probes do not have systems to warn persons inside the facility that the source rack is exposed, nor are they interlocked with other control systems to provide an automatic safety feature that prohibits entry when the source rack is exposed.

2.5.3. Source movement and safety mechanisms

Figure 3 shows the layout of the source control panel in the control room. The design is such that a single key has to be inserted and turned 90° to energize the controls. Removal of the key automatically de-energizes the controls. The same key has

to be used in a separate control panel at the maze entrance during the entry procedure. The main control panel has buttons to raise and lower the source, together with a 'stop' button that holds the source in an intermediate position, with warning lights to indicate its position.

The stainless steel shaft running through the hydraulic damper of the source drive mechanism has a larger diameter at each end which, when in the 'fully up' and 'fully down' positions of the source rack, actuates the two respective microswitches and sends signals to the control panel. The tolerance of these microswitches is unknown. Also, located at ground level at one end of the source rack guide is a microswitch that senses when the shielding plug on top of the source rack is in the 'fully down' position. Pressing the 'source down' or 'source up' button immediately results in the lights 'down' or 'up' being illuminated. When source movement is completed, the microswitch signals sense the position of the source rack and the storage or irradiation lights are illuminated, as appropriate.

If entry is not required, the source rack can be repeatedly cycled by raising and lowering without any constraints. However, if entry is required then certain sequences have to be followed; these bring into play a number of safety features and safety procedures, as described in Section 2.5.4.

2.5.4. Access safety features

At the entrance to the maze there is a motorized, moveable floor section that, during irradiation, is driven back to reveal a deep pit that covers the full width of the maze entrance. At the time of the accident, narrow ledges were present along the sides of the pit which, alone, were not wide enough to permit anyone to walk across. However, the drive motor for the moveable floor section was located in the pit near one such ledge and, together, they provided a potential pathway across the pit. Since the accident, the motor has been moved, the ledges removed and the size of the pit increased (photograph 9). For access, a small control panel at the maze entrance drives back the floor section covering the pit. However, a single key from the main source control panel has to be inserted, and it cannot be removed unless the floor section covering the pit is moved. Thus, the floor position is interlocked with the source controls.

Around the first bend in the maze entrance there is a large, pressure sensitive plate covering the full width of the maze entrance. Walking over the pressure plate with the source exposed would result in the source rack being automatically lowered to the safe position.

2.5.4.1. Entrance sequence

With the source 'fully up', the 'irradiation light' is illuminated, as is the 'no admittance' light. To gain entry to the facility, the following sequence has to be carried out:

(1) Push the 'down' button on the control panel. This illuminates the 'down' light until the microswitches sense the irradiator is 'fully down', at which time the 'down' light goes out and the 'storage' light is illuminated.

(2) The safety procedures require that the operator wait 4 minutes before entering the irradiation chamber in order to allow the ozone and oxides of nitrogen to disperse. This time delay is indicated by the 'entrance' light on the control panel; however, this is a procedural control and there is no interlock to enforce the delay.

(3) The key should be turned from the 'ready' to the 'off' position, and then removed. Even if the 'source down' button has not already been pressed, removal of the key automatically activates the 'emergency dropping' of the source rack to the storage position.

(4) The gamma monitoring probe system should be observed to ensure that the dose rates are acceptable. However, in the event of high dose rates being recorded there are no mechanisms to automatically prevent entry or to trigger an alarm.

(5) The operator should examine the dose rate monitor and confirm, before proceeding, that it is functioning correctly, using a check source attached to the monitor. The facility has three monitors, which are calibrated annually. The monitors consist of a separate rate meter and long probe (approximately 50 cm), which require two handed operation. The detector is of the sodium iodide type and is primarily designed for geological survey work, with a maximum dose rate of 30 μSv/h (photograph 10).

(6) The key has to be taken to the maze entrance panel, where it is inserted and turned to the 'on' position before the motorized section of the floor at the maze entrance can be moved to cover the pit.

(7) While waiting for the floor to be positioned, the operator should take note of the portable monitor reading. If the source rack is shielded it should read 0.2–0.5 μSv/h, and if fully exposed, 3–4 μSv/h.

(8) Proceeding down the maze, the operator crosses the sensitive pressure plate and should observe the state of the warning lights and the readings on his portable monitor. At the time of the accident, there were no warning lights. Should anything unusual be discovered, the emergency 'stop' buttons are pressed, causing the irradiator to be lowered.

2.5.4.2. Exit and exposure sequence

(1) Having completed any necessary work in the irradiation chamber, the operator has to follow 'search and lock-up' procedures. A button has to be pressed at the far end of the chamber, whereupon he/she has 2 minutes in which to complete the sequence.

(2) The operator should make sure that no one is in the irradiation chamber, and then exit.
(3) At the maze entrance control panel, the motorized floor should be moved back to prevent further access.
(4) The key should be removed and taken to the main control panel, where it is inserted and turned to the 'ready' position. The 'ready' light will illuminate if all the safety systems are in a safe condition. Confusingly, at this point in the sequence both the 'no admittance' and 'entrance' lights are illuminated.
(5) Press the 'up' button, the 'up' light is illuminated and the 'storage', 'ready' and 'entrance' lights go out.
(6) When the source rack reaches the 'fully up' position, as sensed by a microswitch, the 'up' light goes out and the 'irradiation' light is illuminated.
(7) At this point, the conveyor system can be started.

Although there are some connections between the circuitry of the three panels in the control room, none provides interlocking mechanisms to prevent entry when high dose rates are detected in the irradiation chamber or to automatically return the source to the safe position if a product jam is detected. These arrangements are required by the standards detailed in IAEA Safety Series No. 107 [9] in order to provide adequate levels of redundancy, diversity and defence in depth for safety systems. Lack of such arrangements places the onus on procedural controls which, as will be seen, contributed to the accident.

2.6. OPERATION AND MAINTENANCE

At the time of the accident, the facility was operating for 24 hours a day, using a 3 × 8 hour shift system. Each shift consisted of one operator at the control panel and one assistant to load the product into the carriers. The irradiation facility is part of a large factory, and electrical and mechanical maintenance staff are available. To allow time off, the factory has six separate shift teams.

The qualifications required for an operator are an engineering degree or a 'special technical education standard'. The State Committee on the Supervision of Operational Safety in Industrial and Atomic Power Engineering provides specific training on the regulatory requirements and local rules of the facility, and also sets periodic examinations on these subjects which operators have to pass to retain their licence to operate. Initially, these examinations had to be taken every 3 years, but the current requirement is an annual examination. Every 3 months, operators have to attend a safety meeting chaired by the unit head. A very low turnover of staff has been experienced and nearly all the operators have been employed since startup of the facility.

Regulations and local rules require that the operators and assistants wear a direct reading quartz fibre electrometer (QFE) and either a film badge or a thermoluminescent dosimeter (TLD). Three portable dose rate monitors of the SRP68 type are available, which are calibrated annually by a laboratory at the Ministry of Health in Minsk.

All the safety systems are positively checked by a member of staff on a monthly basis, and an external organization carries out preventive maintenance every 3 months. Indeed, the facility's log book indicated that, on the day before the accident, such maintenance work had been carried out and the standard found to be acceptable.

3. RADIATION ACCIDENT

3.1. INITIATING EVENTS

The operator involved in the accident was a 34 year old man. He had a degree in engineering and was the most experienced operator at the plant, having commenced employment at the facility during its construction. Thus, he was completely familiar with the facility, the hazards and the safety systems. He was regarded as a skilled operator capable of dealing with operational problems and meeting production targets.

He and an assistant were working on night shift and the accident occurred at approximately 03:40 hours on the morning of Saturday, 26 October 1991. A jam occurred in the transport mechanism because of decoupling of the linkage arms of two carriers, as previously shown in photograph 5. Although this could have been noticed by continual observation of the position indicators on the control panel, there was no intrusive alarm. The operator was in the control room reading a newspaper. While loading the product into the carriers, the assistant first became aware of the jam on hearing the characteristic change in noise of the drive motor. The assistant shouted to the control room to alert the operator, who at the time was not wearing his TLD personal dosimeter or a QFE, both of which were in his lunch box.

3.2. ENTRY AND EXPOSURE

As in many accident investigations, ambiguities exist in the description of exactly what took place during the accident. The operator stated that his own recollection of events was somewhat hazy as he was feeling sleepy at the time. However, both the authorities and those who treated the operator reported that he also appeared reluctant to give any precise details. In the following description,

distinctions are made between the known facts, the probable actions taken and the range of possible options needed to produce the end effect.

There is a high probability that, on being told of the product jam, the operator pressed the 'source down' button before attempting to rectify the situation. He admitted that he did not take the key from the control panel and after the accident it was found in the control panel in the 'ready' position. He may have left it in this position in order to speed up the procedure for restarting irradiation once the transport jam had been cleared, i.e. circumventing the search and lock-up procedures.

As the operator did not take the key with him, he would have had to cross the pit at the maze entrance without the motorized floor section being moved to the closed position. After the accident, no plank or board for bridging the gap was found. However, at the time of the accident the pit was narrower than shown in photograph 9 and the drive motor for the moveable floor was inside it. All evidence indicates that the operator crossed the pit by stepping on to the top of the motor and that he took the portable dose rate monitor with him. After the accident, this monitor was found at the point where the maze entrance joins the irradiation chamber, and was subsequently confirmed to be in proper working order. The next safety feature he would have encountered was the pressure plate in the floor, and it is difficult to envisage how he could have avoided stepping on this. Subsequent tests showed that the pressure plate was in correct working order (tested 25 times) and that it was impossible to jump over it (its position prevented a possible run-up).

Theoretically, it would be possible, but extremely difficult, to cross the pressure plate using the product transport system. This could not have been done while holding a dose rate monitor and there would have been no reason to attempt such a move because of the danger involved.

At this point, even if in his sleepiness the operator had forgotten to lower the source rack at the control panel, it should automatically have returned to the safe position. There remains a possibility that the source movement mechanism had jammed so that the source rack was exposed to some degree. However, the problem appears to have rectified itself, because after the accident it was observed that the source rack was in the 'fully shielded' position; after testing it was found to be operating satisfactorily. Thus, it can be concluded that in all probability the source rack was in a safe position when the operator entered the irradiation chamber.

On entering the irradiation chamber, the train of product carriers would have obscured the operator's view of the source rack had it been in the irradiation position. However, had he looked, he would have seen the position of the counterweights, indicating the position of the source rack.

He walked around the back of the product transport system to where the blockage had occurred (photograph 11(a)) and tried to release the jammed carriage couplings (photograph 11(b)). After about 1 minute, he developed an acute headache and pain in his joints and gonads. He felt generally unwell and had difficulty in breathing. He turned his head to the left and saw the source rack in the irradiation

position. He did not press the nearby emergency 'stop' button, but ran out of the irradiation chamber and told the assistant that he had been irradiated.

It is agreed by all concerned that when he entered the irradiation chamber the controls were in a position such that the source rack should have been in the storage position. However, with the key in the control panel and turned to the 'ready' position, exposure was imminent. This leaves the following questions unanswered:

(1) What caused the source rack to rise to the 'up' position?
(2) Why did the operator not notice the source rack being raised?

Dealing with what caused the source to move to the irradiation position, this may have resulted from:

(a) Accidental and unnoticed depression of the exposure button (several buttons are close together);
(b) Temporary failure of a component in the control circuit, e.g. jammed contacts;
(c) The logic of the electrical circuits (as installed), together with the unusual combination of control settings and safety devices, such that power was provided to the source drive mechanism.

As to the question of why the operator did not notice the source rack being raised, this would not have been accompanied by any audible alarms inside the irradiation chamber and there were no warning lights to indicate its position. The drive mechanism for moving the source rack would certainly have made a noise, but this may have been masked by the noise from the ventilation system and the product transport system (if he had failed to stop it). In addition, he may have been in the maze entrance at the time and therefore been unable to clearly hear the mechanism.

While it has not been possible to accurately chronicle the sequence of events leading to the irradiation, it is clear that:

(i) The specified safe operating procedures were not followed and the safety features were circumvented;
(ii) The safety features could be improved to prevent circumvention (see Section 5).

3.3. RESPONSE TO THE ACCIDENT

Immediately after the operator exited the room, telephone calls were made to the local hospital and the police.

An ambulance was sent and within 20 minutes he was admitted to the hospital in Nesvizh. It was immediately clear to the medical staff, from his description of the accident and the initial symptoms of vomiting, headache, fatigue and tachycardia, that he had been severely irradiated. The medical staff made the decision to refer

him to specialists for treatment, and arrangements were made for him to be moved, via Minsk, to the clinic at the Biophysics Institute in Moscow. He arrived there at 19:00 hours the same day. Details of further medical management are given in Section 6.

The police and the factory reported the accident immediately to the Ministry of Health via their 24 hour emergency number and relevant staff were contacted at home. The factory was asked not to use the facility and to leave all the controls and items as they had been at the time of the accident. On the morning of the same day, before his transfer to Moscow, the operator was interviewed and some dose measurements were taken as part of reconstruction of the accident (see Section 4). Also on the same day, the State Committee on the Supervision of Operational Safety in Industrial and Atomic Power Engineering set up a commission to investigate the accident. The commission included representatives of the regulatory authorities, the plant management and the trade unions. Operation of the irradiation facility was suspended and the plant's licence withdrawn pending implementation of the commission's recommendations for improvement, which included:

(1) Enlarging the size of the pit and moving the motor;
(2) Providing an audible alarm for movement of the source rack within the facility;
(3) Providing visible warning signals inside the facility to indicate the position of the source rack.

It is understood that all these recommendations were implemented and by the time of the post-accident review in November 1992 the plant was back in full operation. In the interim, the operator had died in hospital, having survived 113 days.

4. DOSE ESTIMATION

For convenience, this section brings together the number of attempts that were made to estimate the dose received. However, these estimates spanned a period of time, and it is relevant to Section 6 that the exact timing of when this information became available to the medical team in Moscow be borne in mind.

4.1. PHYSICAL RECONSTRUCTION OF THE ACCIDENT AND CALCULATIONS OF THE EXPOSURE DOSE

On the morning of the accident, the operator (in hospital) and the staff (at the plant) were interviewed in an effort to determine exactly what had happened. In particular, information was sought on where the operator had been standing and the duration of exposure. The initial estimate of exposure time was in the range of

1–4 minutes in the irradiation chamber. However, reconstruction of the probable actions suggested 1½ minutes as a reasonable estimate.

A few simple measurements were made using TLDs located at positions representative of the operator walking around the outside of the carriages in the irradiation chamber and the time he spent trying to rearrange the carriage couplings. From these measurements, the effective dose was estimated to be 12–15 Gy. This was communicated to the Institute of Biophysics in Moscow by telephone and a short report followed several days later. The report did not include any photographs or detailed drawings of the facility, but a simplified schematic diagram of the exposure position was attached.

Subsequently, engineers from the designers of the facility visited the Institute of Biophysics to help the doctors and physicists estimate the dose. As a result of these discussions, the isodose rate distribution closest to the source was constructed; from associated calculations, the effective dose was estimated to be in the range of 8–16 Gy.

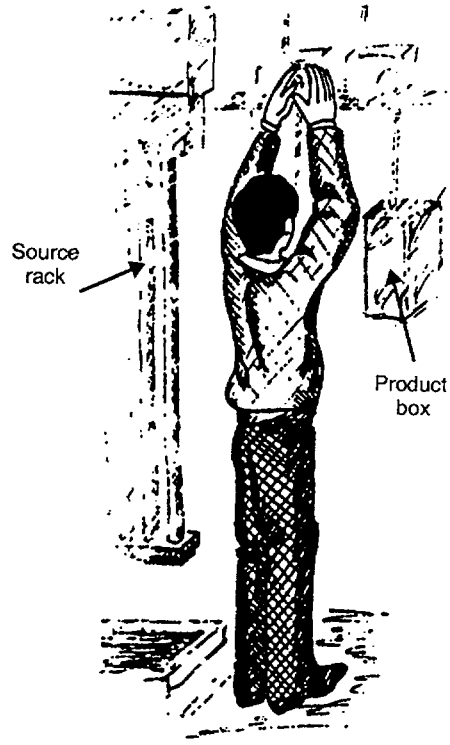


FIG. 5. Position of the operator during exposure (according to the information given to the medical team shortly after the accident).

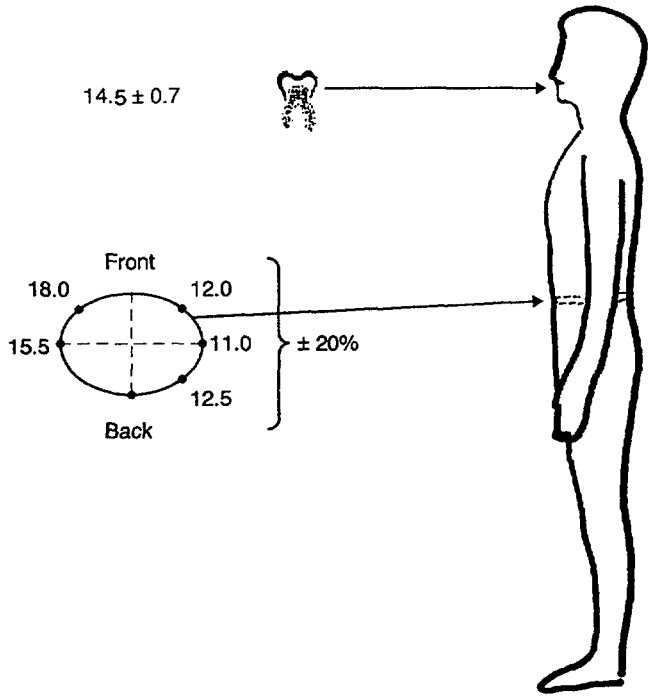


FIG. 6. Exposure doses (Gy) estimated by ESR.

It is relevant to note that the information given in Figs 5 and 6 suggests that the operator had been very close to the source, about 0.5 m from one edge in free space, without any shielding. Reconstruction of the accident during the post-accident review visit identified that this was not a true representation of the exposure conditions. Photographs 11(a) and (b) depict the likely positions of the operator during the major part of his exposure. This is discussed further in Section 4.4.

4.2. BIOLOGICAL DOSE ASSESSMENT

When the operator was in Moscow, samples were taken for analysis of chromosome aberration in the blood and bone marrow lymphocytes. Some problems arose in getting the cell cultures to grow, but by day 5 a dose equivalent of 11 $\pm$ 1.3 Gy was estimated. In addition, a review of the neutrophil and lymphocyte blood counts between days 1 and 8 was made that suggested a whole body dose in the range of 9–11 Gy (see Section 6).

As the patient's symptoms progressed, further biological indicators of dose were given, in particular the way in which erythema of the skin and subsequent lesions progressed; these provided good indications that the left side of the body had been closer to the source than the right side. These symptoms did not develop uniformly, with an apparent increased reaction on the left elbow, the left buttock and the lower left leg, the latter two reactions suggesting sharp cut-off points that were indicative of some shielding, although conflicting factors arose after treatment (see Section 6.5 for further discussion).

4.3. ELECTRON SPIN RESONANCE STUDIES

The electron spin resonance (ESR) technique can be used to estimate doses [14, 15]. Some clothing materials are particularly suitable for ESR measurements and, since clothes are directly linked to the movement, orientation and time of exposure of a person, spatial assessments of dose can be made.

Two days after exposure, the clothing worn by the operator at the time of the accident was received by the Dosimetry Laboratory at the Institute of Biophysics, Moscow. His vest, which was made of cotton mixed with viscose, was chosen as the most suitable apparel from the point of view of radiosensitivity. Samples were taken at waist level and analysed by ESR. The results, shown schematically in Fig. 6, were telephoned to the medical team on 30 October (day 4); these are consistent with the later skin effects discussed in Section 4.2.

Following the death of the patient, a tooth, together with nail clippings from the fingers and toes, were taken for ESR analysis. The dose estimated from the enamel of the tooth (left molar) was 14.5 ± 0.7 Gy. For the nail clippings, the length of time that had passed since exposure precluded estimation of the absolute dose, but did give an indication of the relative dose. As with previous measurements, there was a 20–30% increase in dose on the left side relative to the right side of the body. However, the estimated hand dose was 50% greater than that for the feet.

4.4. EXPOSURE FACTORS

The operator's exposure falls into two main parts: (1) while moving in and out of the irradiation chamber; and (2) while trying to rearrange the carriage couplings.

For item (1), the exposure time is very uncertain, as it is not known how long the source was in the 'up' position. During this phase, the operator would have been shielded to some extent by the loaded product carriages, possibly equivalent to a half value layer. However, at around waist level there would have been a gap of about 10 cm between the upper and lower boxes. The effective gap may have been larger because of air spaces at the top of the lower product boxes. Similarly, there would

have been higher dose rates to the feet because of the 20 cm clearance of the boxes above floor level.

The same considerations apply to his exposure while rearranging the carriage couplings (item (2)). However, other local shielding would have been present. The narrow angle of exposure relative to the plane of the source rack is such that small changes in position could have had a significant effect on the shielding, i.e. from attenuation provided by the stainless steel structure of the source rack and the counterweight frame, from the counterweights themselves, from the product carriages and from self-absorption in the source.

Thus, the operator was exposed in a complex geometrical pattern that was changing with time and in which small movements could have significantly affected the dose received. This is one of the reasons why the ESR measurements were of particular importance.

The initial physical dose assessment provided useful information to the medical team. However, as mentioned in Section 4.1, their perception of the exposure environment differed somewhat from the real situation at the plant. Had there been additional, more detailed dose reconstruction, involving both medical and physics staff at an early stage, some medical queries regarding apparent variations in skin dose may have been resolved. During the post-accident review visit to the plant, relevant items were photographed and video taped. The latter, in particular, when shown to the medical team, was clearly useful in helping to match the observed clinical effects to the possible exposure conditions.

5. LESSONS LEARNED

The primary objective of carrying out a post-accident review is to identify the lessons that can be learned from an accident and then to disseminate this information to all who may benefit from it. One of the problems encountered in this post-accident review was that, while the many individuals in the various organizations concerned were co-operative in providing interviews, there was a lack of readily available and coherent data and documentation. These are relevant to safety and are reflected in the observations and recommendations (in italic type) outlined in Sections 5.1 to 5.7; they are presented under topics relevant to irradiation safety. Although it is clear where the prime responsibilities lie for implementing some of the recommendations, many, if not all, of these have implications for designers, manufacturers, operating organizations, competent authorities and international authorities.

5.1. PRIORITIES

(1) This fatal irradiator accident is the fifth to be reported, joining those at the Stimos plant, Italy [4]; in Kjeller, Norway [5]; in San Salvador, El Salvador [2]; and at the Sor-Van facility, Israel [3]. In addition, a number of irradiator accidents have given rise to serious, but non-fatal, radiation injuries [6–8].

A clear lesson to emerge from the accidents that have occurred over the past few years is that radiation safety in irradiation plants must be given a much higher priority by all concerned, i.e. manufacturers, operating organizations, competent authorities and international bodies.

(2) The report on the San Salvador accident stated that "Many of the recommendations cover procedures and practices already considered to be essential to safe operation". This statement was as valid for the Sor-Van accident as it is for the accident reported on here. The IAEA has published guidance in this area in Safety Series No. 107 [9], which is recommended to those with the responsibility for irradiator safety.

It is strongly recommended that:

(a) A thorough review of radiation safety be carried out at each existing irradiator to take account of: (i) the lessons learned from this and previous accident reports, and (ii) the current guidelines from the IAEA, manufacturers and competent authorities;

(b) All designs of facilities should be in accordance with the standard of Safety Series No. 107 [9].

(3) The prime responsibility for implementing recommendation (2) rests with the operating organizations; however, it is recognized that the expertise available varies significantly, and that the operating organizations may need to seek expert advice.

In planning their work programmes, manufacturers, competent authorities and international organizations should take cognizance of the increased priority advocated in recommendation (1) and the need to respond to operating organizations' requests for expert advice. Priority should be given to those facilities that have been in use for a number of years, and particularly those in developing countries where the radiological infrastructure is probably not as strong.

5.2. INTERACTION OF THE TRANSPORT MECHANISM AND THE SOURCE RACK

(4) In a number of the previous irradiator accidents, a product jam had obstructed the free movement of the source rack and acted as the initiating event. Since

source rack obstruction had been a problem in the early years of the Nesvizh facility, it should be noted that one of the lessons learned from these obstructions had been the provision of a metal grid to prevent any future occurrences.

(5) In this accident it was a product jam, specifically decoupling of the product carriers, that caused the initiating event. It is understood that such decouplings had taken place quite frequently at the Nesvizh facility. Any product jam requires entry of the operator to the irradiation chamber and rapid rectification of the problem in order to minimize lost production time. While the design of the facility's safety systems should ensure safe entry to the irradiation chamber at all times, from the safety and operational viewpoints the need to enter the irradiation chamber should be minimized.

Transport mechanisms and their maintenance should be designed to minimize the potential for product jams.

(6) At the Nesvizh facility, monitoring the progress of the product boxes had been reduced to a minimum. However, even in the original design the system required constant vigilance at the control panel and did not provide any intrusive alarm to indicate a problem. More importantly, there was no interlock between the product transport system and the source control panel to automatically move the source rack back into the storage position in the event of a product jam, and then to reset the controls so that the search and lock-up procedures could be followed. The system relied on the operator to manually initiate the source rack movement and to follow the entry procedures — something clearly not done by the operator in this instance.

To minimize the possibility of operators circumventing safety procedures, irradiators should be designed to ensure that:

(a) There is a sensing system to detect product jams;

(b) Detection of a product jam automatically results in: (i) an intrusive alarm being sounded, (ii) the source rack being fully returned to the safe position, and (iii) resetting of the controls so that the source cannot be re-exposed without the search and lock-up procedures being followed.

5.3. SAFETY SYSTEMS

(7) Safety Series No. 107 [9] recommends a safety philosophy that is based on the concept of defence in depth. The components of the safety system should provide:

(a) *Redundancy:* use of more than the minimum number of items of equipment to achieve a given safety function;

(b) *Diversity:* incorporation of different attributes into the redundant systems as components that perform the same function;

(c) *Independence:* achieved through functional isolation and physical separation of components.

(8) Although gamma monitors had been installed inside the irradiation chamber, their signal was not being used to the best effect. First, the ratemeter displaying the reading could be switched between the output from the two detectors without it being clear to the operator which one was being displayed. Second, and more important, there was no connection between the dose rate control panel and the source control panel.

The safety system must include a monitoring system with built-in redundancy to detect the radiation level in the irradiation chamber. The monitoring system should be integrated with personnel access safety features and warning systems such that:

(a) If the system detects a radiation dose rate above a specified level, or malfunctions, or is turned off, access to the irradiation chamber is prevented;

(b) If the specified radiation level is exceeded, the system should generate visible and audible alarm signals and termination of the irradiation should be shown on the console.

(9) It appeared that, in the 'ready' position of the key switch, the source could be cycled up and down without any audible alarms sounding in the irradiation chamber. In theory, other safety systems should prevent anyone entering the irradiation chamber when movement of the source rack is taking place; therefore, at first sight the alarms might be considered unnecessary. However, as can be seen from this accident, reliance on this being the case is not acceptable and provision of an alarm would have advocated the *redundancy* and *diversity* principles. Indeed, had such an alarm been provided it would probably have prevented the accident.

An alarm that is audible both inside the irradiation chamber and at all access ports must be provided to indicate when the source is neither fully shielded nor in the fully exposed position.

(10) In this and in the earlier accidents in San Salvador and at Sor-Van, ways of circumventing parts of the safety system were found. This is yet another reason for pursuing a policy of *redundancy, diversity* and *independence* in safety systems. However, attention should also be given to assessing how easily safety features can be overcome. For example, in retrospect it is clear that the electric motor located in the pit provided a way of circumventing the safety feature, as indeed a commonly available item such as a ladder would have done.

The effectiveness of safety features should be regularly reviewed. This is particularly important at the design stage, but is also relevant to operating organizations and regulators during the life of the plant.

5.4. INSTRUCTION AND TRAINING OF STAFF

(11) Although there appears to have been a structured training programme at the facility, any accident where the safety procedures have obviously not been followed must call into question the effectiveness of instruction and training. More generally, there will always be a need to review training programmes. The effectiveness of training, and indeed of many other safety aspects, can depend on having a coherent, up to date instruction manual covering all aspects of the plant.

(a) Training should be reinforced regularly and updated when necessary. Particular emphasis should be placed on the functions of the safety systems and procedures, and on the potential consequences of failure to operate them correctly.

(b) A comprehensive instruction manual covering plant layout, safety and warning systems, operating rules, emergency procedures and training should be kept up to date and be readily available to the workforce.

5.5. MONITORING

(12) In the earlier accidents, lack of a portable monitor was a contributory cause; this does not appear to have been the case in this accident. However, it was noted that the dose rate meters available were bulky, which may account for their not always being used. An additional safety precaution should be personal alarm monitors.

(a) Personal alarm monitors should be routinely worn by operators throughout their work shifts;

(b) Procedures should be drawn up to ensure that the personal alarm monitors are routinely checked for satisfactory operation;

(c) Personal alarm monitors should be used in addition to not in place of portable monitors on entry into the irradiation chamber.

(13) Failure of staff to wear their personal monitoring badges while at work is a common feature found in investigations of accidents and incidents. This leads to loss of dose information, which could be valuable in responding to an accident. However, it is also an indicator of the general lack of attention that staff pay to radiation safety.

The importance of wearing personal monitors by staff should continually be reinforced by managements and regulators.

(14) Assessments of dose distribution at waist level, using ESR techniques on the clothing worn by the operator, proved to be valuable. Indeed, in retrospect, it would have been useful to have extended measurements to cover all parts of the body.

When choosing coveralls, etc. to be worn by irradiation plant workers, consideration should be given to materials that facilitate ESR measurements.

5.6. INSPECTION AND AUDITS

(15) In this and in the earlier accidents it has been shown how, over time, workers can become complacent towards hazards and start to ignore safety aspects, e.g. bypassing interlocks and failing to wear personal monitoring badges. Routine auditing can bring such matters to light. Audits are also an indicator to staff of the importance that management attaches to radiation safety, thus promoting an ethos of safety.

Operating organizations should carry out routine internal audits (at least annually) of all aspects of radiological safety. A formal report should be presented to the management and any appropriate action taken.

(16) The primary responsibilities for safety rest with the manufacturer and the operating organization; nevertheless, the regulatory programme enforced by the competent authority can influence how well these responsibilities are discharged.

Competent authorities should ensure that they have an appropriate programme of inspection and enforcement for irradiation facilities. Existing programmes should be reviewed in the light of this and other accidents.

5.7. CO-OPERATION

(17) The medical team's perception of the exposure environment differed somewhat to the real situation at the plant. Provision of photographs or video tape footage of the site of an accident can be helpful to the medical team's understanding of the reasons for or prediction of the effects. In some cases it may be useful for both medical and physics staff to be involved at an early stage of accident reconstruction.

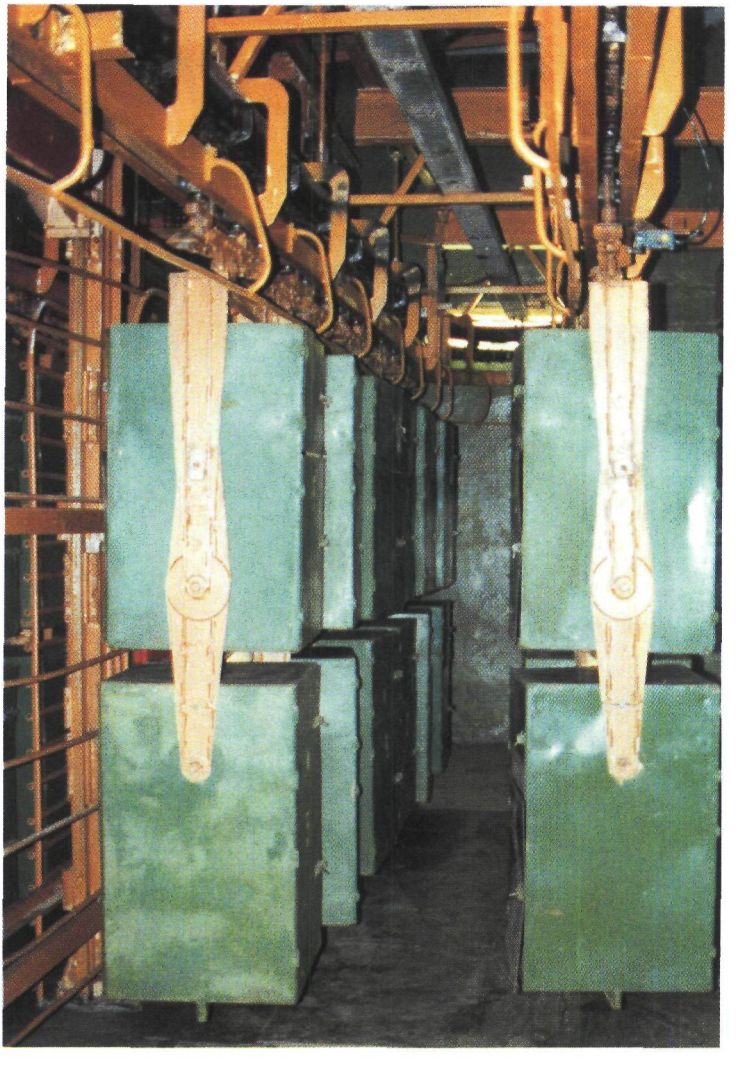
It is always useful to have a multidisciplinary team involved in accident reconstructions.

Text cont. on p. 45.

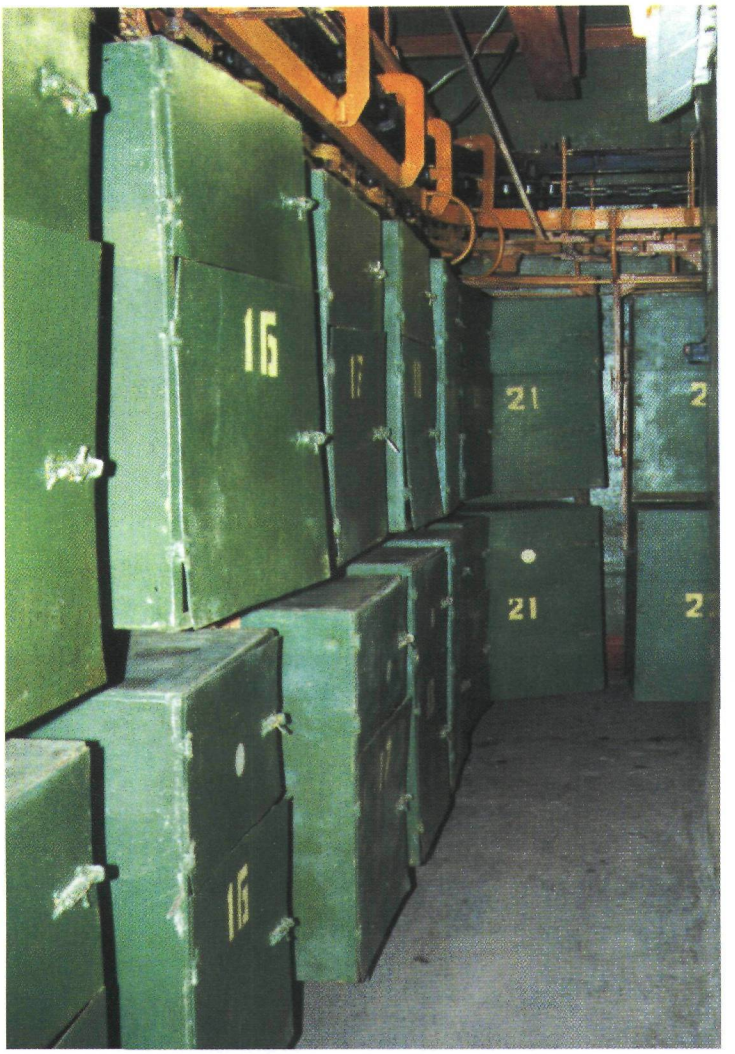
PHOTOGRAPHS

Photograph 1. Source rack frame and protection grid. The orange metal frame is the upper part of the shielding plug for the source rack. Spaces at both sides of the frame allow the counterweights to slide down.

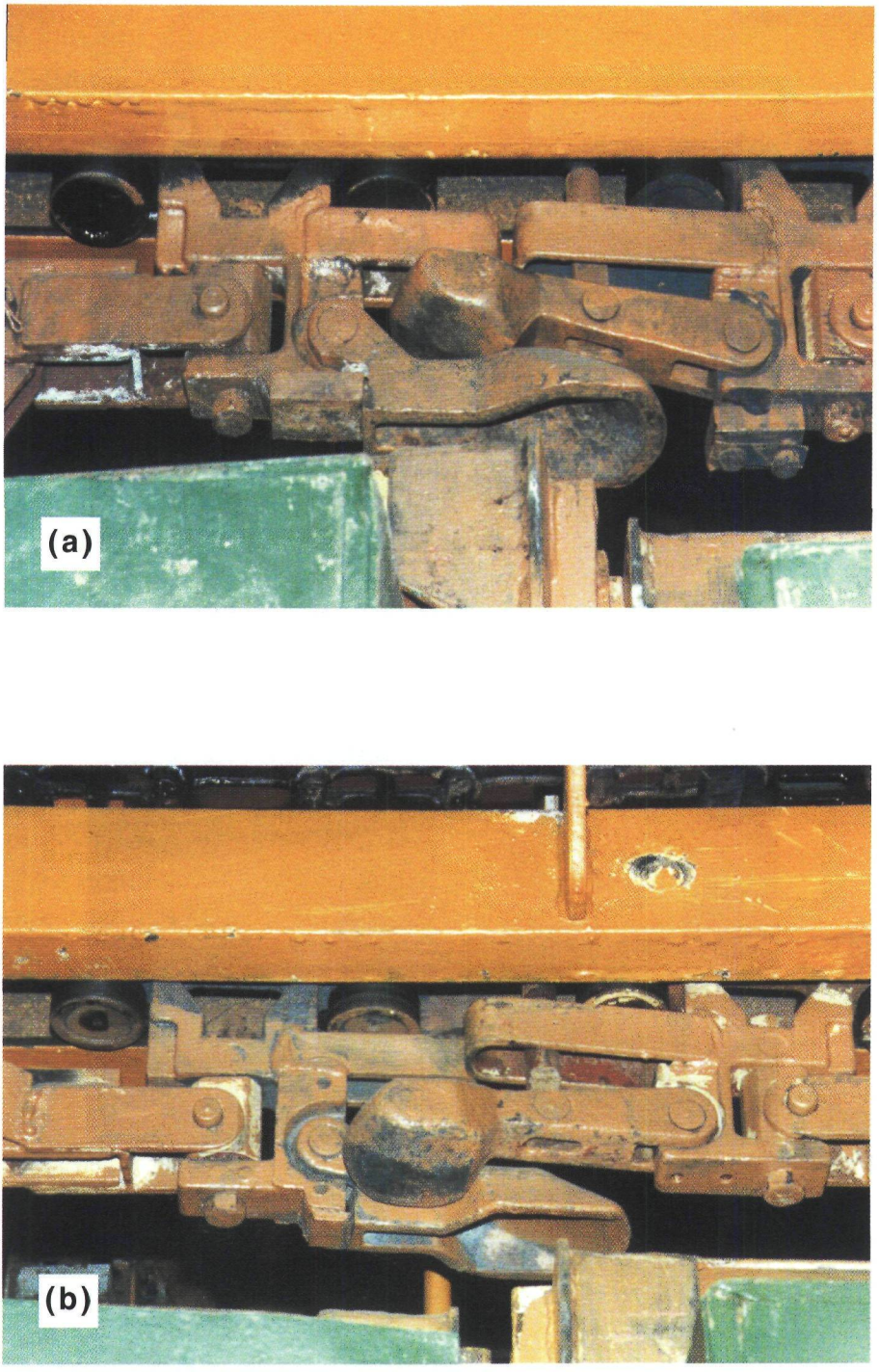
Photograph 2. Counterweight in the upper position (source in the shielded/storage position).



Photograph 3. Conveyor system with cradles and transport boxes.



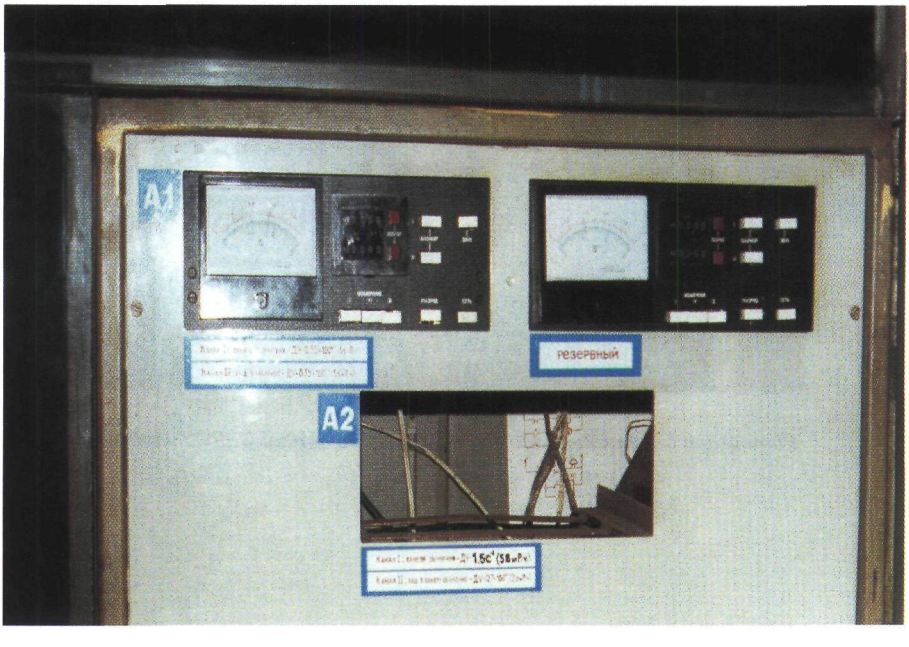
Photograph 4. Distribution of carriages inside the irradiation chamber, indicating the confined space when fully loaded.



Photograph 5. Linkage arms: (a) normal position; and (b) abnormal position.

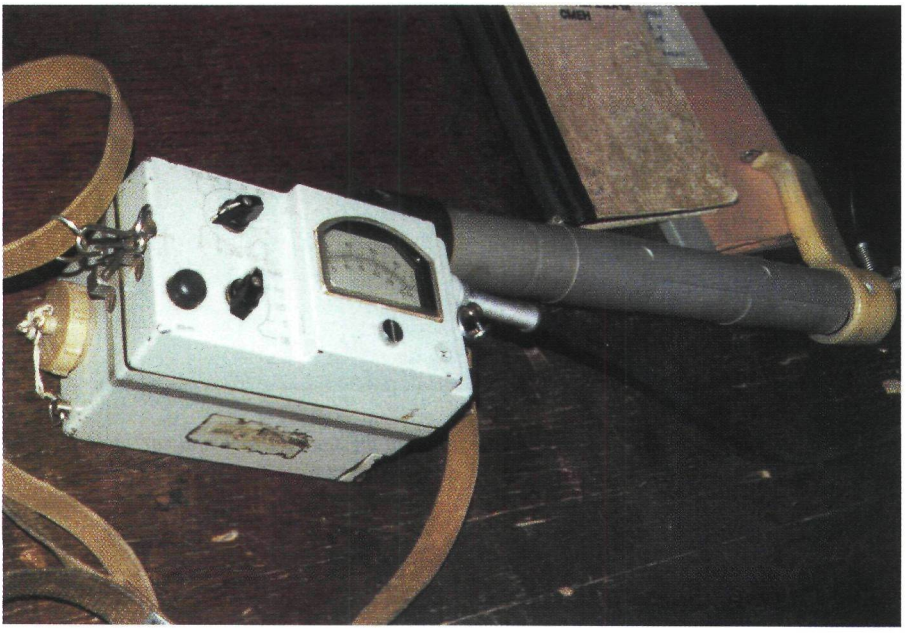
Photograph 6. Operator restoring conditions to normal with a metal rod.

Photograph 7. Lead shielded gamma monitoring probe inside the irradiation chamber.

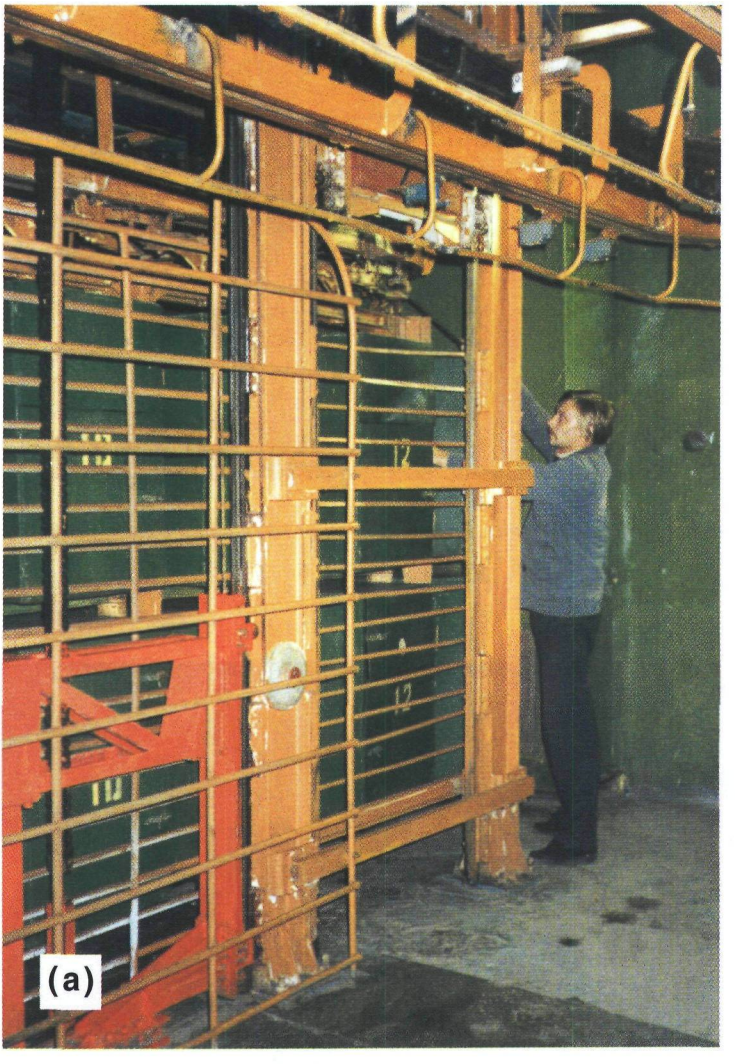


Photograph 8. Gamma monitoring probe system in the control room.

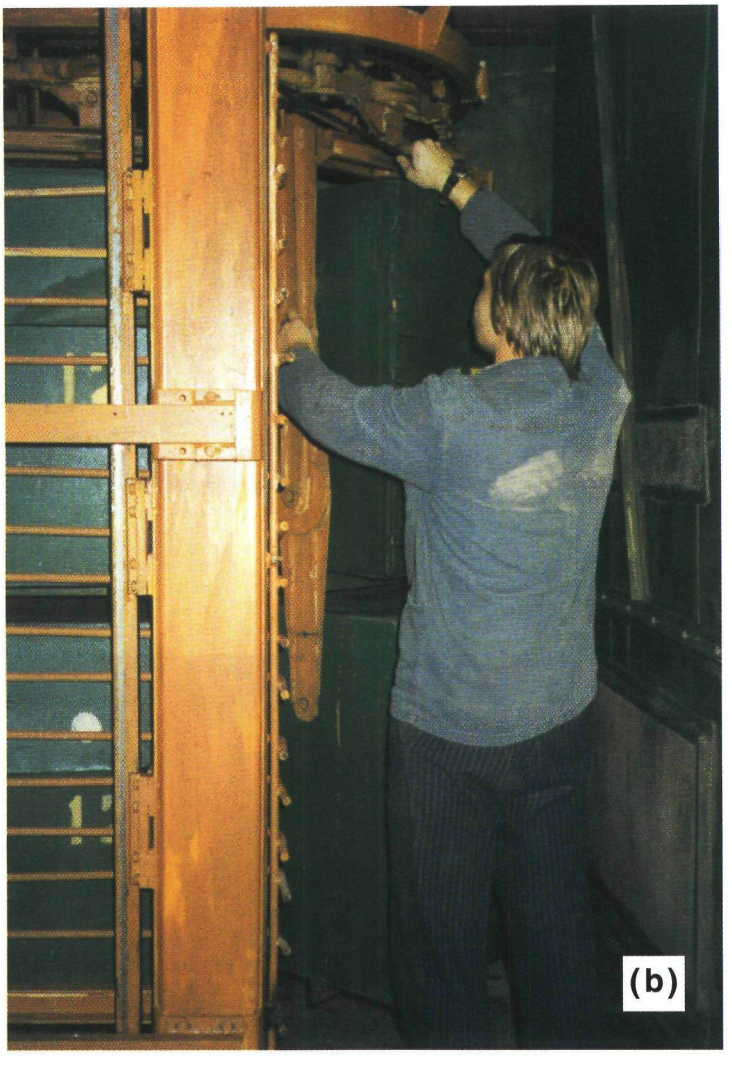
Photograph 9. Dry pit with moveable floor section at the maze entrance.



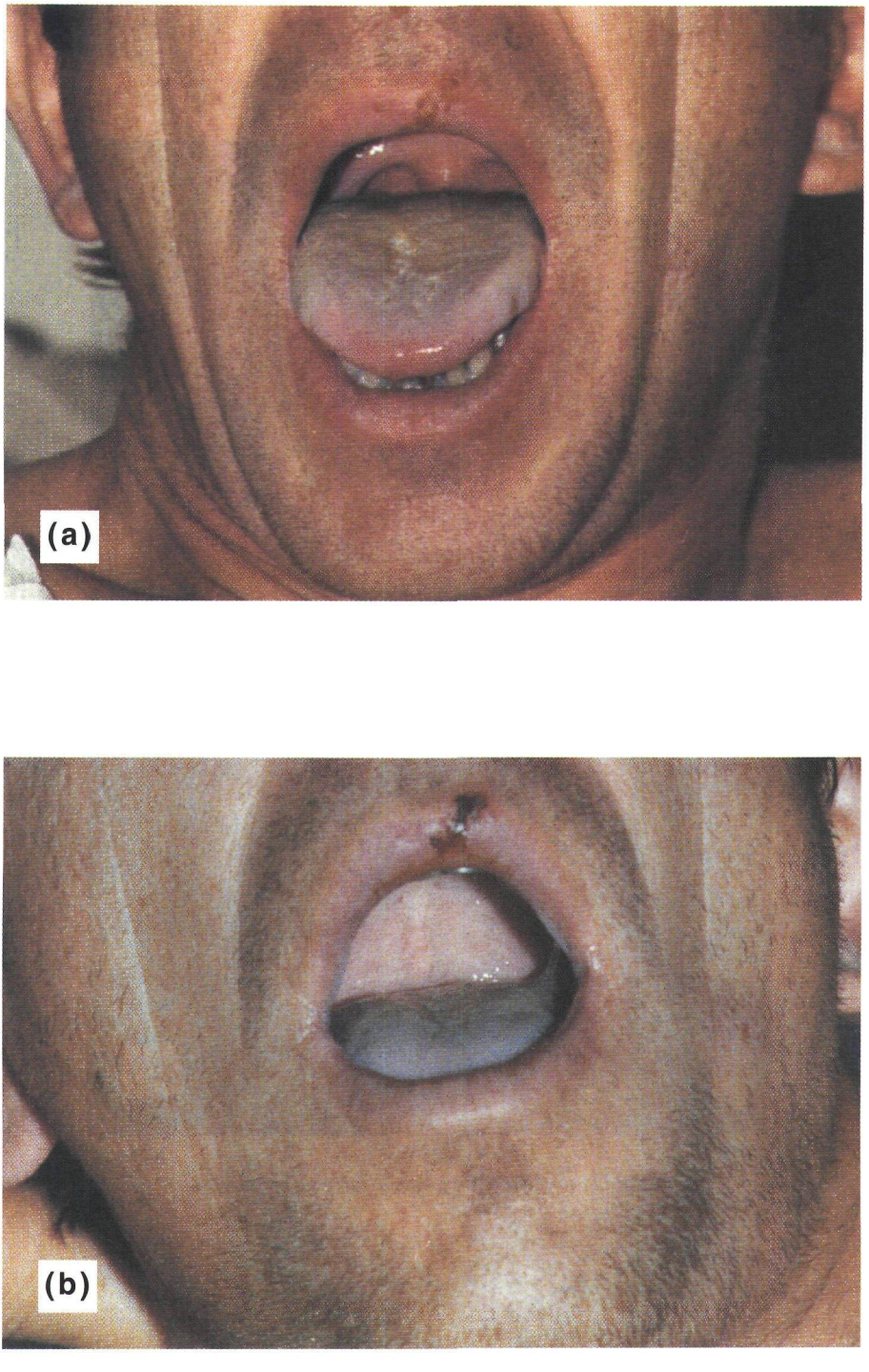
Photograph 10. Portable dose rate monitor used during the entry procedure.



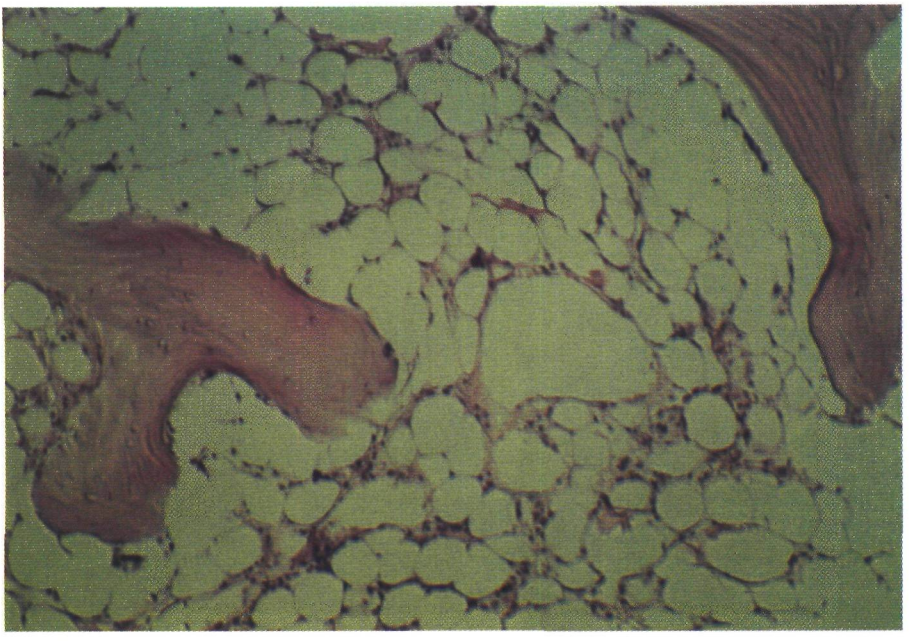
Photograph 11. Position of the operator in relation to the source frame and carriages during reconstruction of the accident: (a) at the back of the product transport system; and



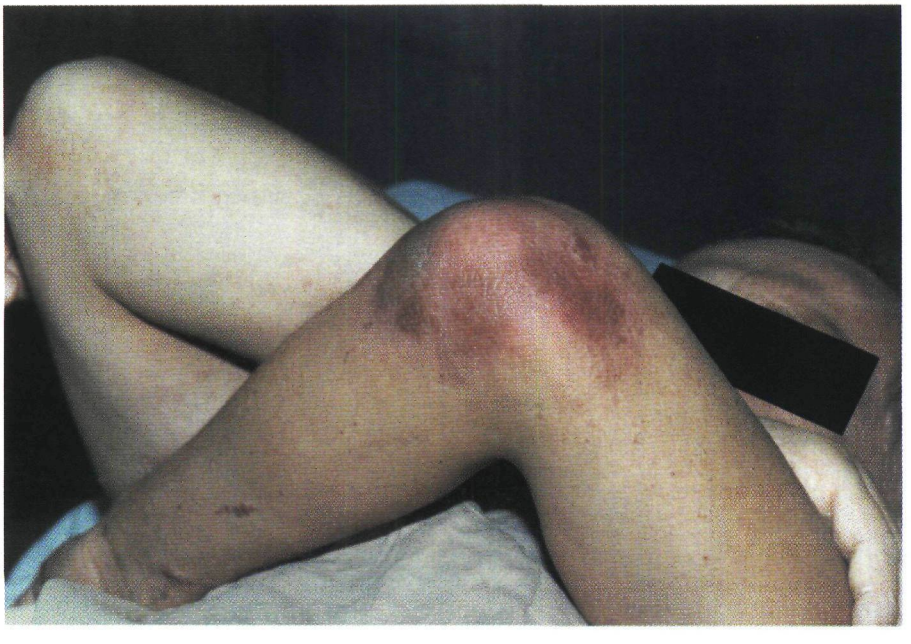
(b) trying to release the jammed carriage couplings.



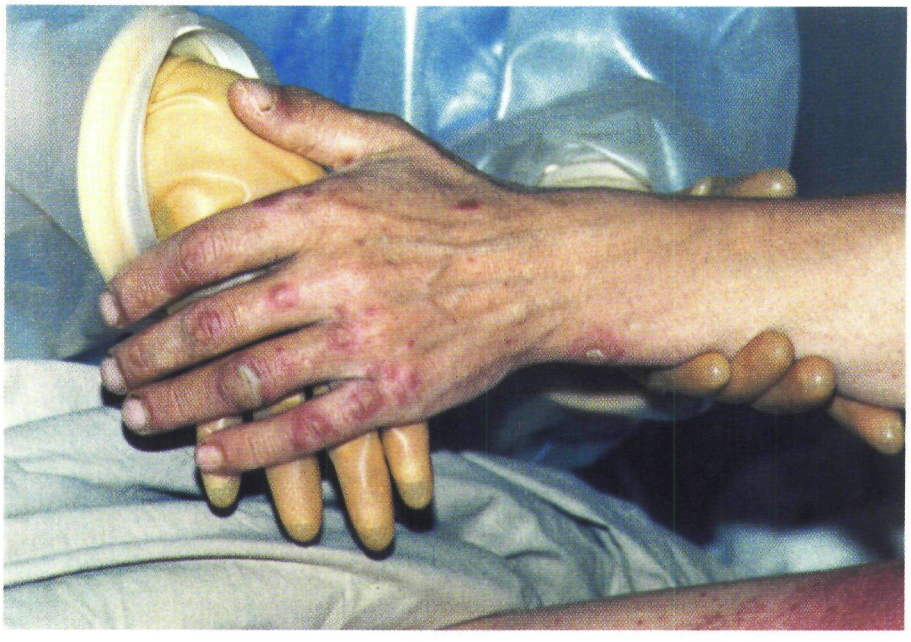
Photograph 12. Herpes labialis and mouth mucositis: (a) day 4; and (b) day 6.



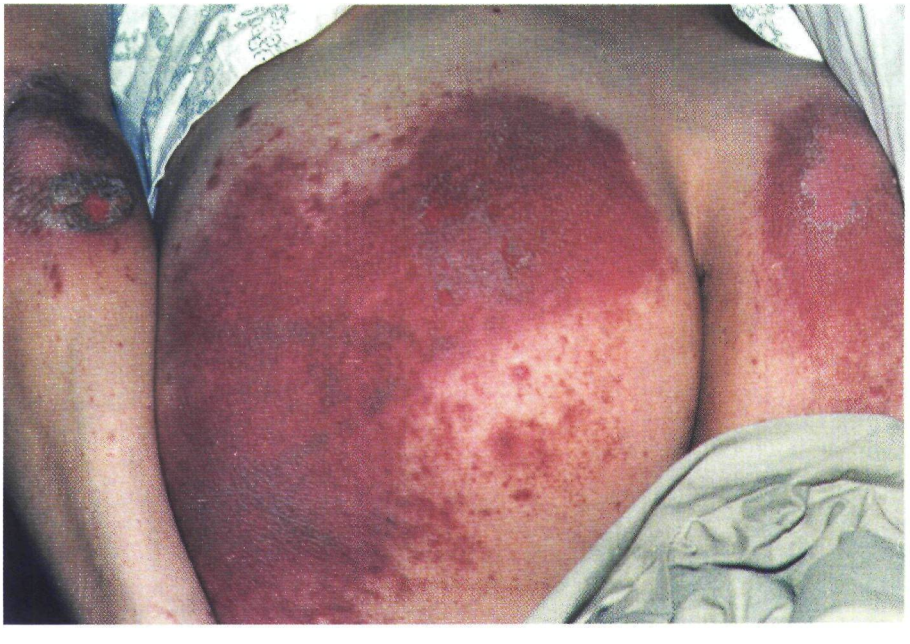
Photograph 13. Histology of the bone marrow biopsy: complete cell aplasy, with only a few macrophages to be seen (×100) (day 16).



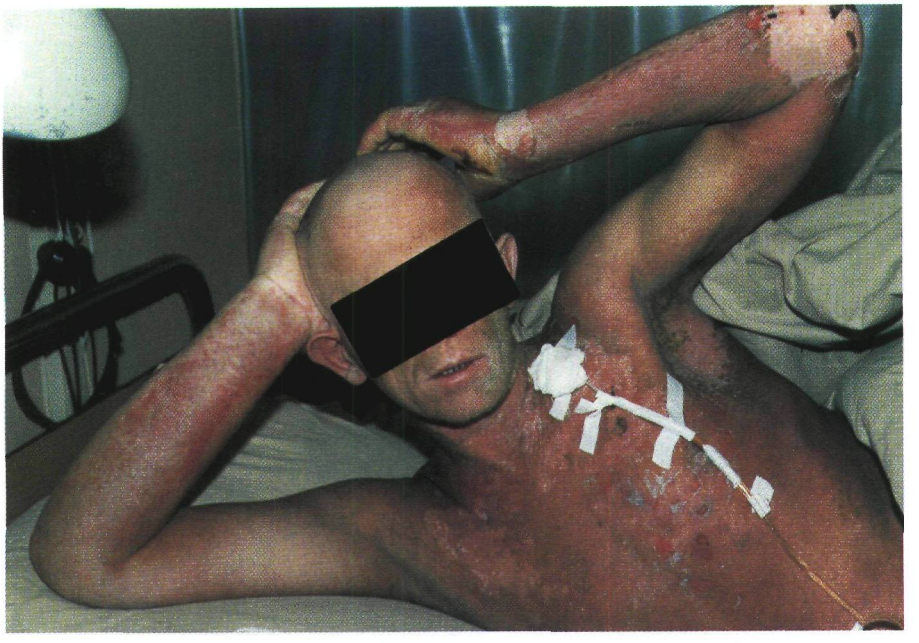
Photograph 14. Skin injury to the left elbow (day 16).



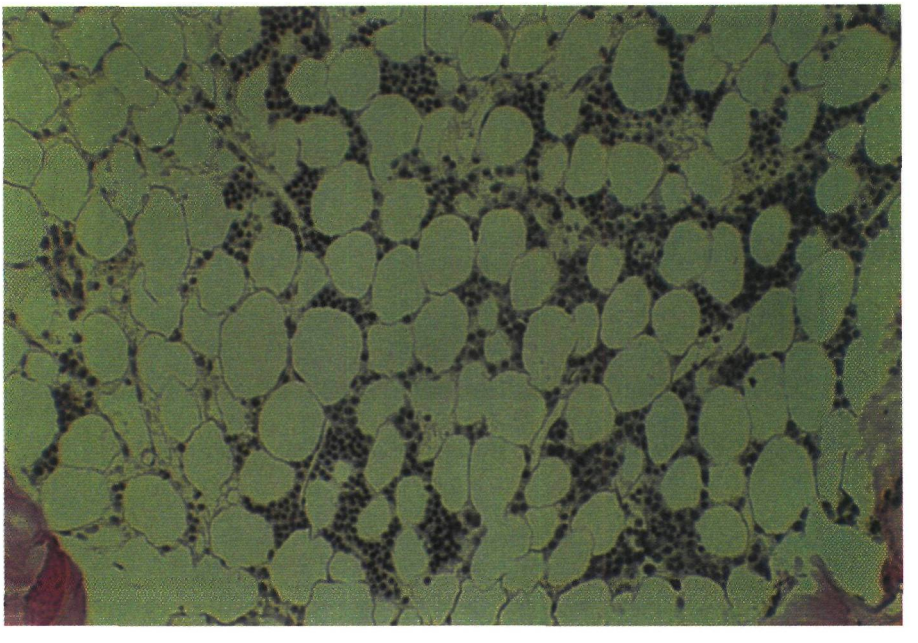
Photograph 15. Skin injury to the left hand (day 18).



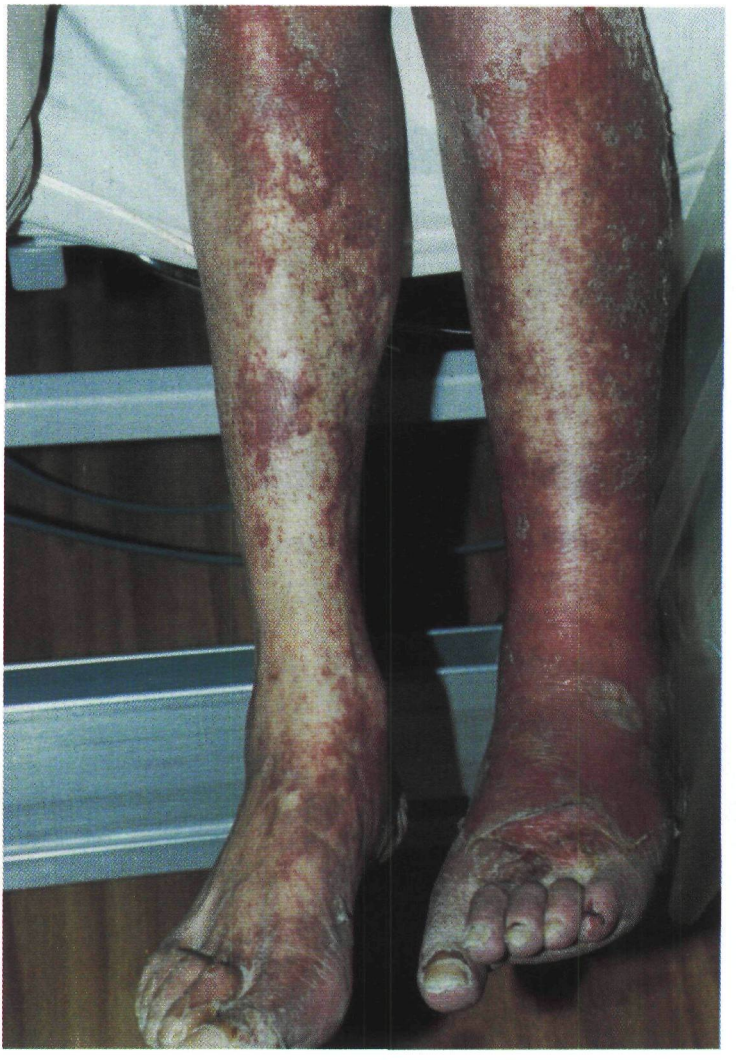
Photograph 16. Skin injury to the buttocks (day 18).



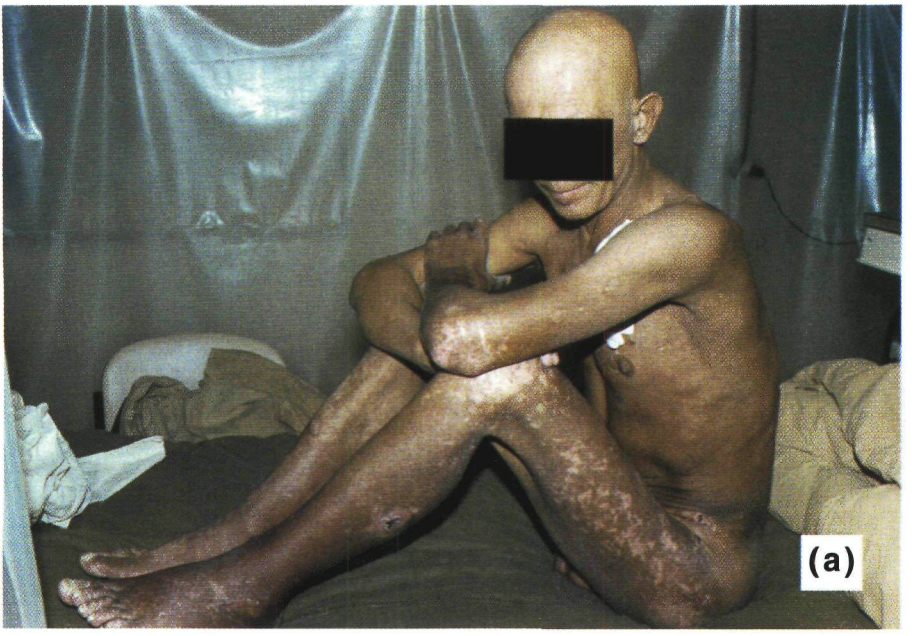
Photograph 17. Almost total body erythema and other injuries (day 32).

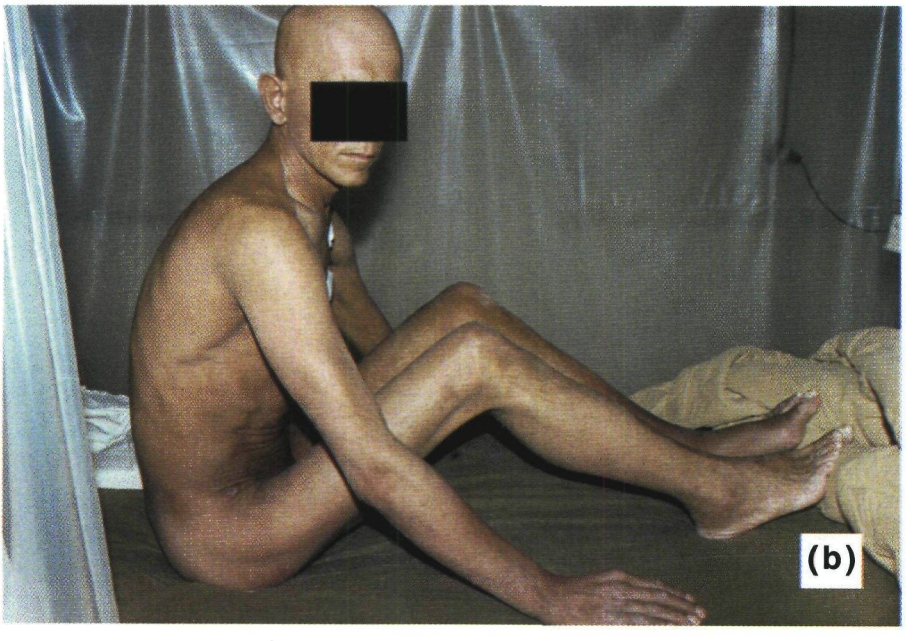


Photograph 18. Histology of the bone marrow biopsy: a noticeable increase in cellularity (×60) (day 44).

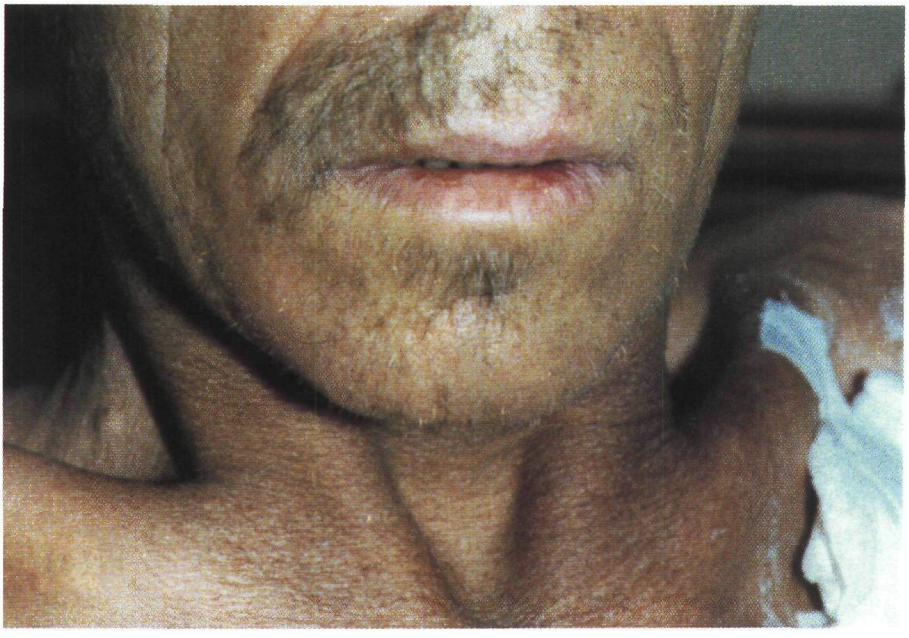


Photograph 19. Skin injury to the legs; phlebitis of the left leg (day 53).

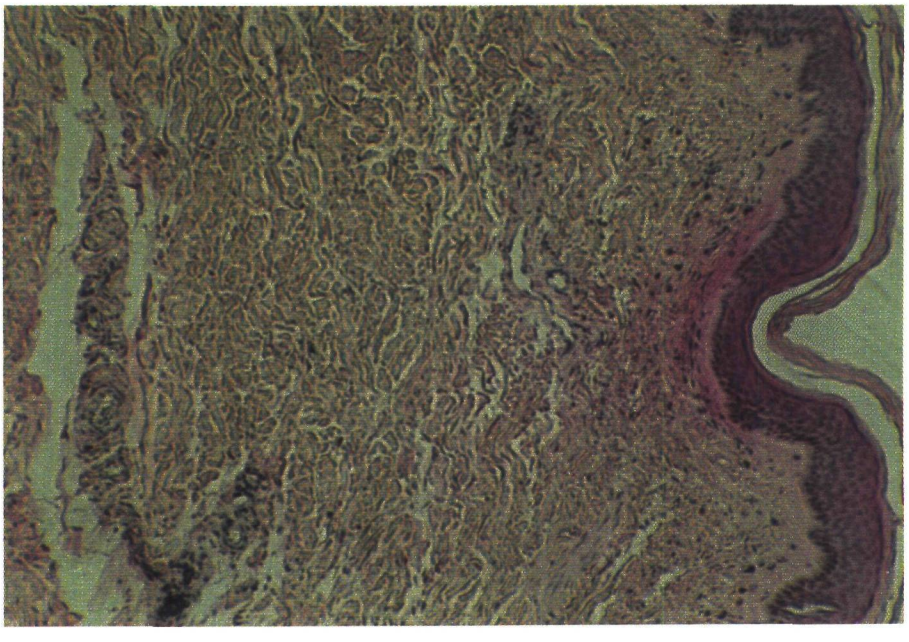




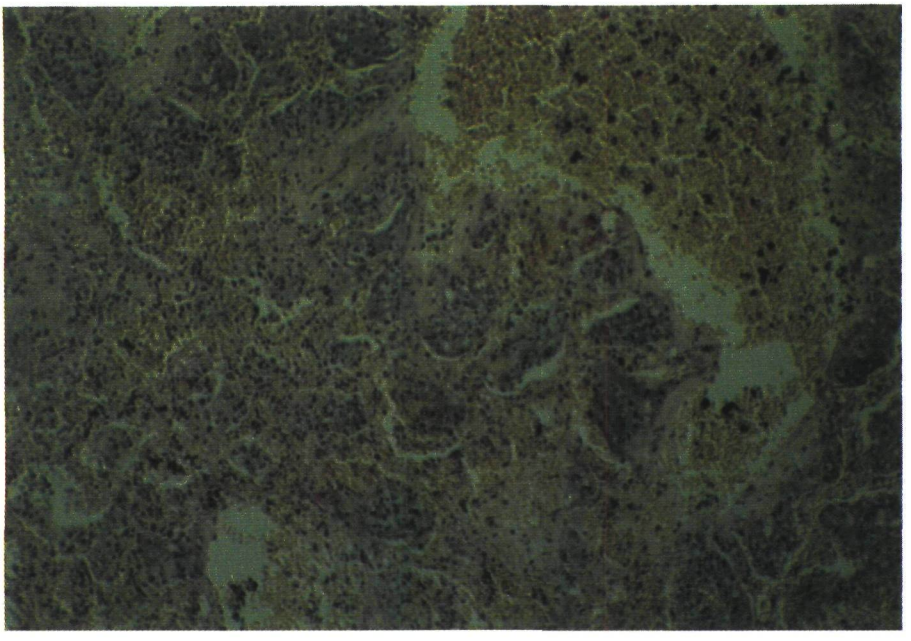
Photograph 20. General view of the patient: (a) from the left side; and (b) from the right side (day 74).



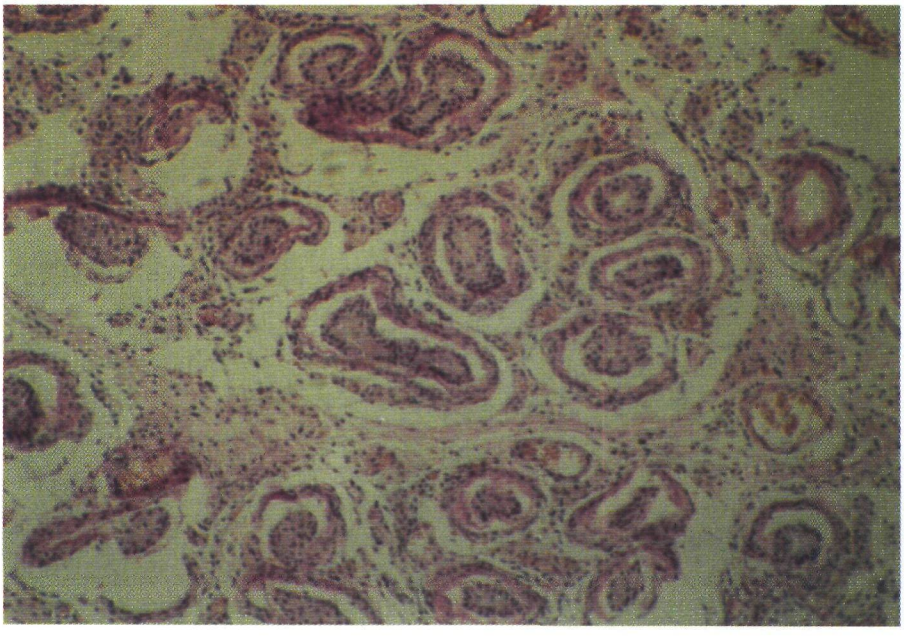
Photograph 21. Growth of hair, more evident on the right side (day 89).



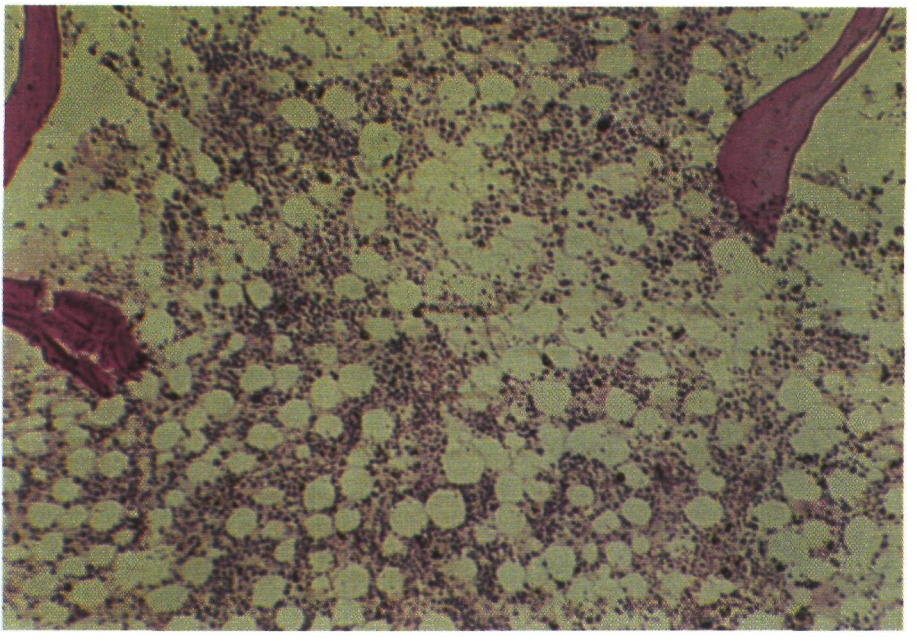
Photograph 22. Post-mortem examination: skin of the left elbow – atrophy of the skin appendices and a great deal of pigment in the basal cells (×60).



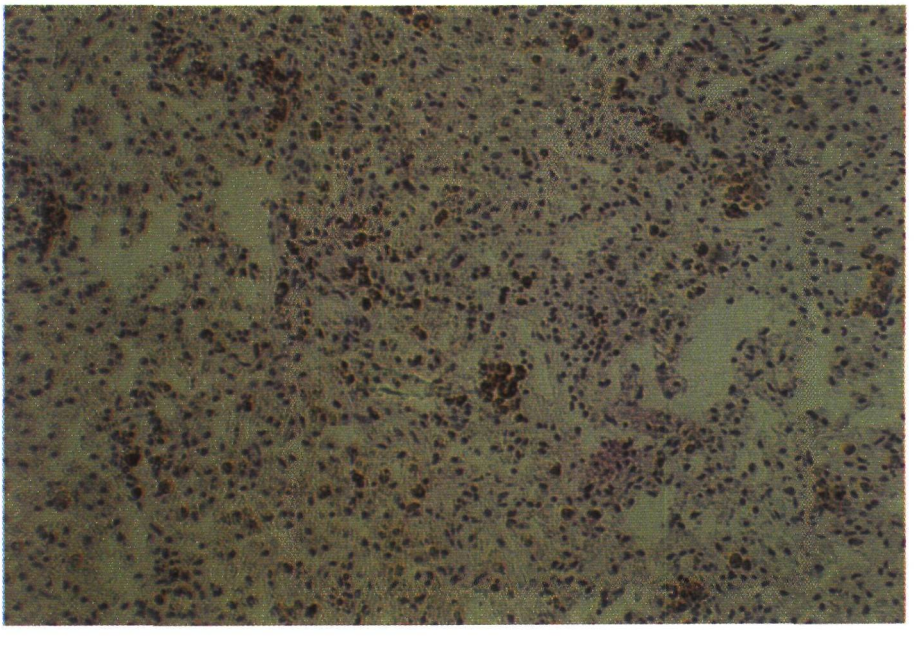
Photograph 23. Post-mortem examination: right lung – foci of fungal infection destroying the organ tissue (×60).



Photograph 24. Post-mortem examination: testes – oedema of tissues, spermatogenic epithelium is dead (×60).



Photograph 25. Post-mortem examination: bone marrow – almost normal cellularity.



Photograph 26. Post-mortem examination: lymphatic nodules – scanty cellularity, with many haematosiderini (×60).

(18) Lack of documentation relating to the plant suggested that there had been only limited contact between the manufacturers and the operating organization; this was possibly due to changes in organizations and their responsibilities in the former USSR republics.

To ensure that lessons are learned from radiation accidents arising from a whole range of design and operational problems in many irradiation plants, it is important that ongoing contact is maintained between the manufacturers and the operating organizations.

5.8. INITIATIVES BY THE IAEA

Following the irradiator accident in San Salvador, the IAEA enhanced its work on radiological protection in irradiation facilities. This was given further impetus by the accidents at Sor-Van and in Nesvizh, and some relevant aspects should be noted.

5.8.1. Training

The experience gained from the accidents in San Salvador and at Sor-Van was given prominence in the programme of regional training courses in radiological protection. In addition, a series of 2 week regional training courses specifically on irradiator safety for senior staff commenced in 1991. Five such courses have taken place in three different world regions (Latin America, the Middle East and Europe, and Asia and the Pacific).

A feature of all the fatal accidents that have occurred at irradiators has been operator ignorance or negligence as to the consequences of not following the proper procedures. There is clearly a need to provide simple, but effective, training supplements for operators. A training video tape is a good way of reaching a wide audience and the IAEA, in consultation with manufacturers, operating organizations and national bodies, has produced such a training tape [12], which is available to Member States. This should be used to supplement normal training regimes and should not be regarded as a substitute.

5.8.2. Dissemination of information

The information disseminated on accidents and incidents can take many forms. IAEA post-accident review reports necessarily take some time to complete as information on all aspects has to be compiled, analysed and reported on in depth. To ensure early dissemination of the key points of such accidents, a summary, based on the findings of the local authorities, was prepared and distributed as soon as possible after the accident. Distribution of this summary was on an informal basis, primarily

to those known to have a specific interest in this area or to those who had previously asked for advice.

To promote dialogue on radiation safety at irradiators and to disseminate information further, the IAEA organized a Technical Committee Meeting to review Radiological Accidents in Industrial Irradiation Facilities and their Implications for Competent Authorities, Designers and Manufacturers (Vienna, 19–22 August 1991). The participants heard presentations on fatal accidents in Italy [4], Norway [5], El Salvador [2] and Israel [3], which prompted some thought and ideas on the problems of disseminating information, particularly in developing countries. For example, manufacturers often have difficulty in identifying competent authorities with regard to new facilities or better safety systems. It was agreed that the IAEA would, in such cases, be able to use its good offices to identify competent authorities.

Some significant steps have been taken in the dissemination of information. In the longer term, more formal arrangements may have to be made and the IAEA is keeping the matter under review.

The IAEA is also considering a pilot programme (International Review of Irradiator Safety (IRIS)) to provide Member States with adequate advice on radiation safety at gamma irradiators. IRIS will consist of a Secretariat to obtain and collate data on irradiator types and locations, an Advisory Group to direct and monitor activities, and on-site review teams to provide practical assistance to Member States. IRIS will form part of an integrated system of assistance, including video tape training packages, regional training courses and IAEA publications.

6. MEDICAL MANAGEMENT

6.1. INTRODUCTION

Close observation of the patient suffering from acute radiation sickness (ARS) over a period of time (113 days) provided a great deal of information on the clinical manifestations, and very detailed diagnostic findings and therapeutic measures. For a comprehensive study of the case, the general course of disease was subdivided into a number of time periods. For each of these periods, the special tasks that the medical team had to consider were the level of information received, the main clinical findings and the treatment regime. From the extensive experience gained by the clinic at the Institute of Biophysics, where the patient was treated, five periods were identified.

During the first period (days 0–7), the main task was the urgent collection of information on dose assessment and evaluation of the uniformity of dose distribution. This was necessary for decision making related to the treatment of bone marrow and gastrointestinal syndromes, which began almost immediately.

The second period (days 8–39) saw severe clinical manifestations of all the injured systems and demanded very intense therapeutic interventions under careful clinico-laboratory monitoring.

During the third period (days 40–70), some results of the treatment were evident, with the patient surviving the bone marrow and gastrointestinal syndromes. However, at that time new complications arose, possibly related to the severity of the treatment.

The fourth period (days 71–101) was characteristic only for the patient, who developed new lung infections and progressive metabolic changes. This required additional changes in the therapeutic tactics.

The fifth period (days 102–113) was terminal, characterized by progressive pulmonary insufficiency. Intensive re-animating measures were necessary, but hopeless.

Descriptions of medical management have been made according to these time periods.

6.2. CLINICAL COURSE OF ARS

6.2.1. Initial medical management (days 0–7)

At the moment when the operator saw the source in the upper position, he noted a metallic taste in the mouth and a feeling of heat on the face. He left the irradiation room and 5–6 minutes later experienced nausea and vomiting, which recurred frequently over the next few hours. He realized immediately that he had been exposed and, in accordance with instructions, telephone calls were made to the local hospital and the police. Twenty minutes later he was admitted to the hospital in Nesvizh.

At the time of admission, he was in an excited state but nevertheless complained of fatigue, a headache, an ache in the abdomen, and pains in the hands and feet. He was pale and continued to vomit. Fifty minutes after exposure he had a single attack of diarrhoea. The first medical examination showed tachycardia, a normal blood pressure, which dropped after 2 hours, and an elevated body temperature (38.5°C). His psychological state lowered rapidly, although he stopped vomiting 6 hours after exposure.

The first blood analysis (2 hours after exposure) showed early neutrophilic leukocytosis (13×10^9/L), with absolute lymphopenia (0.9×10^9/L). The biochemical test results were normal. When physicians in the local hospital realized that this was a severe case of radiation exposure, emergency treatment was given. A vein was catheterized for continuing infusions. The patient was transferred to Minsk 4 hours after exposure and then to Moscow, where he was directly admitted (16 hours after exposure) to the clinic at the Institute of Biophysics, a specialized

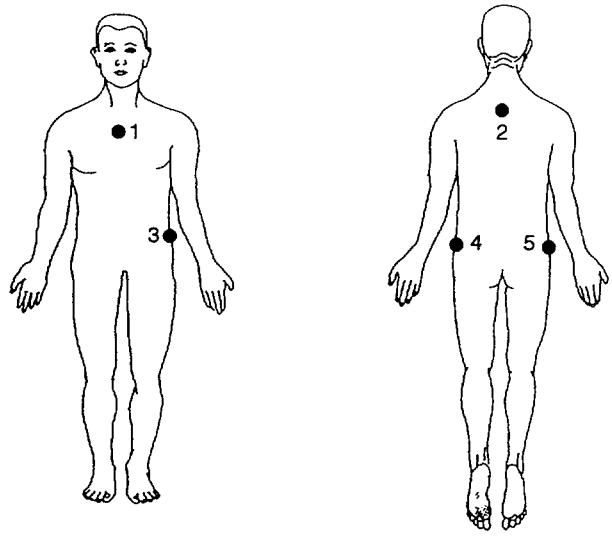


FIG. 7. Schematic representation of the bone marrow punctures and biopsies performed: (1) sternum; (2) third thoracic vertebra; (3) crest iliaca anterior sinistra; (4) crest iliaca posterior sinistra; and (5) crest iliaca posterior dextra.

hospital for radiation injuries. He did not require any special support for the journey by ambulance from Nesvizh to Minsk (200 km) or by aircraft from Minsk to Moscow (800 km).

At the time of admission to the clinic in Moscow, the patient had light erythema of the face, neck and hands, and swelling of the parotic glands (greater on the left side). Amylasuria was up to five times higher than normal and his body temperature was 37.6°C, but there was no nausea or vomiting.

From the local hospital's information and an interview with the patient, the physicians in Moscow realized that they were faced with a severe case of irradiation. Therefore, the patient was immediately placed in isolation (22 hours after exposure) and provided with a prophylactic; enteral selective decontamination and heparinization were started simultaneously. Blood samples were taken for peripheral cell counts, human leukocyte antigen (HLA) (A and B) typing and cytogenetic analysis. Bone marrow from five different sites in the body was taken for dose estimation and evaluation of dose distribution (Fig. 7). The first sternal aspiration was done 2 hours after admission (18 hours after exposure), and the third thoracic vertebra, the anterior and posterior left iliac crests and the posterior right iliac crest were punc-

tured 8 hours later.[1] An electroencephalogram examination was also performed and found to be normal. The patient's sister was called to the clinic for HLA typing as a potential donor.

Several calls for international assistance were made. R.P. Gale (Bone Marrow and Stem Cell Transplantation, Salick Health Care, Inc., United States of America) was asked to provide haematopoietic growth factors. Through the Service central de protection contre les rayonnements ionisants (P. Pellerin) and the Centre de radiopathologie (H.P. Jammet) (both in France), communication with the French Registry of Bone Marrow Unrelated Donors was established, and blood samples of the patient and his sister were sent for typing to J.J. van Rood at the Leiden Laboratory, Netherlands.

As a result of these measures, treatment with growth factors (granulocyte macrophage colony stimulating factor (GMCSF) and interleukin-3 (IL-3)) was started on days 1 and 6, respectively:

(1) The results of domestic HLA typing were confirmed by the Leiden Laboratory and showed haploidentity between the patient and his sister;
(2) A potential unrelated donor for a bone marrow transplant (BMT) was found in France.

The general condition of the patient was satisfactory between days 1 and 5. The erythema evident on day 1 started to diminish on day 2 and had completely disappeared by day 6. Swelling of the parotic glands also decreased.

Herpetic lesions (herpes simplex) appeared on the upper lip, the left side of the nose and the left cheek (photograph 12(a)). These lesions showed favourable evolution, with a crust on the lip and a tendency to healing on the cheek (photograph 12(b)). This evolution was mainly attributed to the antiviral treatment administered to the patient on admission.

The rapidly decreasing granulocyte and thrombocyte counts were the major haematological signs during this period, indicating a high radiation dose. The lymphocyte counts were below 10^{11}/L from day 2. The granulocytes fell from 4×10^{12}/L on day 2 to 0.5×10^{12}/L on day 6. The thrombocytes also fell, from 140×10^{12}/L on day 2 to 80×10^{12}/L on day 6. These haematological data confirmed that the case was very severe. From the reference curves of the blood cell counts elaborated previously [16], the mean whole body dose was estimated to be about 12 Gy. Annex I shows how this was done.

The results of cytogenetic analyses are given in Annex II. It was impossible to evaluate the dose from cytogenetic analyses of the peripheral blood lymphocytes

[1] Such early bone marrow sampling for cytogenetic analysis was necessary for possible dose assessment by the so called direct method, avoiding cultivation. This method is only informative during the first 24–30 hours after exposure.

because of: (1) the very low level of circulating lymphocytes; (2) their inability to undergo mitosis; and (3) failure of the attempt to produce cultures. The frequency of aberrant bone marrow cells was 100%. From previous experience, the whole body dose was estimated to be higher than 6 Gy, and probably between 8 and 10 Gy. On day 5, this estimate was refined and the dose was evaluated at about 11 Gy. The results of ESR were received on day 7, again confirming the high level of exposure, i.e. between 11 (right side) and 18 Gy (left front) at waist level (Fig. 6).

Day 6 marked the end of the so called latent period, which was, however, not as pronounced, since several clinical signs had appeared:

(a) Mucositis in the mouth (photographs 12(a) and (b)), with oesophagic pain;
(b) Diarrhoea with watery stools (0.6–0.9 L/d);
(c) Some loss of body weight;
(d) Progressive cytopenia;
(e) Moderate fever (about 38°C).

During this period it was decided not to perform a BMT, but rather to continue the treatment with haematopoietic growth factors (GMCSF and IL-3).

6.2.2. Clinical course (days 8–39)

This period corresponds to the critical phase of ARS, resulting from a combination of haematological syndrome, gastrointestinal syndrome and skin injuries.

Fever was constant, between 38 and 39°C. The haematological syndrome was characterized by deep pancytopenia, confirmed by complete bone marrow depression (photograph 13). However, the bone marrow investigations performed on days 23 and 27 showed young forms of myelopoietic cells. At this time, the peripheral blood count showed the appearance of a few granulocytes and monocytes. From day 33 reticulocytes were increasingly found. These changes, which indicated the reversibility of the pathological process, provided some hope to the physicians. However, the lymphocyte counts decreased continuously up to day 18. The level of erythrocytes was constantly low, demanding repeated erythromass transfusion. Likewise, the continuous decrease in thrombocytes required almost daily thrombomass transfusions. The patient received antibiotherapy of broad spectrum, including antiviral drugs.

Mucositis in the mouth was still moderate, with small erosions, and recovery began on days 14–15, exhibiting epithelization on days 28–30.

Manifestations of the gastrointestinal syndrome were moderate (three to nine stools per day, with a volume varying from 0.5 to 1.5 L/d) owing to total parenteral feeding. Any attempt to begin enteral feeding led to a deterioration in the syndrome. Between days 36 and 39 there were signs of intestinal bleeding, which required transfusions of large quantities of red cells and platelets, as well as large volumes of liquids. The gastroduodenal endoscopy showed a large number of small erosions and

haemorrhages. The whole mucosa bled. Treatment with heparin was stopped. The most significant result of this syndrome was a rapid deterioration in the general state of the patient, whose weight dropped from 70 kg on the day of admission to around 60 kg on day 39.

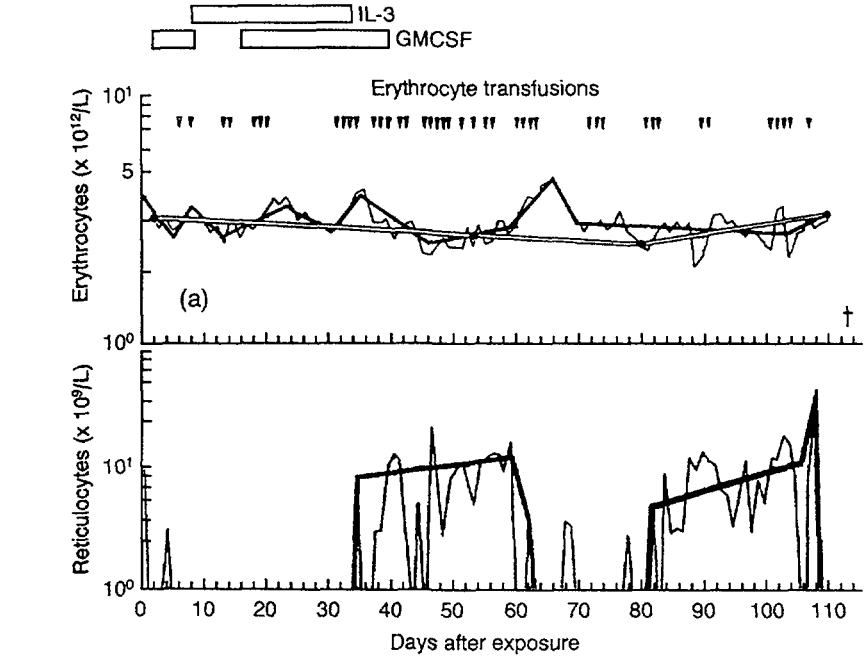
Skin injuries appeared on day 11, with epilation that was more evident on the left side of the body, beginning on the head and extending to the chest and pubis.

Secondary erythema appeared between days 11 and 15 on the left side of the face, ear and neck. Dry desquamation occurred at these places on days 24–25. From this time, the patient demonstrated a gradual extension of skin injuries, which appeared successively on various parts of the body. On day 11, erythema with skin oedema appeared on both elbows and both iliac crests. However, some time later all the signs were more pronounced on the left side of the body. Photograph 14 shows skin injury to the left elbow and photograph 15 the dorsal surface of the left hand, with marked localizations on the finger joints. After a few days, blisters and small erosions appeared on these areas. Also on day 11, erythema appeared on the left buttock, and extended to the right side within a few days (photograph 16). At the end of the first month, the gradual process of skin lesion extensions resulted in almost total body erythema (photograph 17). Wet desquamation was especially marked on the left hand and left leg. Some signs of skin recovery were visible at the beginning of the second month, with skin injuries not as painful as expected. Severe pain appeared in both feet around day 20 and persisted for 1 week. The character of these pains was not typical of classical radiation injury. A question was raised on the possible combination of three causes, i.e. radiation, the side effects of the growth factors and some local circulatory disorders. After a reduction in the growth factors dose, the pain diminished and was only exacerbated by contact and pressure. Painful balanoposthitis developed on day 28, but this was cured within 1 week.

Skin biopsies of the left iliac region were carried out on days 3 and 16. On day 3, no significant signs of radiation injury were shown; dystrophic changes were found in one of five to six normal cells, while skin appendices were normal, indicating a skin dose of lower than 20 Gy. On day 16, more specific changes were observed, such as a decrease in epidermis cellularity, dyskeratosis, which consisted of a large increase in the number of melanocytes, and marked infiltration surrounding the dermal vessels. These clinical findings confirmed the possibility of spontaneous skin recovery. At this time, the pathologist estimated the skin dose to the left iliac region to be around 8–10 Gy.

Regular chest X ray examinations showed almost normal lung pictures on days 9 and 23, with the exception of a slight vascular net. On day 38, a solid shadow could be seen in the middle lobe of the right lung and some infiltrations in both lungs. However, there were no clinical symptoms of any lung disease at this time.

In this critical period, no patent bacterial infection was evident; the lung shadow found on the X ray on day 38 was suspected to be a localized fungal pneumonia and treatment with amphotericin B was started.



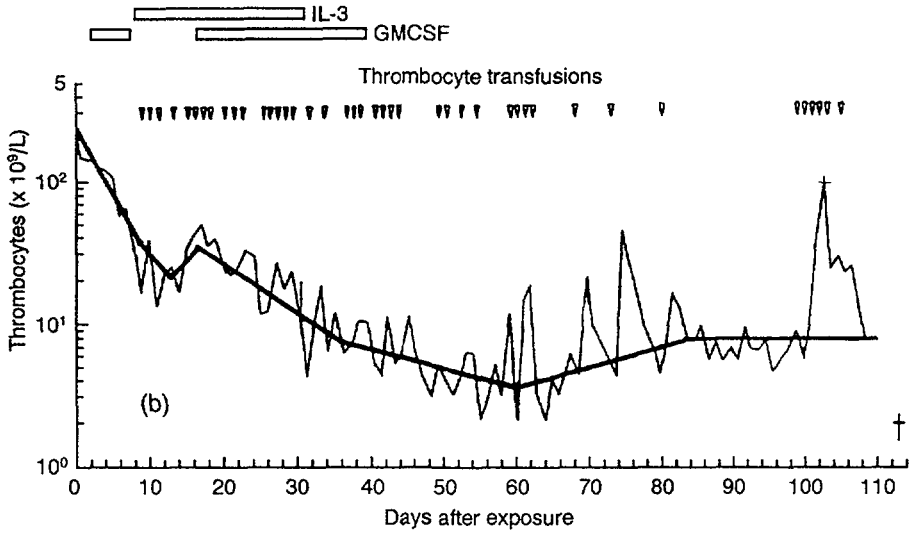
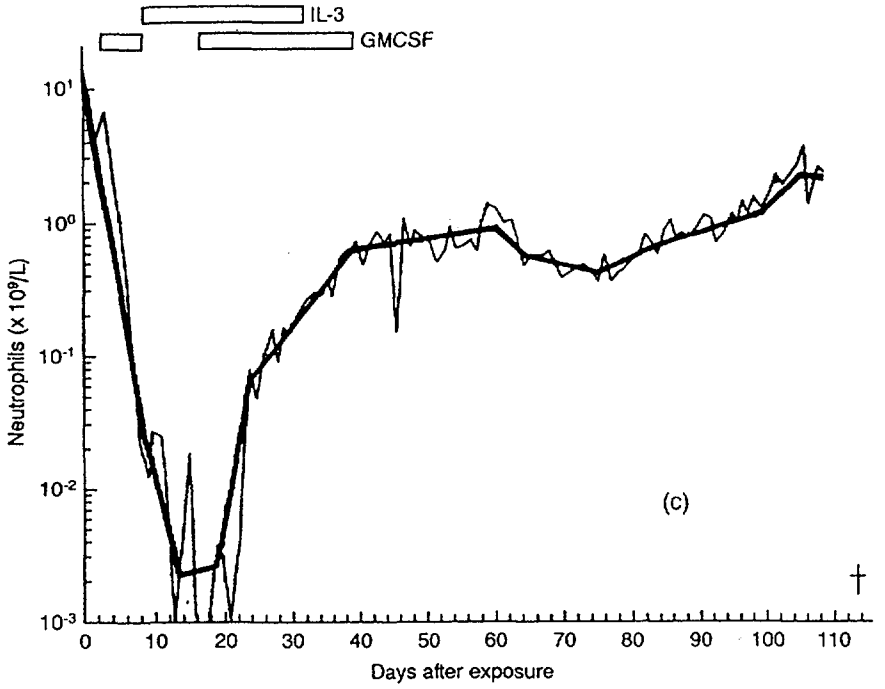
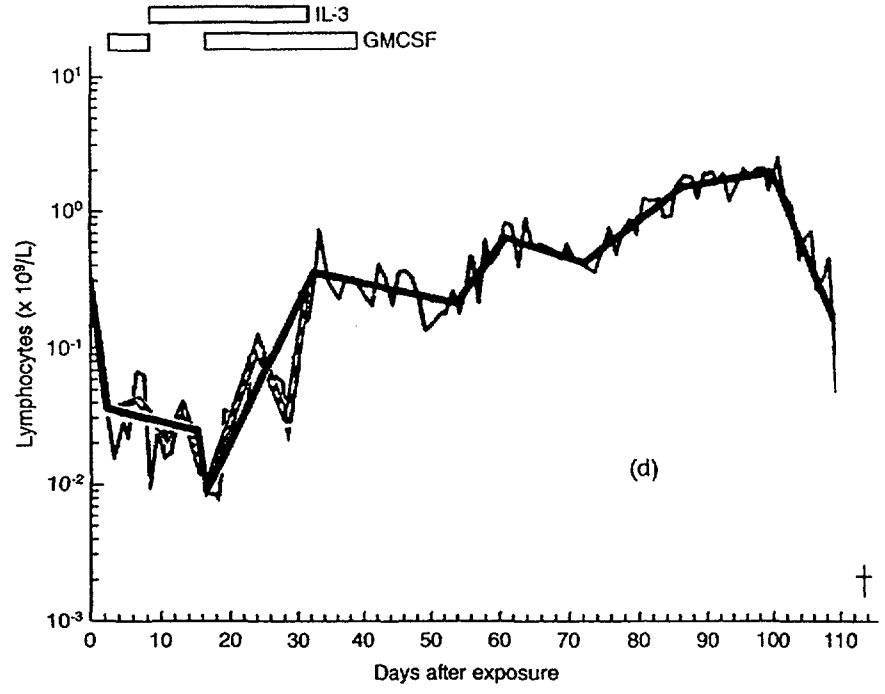


FIG. 8. Counts during the whole clinical course of ARS, and their dependence on treatment with growth factors: (a) erythrocyte and reticulocyte counts; (b) thrombocyte counts;





(c) neutrophil counts; and (d) lymphocyte counts.

From the beginning of this period, a gradual increase in infection of the liver started. Biochemical tests showed only an insignificant rise in transaminase and creatine phosphakinase, with significantly progressed hypoalbuminaemia, which required intensive albumin transfusions.

6.2.3. Clinical course (days 40–70)

During this period, the general state of the patient was relatively stable, and his mental state had even improved; his fever after day 50 was neither as constant nor as high as earlier.

The neutrophil counts in the blood showed a plateau, with small variations (between 400 and 1000 $\times$ 10^9/L). The lymphocytes also showed a plateau, but only at a lower level. Thrombocytes were still at a low level and repeated thrombocyte transfusions were necessary. The erythrocyte counts continued to decrease slightly during the first days of this period; the reticulocyte wave that had appeared in the previous period lasted up to the end of the second month and had completely disappeared by day 62 (Figs 8(a) to (d)).

Bone marrow examinations were done on days 44 and 62 and demonstrated an increase in cellularity (photograph 18).

Gastrointestinal syndrome manifestations began to decrease after day 40; however, anorexia was persistent and there were some episodes of vomiting. The patient received partial parenteral feeding.

Some signs of hepatitis, revealed by biochemical findings, were constant and became more evident by the end of this period.

The oropharyngeal syndrome was characterized by only a slight atrophy of the mucus. Epithelization was evident in most of the skin lesions; however, the new skin was atrophic and dark brown, atrophy being more marked on the left side of the body. Phlebitis in a vein of the left leg (vein saphena) persisted. The skin of the left leg was hyperhaemic, with oedema of the underlying tissues and superficial erosions (photograph 19); pain was exacerbated during this period. A skin biopsy showed fibrinoid swelling in the skin blood vessels and moderate dystrophy of the appendices.

X ray examinations carried out on day 51 showed slight amelioration of the right lung lesion. Tomography on day 54 showed increased infiltration in the left lung, and some tissue destruction was suspected. Some time later (day 58), clinical signs of bilateral pneumonia appeared. An X ray examination performed on day 67 showed an enlargement of and an increase in the density of the right lung shadow and the appearance of a new shadow in the lower lobe of the left lung. X rays on day 70 again showed some signs of pneumonia which, however, gave no indication of the etiology (causal agent) of the lung injury. During this time, there were no classical symptoms of radiation pneumonitis. This was also confirmed by the negative results of repeated transcutaneous and transbronchial lung biopsies. However, the patient received all the necessary treatment for pneumonia.

6.2.4. Clinical course (days 71–101)

This period represents a transition between the previous relatively stable period and the terminal phase. It was characterized by:

(1) Progressive amelioration of the general state of the patient, who became more active and started to feed himself, although parenteral nutrition was maintained. However, the loss of weight continued, resulting in an almost 20 kg loss by the end of this period. The peripheral blood count showed a gradual increase in all the cells, except for the thrombocytes, which were still at a low level (Fig. 8(b)). The bone marrow biopsy performed on day 82 indicated little change: a few cells with a normal pattern of immature and mature cells. The patient's temperature was almost normal during this period and there were no signs of a gastrointestinal radiation syndrome.

(2) The skin exhibited complete re-epitheliation, but with dystrophic changes. The hair started to grow on the right side first, especially in areas where epilation was incomplete. Comparison of the left and right sides of the body demonstrated clearly that exposure had been greater on the left than on the right side. The healing process on the left and right sides differed; dark hyperpigmentation with spots of depigmentation were exhibited on the left side (photograph 20(a)), while the right side looked almost normal (photograph 20(b)). A difference in hair growth was also apparent, particularly on the face, where the patient's moustache reappeared on the right side only (photograph 21).

(3) The skin biopsies performed on day 82 at three different sites of both the iliac crests, i.e. anterior and posterior right and anterior left, showed a basic layer in rather good condition, associated with some uniform atrophic changes in the dermis and epidermis, such as an increase in the connective tissue and a slight decrease in the dermal vascular system. These pathological changes appeared to be of the same nature on both sides of the body, although the dynamic was quicker on the left side. In addition, the sweat glands were found to be atrophic.

(4) The lungs continued to be of concern to the medical team; the shadows (right middle lobe and left lower lobe) were persistent and their aetiology remained questionable. All attempts to find the cause of the lung opacities were unsuccessful, since no microbic or fungal agent could be traced. On day 100, an X ray examination of the chest revealed considerable infiltration in the lower left pulmonary lobe. The evident toxicity of the high doses of amphotericin B and the uncertain nature of the lung infection led to discussions on an open lung biopsy.

(5) Hepatitis, revealed earlier by biochemical findings, was particularly evident around day 80; it was assessed to be of the persistent cholestatic type. The possibility of a toxic effect of the antibiotic on the liver was thought to be significant, since antibiotherapy had been reinforced to treat the pneumonia.

(6) At the end of this period, 3 months after exposure, signs of renal failure appeared.

6.2.5. Clinical course (days 102–113)

An open biopsy of the left lung was decided upon and carried out on day 102, but no infection was revealed. The patient withstood the operation relatively well, but 2 days later (day 104) his respiratory condition suddenly worsened, resulting in a typical acute adult respiratory distress syndrome.

The general condition of the patient deteriorated, with a sudden collapse on day 104, accompanied by a rise in body temperature. Alterations in the main metabolism process were observed and acidosis appeared. During this time, the patient demonstrated evident symptoms of respiratory insufficiency, with hypoxaemia, chest pains and a slight cough, although there was uncertainty as to their specific cause.

Active therapy, including hyperbaric oxygenation following artificial lung ventilation (ALV), proved to be ineffective, even harmful; hypoxaemia increased rapidly and, as a result of ALV, a pneumothorax developed and new symptoms of severe pneumonia appeared. A severe respiratory syndrome, intoxication and hyperosmolar state with increasing renal insufficiency led to encephalopathy of mixed genesis.

The patient's blood pressure decreased sharply on day 112, and he died the following day while in a hypoxaemic coma, mainly because of respiratory distress.

6.3. MEDICAL TREATMENT AND A REVIEW OF ITS EFFECTIVENESS

The specialized hospital in which the patient was treated, the clinic at the Institute of Biophysics, has many years of experience in the management of radiation induced injuries. The main objectives of the treatment were to reduce the period of bone marrow aplasia, maintaining circulating blood cells at an acceptable level; to avoid infection and haemorrhaging; to protect the gastrointestinal tract (GIT) from as much harm as possible; and, finally, to support the metabolic functions.

As soon as the patient was admitted to the Moscow hospital he was placed in an overpressurized isolated room that was provided with sterilized air. From the first days of hospitalization he was given intensive anti-infection treatment, including classical antibiotics as well as antiviral and antifungal drugs. During the course of the disease, precise antibiotherapy was adapted to actual clinical findings. From the start, the patient also received enteral selective decontamination. On day 6, he was placed under total parenteral nutrition, providing 2500 kcal/d. On the first day of admission (day 0), immunoglobulin and heparin were provided.

Information on dose level and its distribution are of prime importance for some crucial therapeutic decisions. In this case, it was recognized early that the dose was

very high, around 10 Gy or more. From the initial information received from the patient and from a description of the accident circumstances, the physicians could not exclude some non-uniformity of exposure. This was in fact later demonstrated, with a factor of about 1.5 shown between the least exposed and the most exposed parts of the body. Nevertheless, because of the high level of dose, the relatively heterogeneous dose distribution did not constitute a major parameter for decision making.

After long and controversial discussions with foreign specialists in an international consultation held on 3 November 1991 (participants: A.K. Guskova, A.E. Baranov, H.P. Jammet, R.P. Gale and A. Butturini, as well as T.M. Fliedner by telephone) it was decided not to perform a BMT, either from the haploidentical donor (the patient's sister) or from the donor found through the French Register, because the hazards, as judged by the physicians responsible for the patient, outweighed the benefits. Therefore, the decision was made to stimulate haematopoiesis with growth factors and to carry out replacement treatment with classical transfusions of red blood cells and thrombocytes (T-leukocytes depleted), the frequency and volume of which were accordingly adjusted. The total number of perfused cells was very high, far above that usually found in an ordinary hospital department. Transfusions started on day 6 and were necessary during the whole course of the illness.

It should be emphasized that, in such severe cases, the need for repeated transfusions of red blood cells and platelets is very high. These proved to be very effective as the patient overcame the haemorrhagic syndrome and intensive bleeding.

Before any decision was made on whether or not to carry out a BMT it was decided to stimulate haematopoiesis by growth factors. Two growth factors were used: GMCSF, which is a common stimulator of myelomonocytic progenitors, and IL-3, which is a large spectrum stimulator of the most primitive stem cells.

Treatment with GMCSF (slow intravenous infusion ($11 \cdot 4\ \mu g \cdot kg^{-1} \cdot d^{-1}$)) was started on day 1 and a further 6 $\mu g \cdot kg^{-1} \cdot d^{-1}$ was initiated on day 2. However, treatment was interrupted on day 6 because some clinical signs appeared that may have been drug related rather than due to radiation. These possible side effects included fever, oedema, pain, arthropathies and thrombophlebitis, which could have been third grade GMCSF complications. For this reason, GMCSF was replaced by IL-3, which was injected (slow intravenous infusion ($10\ \mu g \cdot kg^{-1} \cdot d^{-1}$)) from days 6 to 31. As the general state of the patient improved, and as the supposed side effects decreased to a level consistent with radiation exposure, GMCSF was again used from days 16 to 39. Consequently, the patient received both growth factors from days 16 to 31.

Regarding the haematopoietic system, the two waves of reticulocytes that appeared in the circulating blood on days 34 and 82 (each lasting about 1 month) can be interpreted as follows: the first wave was directly related to the use of growth factors, according to the bone marrow examinations, while the second was due to

spontaneous recovery, probably influenced by the treatment. Additional evidence of the effectiveness of this treatment was that no such recovery was shown in the platelets, on which GMCSF and IL-3 have no influence.

At the high level of dose received, more severe GIT injuries (including mucosas) would have been expected, which could have resulted in the patient's death. Therefore, the beneficial effect of the two growth factors on the stem cells of various tissues should be taken into consideration.

An intensive detoxication therapy was started on day 0, and continued throughout the entire course of the disease. It consisted mainly of forced diuresis (half the normal physiological solution, with diuretics added) and of polyvinyl pyrolidol. In addition, the patient received fresh frozen plasma (10–15 $mg \cdot kg^{-1} \cdot d^{-1}$), with human albumin added.

Radiation injury to the skin was treated mainly with 'Lyoxazol', especially developed by the Pharmaceutical Laboratory at the Institute of Biophysics.

Because of the respiratory distress that appeared in the weeks before the patient's death, AVL with hyperbaric oxygen was provided from 5 days after the open lung biopsy, i.e. on day 107, until death.

Survival of the patient for more than 3 months was certainly related to the strong aseptic regime under which he was kept, including total isolation, prophylactic antibiotherapy, enteral decontamination and parenteral nutrition. Even when a fungal infection occurred in the right lung it was discovered by systematic X ray checking. The herpetic lesions that occurred at the very beginning of the clinical course did not spread to the pulmonary tissues, as usually happens in such severe cases.

A detailed flow chart, including a list of all the drugs, doses and administration dates, is presented in Annex III.

6.4. PATHOMORPHOLOGICAL FINDINGS

A post-mortem examination was performed a few hours after death. The main findings from the macro and micro examinations of organs and tissues are described in Sections 6.4.1 to 6.4.11.

6.4.1. Whole body study and skin injury

The cachectic state of the patient, with a weight loss of 20 kg, had been underlined by the pathologists. There were several very characteristic findings:

(1) *Hyperpigmentation of uneven distribution,* which may have been related to radiation and adrenal gland deficiency.

(2) *More or less pronounced epilation,* with new hair follicles appearing on the right side of the face, while some regions of the body appeared to be almost normal: right scapula, upper part of the right arm, right part of the chest and the abdomen, and the right thigh.

(3) *Deep and limited necrosis* in the sacrum region, related to prolonged decubitus and subinfection, and *more recent lesions* on both heels, the back and the head.

(4) Using microscopy, the skin on the right side of the body was found to be relatively less damaged. The left side showed *significant signs of atrophic radiation dermatitis* (photograph 22). *Microbial penetration* took place in the deep layers of derma in necrotic areas, the microscopic picture showing *oedema* around the blood vessels and a number of *drainage cells.*

6.4.2. Lungs

The macro and microchanges in the lungs were very polymorphic. Lung tissue was compact and full blooded, especially in the middle lobe of the right lung. In the lower right lobe, a subpleural bulla (with a diameter of about 4 cm) was found to be filled with blood and clots. In a somewhat central position, a large cavity, with hard walls and some inflammatory foci, was located. Two greenish yellow foci were clearly to be seen in the left lung. Histological examination of several slides showed: (1) foci of fungal infection (aspergillus) in the middle right lobe, some of which were typical of previous infections, while others were at the necrotic stage (photograph 23); (2) a typical microbic infection in the lower left lobe, without visible fungal lesions; (3) plethora and oedema of the blood vessel walls, with a great deal of severe haemorrhaging; and (4) general alveolar epithelium damage, with desquamation and disseminated foci of gealinosis and introalveolar sclerosis. These findings corresponded slightly to typical radiation pneumonitis.

6.4.3. Gastrointestinal tract

The stomach was found to be filled with a quantity of blood, but did not exhibit any lesions in the mucosa, which could be the explanation for this important bleeding. The mucosa was autolysed. The ileum was cyanotic, with severe haemorrhaging (about 50 cm) and almost complete denudation. The rest of the GIT was almost normal, except for a mucosa that was significantly thinner than usual. Mucosal and submucosal oedema, with atrophy of the glands, was distributed throughout the whole GIT. In some places, dystrophic changes in the muscular layers were found, and some punctial haemorrhagia were detected in the mesenterium. It was concluded that partial recovery of the digestive system had taken place.

6.4.4. Liver

The normal organ size and mass (1.9 kg) were significantly decreased and showed deep dystrophic changes that varied from one region to another. Circulatory disturbances were very general and pronounced. In some places, necrotic foci in parenchyma were found.

6.4.5. Kidneys

Both the kidneys showed tubularopathy, with dystrophy and oedema of the channels. Interstitial oedema and an increase in glomerulus cellularity were noted.

6.4.6. Adrenals

Both the glands showed oedema and extravasion of blood in the medullo-cortico parts, with a marked decrease in cellularity in the cortical layer.

6.4.7. Testes

Almost complete destruction of the spermatogenesis epithelium was seen (photograph 24).

6.4.8. Bone marrow

The bone marrow showed some signs of haematopoiesis recovery from total aplasia, which was especially marked in the vertebrae. However, disturbances in bone marrow vascularization were significant in some places (photograph 25).

6.4.9. Spleen

A total reduction in follicules was found, despite the normal size and mass of the organ. Only a small number of lymphocytes, plasmocytes and macrophages could be seen in red pulpa.

6.4.10. Lymphatic nodules

Most of these nodules were shown by a connective tissue frame, with a deep depression in the lymphopoietic tissue (photograph 26).

6.4.11. Thyroid gland

This was almost normal in size, with slightly planed cells.

6.5. CONCLUSIONS

(1) The male operator of the gamma ^{60}Co sterilization unit was exposed to radiation for approximately 1½ minutes and he was about 0.2 metres away from the gamma source at the time the accident occurred. Stupor, vomiting and pains in the stomach appeared within 5–6 minutes; the patient had a single bout of diarrhoea after approximately 50 minutes; shivers, fever and a drop in arterial pressure subsequently appeared (2.5–6 hours after the accident); the number of lymphocytes in the peripheral blood was 0.9 and 0.25 $\times$ 10^9/L at 2 and 15 hours after exposure, respectively.

The exposure conditions and the appearance of the above symptoms within the first few minutes and hours were a clear indication that the exposure dose had been very high (>10 Gy) and that the patient was suffering from acute ARS.

(2) The patient received first aid (tranquillizers, pain killers, detoxificants) at the local hospital, to which he was admitted within 20 minutes of the accident. After 4 hours he was sent to Minsk, and 16 hours after the accident he was admitted to the clinic at the Institute of Biophysics in Moscow, a specialized centre that provides medical assistance in the event of radiation emergencies and accidents.

When severe ARS is suspected, following a relatively evenly distributed exposure, the patient must immediately be sent to a specialized clinic of national or international standard. A description of the geometry of exposure, the exposure time and the source strength must be sent with the patient, as must the clothing and any watches, rings, etc. he/she was wearing at the time for purposes of rapid dose evaluation using ESR techniques. At the same time, the patient's blood relatives should be brought to the hospital as possible bone marrow donors. These two requirements were not complied with in this particular case.

(3) At the clinic, blood samples were taken immediately from a vein and from various parts of the bone marrow in order to evaluate the exposure doses using haematological and cytogenetic methods. It proved impossible to evaluate the mean dose from the number of aberrations in a culture of lymphocytes from peripheral blood because of the absence of metaphases. However, within 2–5 days the cytogenetic tests performed on the bone marrow showed that the absorbed doses in various parts of the body were similar and amounted to approximately 11 Gy. On day 7, following tests on the patient's vest using ESR techniques, it was found that the absorbed doses at waist level were 18 and 11 Gy on the left (front) and right hand side, respectively. This confirmed that gamma radiation exposure was relatively even, with dose levels of >10 Gy.

The above techniques must, in the first instance, be used to evaluate the distribution of the absorbed doses over the body of the affected person. Measurement of the absorbed doses in a human phantom under modelled accident

conditions can provide significant additional information on the inhomogeneity of exposure. This type of modelling was not performed during the days immediately following this incident.

(4) From the magnitude and distribution of the exposure doses and clinical prognoses 2–5 days after the accident it was clear that there was so called irreversible myelosuppression. However, a BMT was not performed for the following reasons: (a) it was unclear at that point whether the patient would survive the transplant because of damage to the intestines and the skin; (b) no HLA from an identical related donor was available and the high risk of using an unrelated donor could have produced fatal secondary illnesses and other BMT complications; and (c) there was some probability that haematopoiesis might spontaneously restore itself.

The possibility of using the haematopoietic growth factors GMCSF and IL-3 remained; the first was administered from days 1 to 6 and from days 16 to 39 after the accident, and the second from days 6 to 31.

The first signs of myelopoiesis restoration were registered on days 22–23 after exposure, when dividing and mature neutrophils appeared in the bone marrow and peripheral blood. After 2 weeks, the blood neutrophil level had risen to 500 cells/mL.

As can be seen, haematopoiesis was restored in this very severe case without a BMT. Specially planned experimental research should be carried out to assess what role a BMT and/or haematopoietic growth factors can play in curing severe ARS in humans suffering from so called irreversible myelosuppression.

(5) The therapy included: (a) early empirical prophylaxis/curing of the herpes virus as well as the bacterial and systemic mycotic infections; (b) replacement therapy involving the transfusion of adequate quantities of blood constituents (thrombocytes, erythrocytes, albumin and gamma globulin); (c) possible prophylaxis and therapy of supposed microangiothrombopathic disorders via round the clock infusion of heparinized (500 units/h) plasma; (d) careful monitoring and correction of the water electrolyte and acid alkali balance; (e) total parenteral feeding; and (f) treatment of radiation induced dermatitis using the special local agent 'Lyoxazol'.

It can be assumed that this supportive and replacement therapy, and the early use of the haematopoietic growth factors, helped to combat the acute myelosuppression, intestinal syndrome and dermatitis caused by the radiation and to keep the patient alive for 3.5 months after exposure.

Modern supportive and replacement therapy for severe ARS should include early and long term empirical prophylactic and curative administration of antiviral, antimycotic and antibacterial drugs, and transfusion of adequate quantities of thrombocytes, erythrocytes, albumin, gamma globulin and plasma. Clearly, this type of treatment can keep a person alive for 60–100 days if they were healthy before exposure and even where the overall, relatively evenly distributed exposure doses were of the order of 11–18 Gy.

(6) At the end of the third month, the patient still had aspergillosis of the lungs, which had appeared at the beginning of the second month. Impairment of many organs slowly increased, resulting in: (a) haemo and myelosuppression, with a very low thrombocyte level; (b) hepatitis; (c) kidney disorders: polyuria and metabolic acytosis; (d) a progressive reduction in body weight: even though the patient's appetite remained good, his calorie intake was sufficient and he showed no signs of diarrhoea; (e) pre-clinical microfocal diffuse sclerosis of the lungs, which was found during the diagnostic biopsy of the left lung.

At the beginning of the fourth month, macrofocal pneumonia developed in the lower part of the left lung, with no clear systemic and local symptoms or breathing insufficiency. The open biopsy of the left lung, performed on day 102, did not reveal the cause of pneumonia.

The patient died of breathing insufficiency 11 days after the biopsy as a result of the operation carried out for acute adult respiratory distress syndrome. The autopsy did not reveal the nature of the macrofocal changes in the lower part of the left lung. An active focus of aspergillosis was found in the middle part of the right lung. There were signs of the acute adult respiratory distress syndrome, oxygen toxicity of the lung, and slight, probably radiation induced, diffuse pulmonary fibrosis.

It is clear that, at overall gamma radiation doses of around 11–18 Gy of high strength, after 3 months a polyorgan chronic insufficiency syndrome will develop that is radiation induced and/or is of toxic or infection origin. Special experimental research is needed to find the main cause of this chronic haematopoiesis and organ insufficiency, and analysis of all the clinical observations for this dose range.

6.6. LESSONS LEARNED

6.6.1. The medical community

(1) As soon as the severity of the overexposure was diagnosed, i.e. in less than 1 hour, the patient was transferred to a very specialized hospital.

The efficiency demonstrated by the medical teams in charge of the patient during day 1 emphasizes the need for: (a) physicians trained to deal with radiation injuries when there is a certain probability of accidental exposure; (b) predefined plans to evacuate the patient as quickly as possible to an appropriate hospital; and (c) specialized physicians with the appropriate medical tools in a hospital specialized to handle severe cases of radiation overexposure. As such overexposure is rare, conditions may not always be filled, therefore international information and collaboration should be organized (see Section 6.6.2). The addresses of specialized centres should be well known in advance.

(2) Diagnosis of acute exposure was carried out very early on the basis of the prodromal symptoms and other early clinical signs.

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. For example, this was not the case in the accidents that occurred in Italy in 1975 and in El Salvador in 1989. This point underlines the importance of the education and training of all workers involved with radiation biological effects.

(3) The medical team in Moscow received from the plant information on the source worker geometry that was not accurate enough, making decisions on therapy very difficult.

Correct management of the patient strongly depends on excellent co-operation between plant personnel, including engineers, physicists and administrators, as well as those persons concerned with investigation of the accident and those health physicists and physicians involved in dealing with the patient. The physician responsible for the treatment should participate in the dosimetric investigations, since the prognosis and choice of treatment strongly depend on dose levels and dose distribution.

(4) While the plant personnel reacted very quickly and efficiently, they considered that evacuation of the patient in good condition was of primary concern under the circumstances.

In order not to lose time or valuable information that would be (or might be) necessary in the early course of illness resulting from radiation exposure, plants and local hospitals should be provided with a list of actions that must be undertaken as soon as possible after such a accident. These actions do not include treatment of radiation injuries, but do provide the first basis for diagnosis, prognosis and treatment. For example, quick actions should include:

(a) Sampling of the clothes worn by the worker at the time of the accident (for further dosimetry by ESR); these samples should be retained for possible reassessment;

(b) Reading of all personal dosimeters (all staff members);

(c) Blood counts (complete);

(d) General medical examination of all the systems and organs, particularly the skin and visible mucosa, in order to detect the first wave of erythema as well as other symptoms related to exposure.

(5) A blood examination was performed on the patient within 2 hours of the accident, and bone marrow samples were taken on arrival at the clinic in Moscow, i.e. within 12–25 hours of the accident.

In addition to all the information on accidental circumstances mentioned in item (3), including physical dosimetry, early diagnosis relies on several types of clinical and biological tests. All are complementary and may include (depending on the severity and development of the illness): cytogenetic analysis (blood and bone marrow), complete phenotyping, daily blood counts and repeated bone marrow examinations, cell and stem cell cultures, and quantitative bone marrow scintigraphy (to test the regeneration capabilities of the bone marrow).

(6) The physicians decided not to perform a graft on the patient, weighing the advantages and risks of alternative treatments, and opted for the long term effects of acute exposure.

Since it has now been proved that persons exposed to high dose levels can survive for more than 2 months, physicians should be prepared for the malfunctioning of several organs and for the failure of several physiological functions caused by the combination and intricacy of many pathogenic factors. Because of the severity of some of these malfunctions and failures, there is a strong need for close collaboration between specialists in various medical fields.

6.6.2. International collaboration (medical field)

(1) Therapeutic decisions can have serious consequences. In this case, very specific drugs were required that are neither currently used nor easily available, therefore the physicians in charge of the patient requested advice and help from foreign experts.

For the medical management of seriously irradiated cases, international collaboration should be considered of great importance. Significant points may include:

(a) Physical reconstruction of the accident;
(b) The search for a suitable bone marrow donor in bone marrow banks;
(c) Provision of modern, expensive and uncommon medicaments;
(d) Consultation of specialists from various countries (as such, accidents are rare and experience is limited);
(e) Some specific examinations (physical and biological) that may be done in other countries.

As all these points cover very different fields, it may not be possible to find individuals or national organizations able to handle the whole situation. Therefore, it is absolutely necessary to co-ordinate this collaboration, which can only be done by an international organization.

Annex I

ESTIMATION OF WHOLE BODY DOSE FROM BLOOD CELL COUNTS

Figure I-1 is a graph of the white blood cells as a function of days after exposure. The m and n points on curve (a) indicate the level of lymphocytes on days 2 and 3 after exposure, respectively. These points are also shown in Fig. I-2. A calibration curve is obtained using the reference curves of blood cells determined previously [16]; corresponding doses of 13 and 11 Gy, respectively, were estimated. Point 0 on curve (b) in Fig. I-1 indicates the day on which the number of neutrophils in the peripheral blood dropped below 0.5 × 10^9/L. This is found in Fig. I-3 and shows the dose to be about 12 Gy.

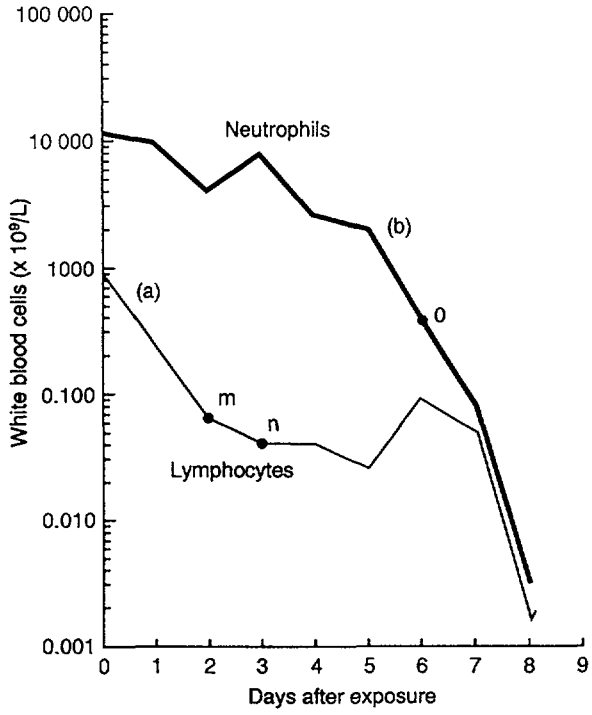


FIG. I-1. Lymphocyte and neutrophil counts for the first period (days 0–7). The m, n and 0 points (for explanation, see text) were critical for dose assessment.

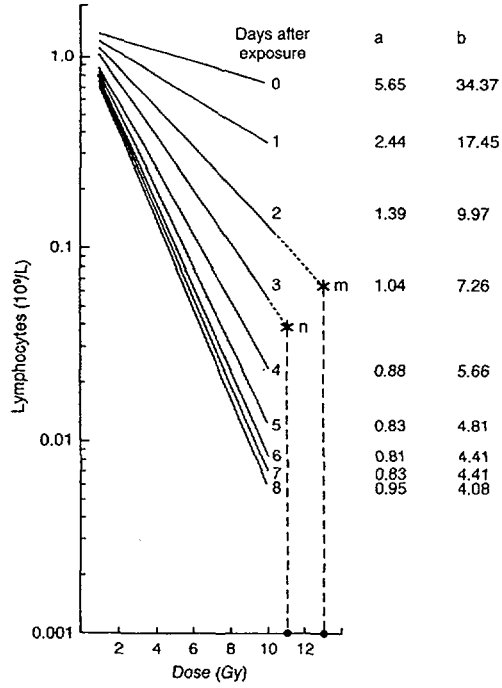


FIG. I-2. Assessment of exposure dose using lymphocyte counts, with the same m and n points (for explanation, see text) as those given in Fig. I-1 (dose calculation: dose = a − b log (lymphocyte counts), where a and b are constants).

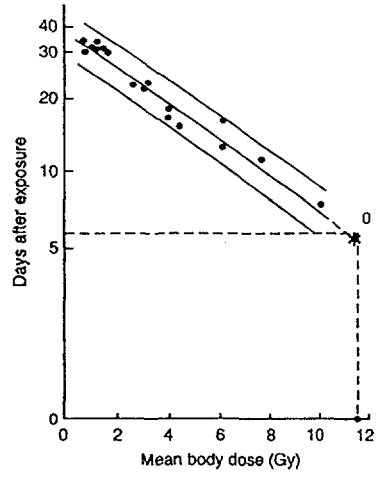


FIG. I-3. Days after exposure against the mean body dose (for explanation of the 0 point, see text).

Annex II

RESULTS OF CYTOGENETIC ANALYSES

TABLE II-I. RESULTS OF CYTOGENETIC ANALYSES OF THE 'DIRECT' BONE MARROW SAMPLES PERFORMED AT THE EARLIEST STAGE AFTER EXPOSURE (26–27 OCTOBER 1991) (see Fig. 7)

Location of bone marrow punctures	Time of puncture after exposure (h)	No. of metaphases analysed	Aberrated cells (%)	Evaluated dose (Gy)
(1) Sternum	18	25	100	>6
	25	50	100	>8–10
(2) Third thoracic vertebra	25	50	100	>6–10
(3) Crest iliaca anterior sinistra	25	50	100	>6–10
(4) Crest iliaca posterior sinistra	25	50	100	>8–10

TABLE II-II. RESULTS OF CYTOGENETIC STUDIES OF BONE MARROW LYMPHOCYTE CULTURES PERFORMED DURING THE FIRST MONTH AFTER EXPOSURE (see Fig. 7)

Location of bone marrow punctures	Date	No. of metaphases analysed	Frequency of dicentrics per 100 cells	Evaluated dose (Gy)	95% confidence intervals
(1) Sternum	26.10.1991	35	588.6	10.9	9.7–12.3
(2) Third thoracic vertebra	27.10.1991	30	530.0		
	31.10.1991	64	590.6		
	Weighted average		571.3		
	Total	94		10.6	9.9–11.8
(3) Crest iliaca anterior sinistra	27.10.1991	56	598.2		
	12.11.1991	8	700.0		
	Weighted average		610.9		
	Total	64		11.1	10.1–12.3
(4) Crest iliaca posterior sinistra	27.10.1991	25	564.0		
	12.11.1991	11	690.9		
	Weighted average		602.8		
	Total	36		11.1	9.8–12.4
Weighted average			590.0		
Total		229		10.9	10.2–11.8

TABLE II-III. DISTRIBUTION OF DICENTRICS AMONG METAPHASES OF THE FIRST MITOSIS IN BONE MARROW LYMPHOCYTE CULTURES PERFORMED DURING THE FIRST MONTH AFTER EXPOSURE (see Fig. 7)

Location of bone marrow punctures	1	2	3	4	*Total*
No. of metaphases analysed	35	94	64	36	229
Frequency of dicentrics	306	357	391	217	1351
Frequency of dicentrics per cell	*No. of cells with dicentrics*				
0	0	1	0	0	1
1	0	3	0	0	3
2	4	5	3	1	13
3	4	9	7	5	25
4	6	12	12	6	36
5	3	15	13	6	37
6	5	17	4	5	31
7	3	11	5	4	23
8	3	9	8	3	23
9	3	5	5	2	15
10	1	3	2	3	9
11	2	3	1	0	6
12	0	0	1	0	1
13	1	0	2	0	3
14	0	0	1	0	1
15	0	1	0	0	1
16	0	0	0	1	1

TABLE II-IV. RESULTS OF CYTOGENETIC ANALYSES OF PERIPHERAL BLOOD LYMPHOCYTE CULTURES AND BONE MARROW LYMPHOCYTE CULTURES PERFORMED 1.5 TO 3.5 MONTHS AFTER EXPOSURE (FREQUENCY OF DICENTRICS IN THE FIRST CELL'S MITOSIS) (see Fig. 7)

Date	Sample analysed	No. of metaphases analysed	% cells with dicentrics	Frequency of dicentrics per 100 cells
	Peripheral blood	130	6.9	42.3
09.12.1991	(1) Bone marrow, sternum	26	11.5	69.2
16.01.1992	(1) Bone marrow, sternum	151	8.6	55.0
	(3) Bone marrow, crest iliaca anterior sinistra	57	12.3	78.9
	(5) Bone marrow, crest iliaca posterior dextra	196	4.6	24.5
06.02.1992	(4) Bone marrow, crest iliaca posterior sinistra	86	9.3	70.9

Annex III

LIST OF DRUGS, DOSES AND ADMINISTRATION DATES

No.	International non-proprietary name (INN)	Daily dose or range (g)	Daily dose or range (IU)	Daily dose or range (L)	Total dose	Start of administration (date)	End of administration (date)
1	Acyclovir	0.5–1.5			31.5	20.10.1991	28.12.1991
2	Albumin 10%			0.3–0.6	7.2	07.11.1991	13.12.1991
3	Alvesin[a, b]			0.5–1.5	34.15	26.11.1991	10.02.1992
4	Aminocaproic acid	5.0			5.0	02.12.1991	02.12.1991
5	Amphotericin B	0.05–0.1			3.35	02.11.1991	04.02.1992
6	Azlocillin	20.0			4680.0	03.11.1991	13.01.1992
7	Cefazoline	2.0–3.0			15.0	01.11.1991	17.01.1992
8	Cefotaxime	1.0–4.0			46.0	06.01.1992	10.02.1992
9	Ceftazidime	2.0–3.0			89.0	30.10.1991	29.12.1991
10	Ceftriaxone	2.0			22.0	05.12.1991	25.12.1991
11	Chloramphenicol	2.0–3.0			49.0	11.12.1991	10.12.1992
12	Ciprofloxacin	0.5			10.5	14.01.1992	03.02.1992
13	Cytotect 10%[a, c]			0.100	0.200	29.10.1991	30.10.1991
14	Deferoxamine	0.5–1.0			17.0	17.01.1992	04.02.1992
15	Diclofenac[d]	0.075			2.32	14.12.1991	19.01.1992
16	Folic acid	0.04			1.44	30.12.1991	03.02.1992
17	Furosemide	0.02–0.32			1.42	26.10.1991	08.02.1992
18	Gancyclovir	0.25–0.5			1.00	06.02.1992	10.02.1992
19	Gentamycin	0.16–0.24			3.04	01.11.1991	03.12.1991

Annex III (cont.)

No.	International non-proprietary name (INN)	Daily dose or range (g)	Daily dose or range (IU)	Daily dose or range (L)	Total dose	Start of administration (date)	End of administration (date)
20	GMCSF	$(0.2–0.6) \times 10^{-3}$			13.2×10^{-3}	28.10.1991	04.12.1991
	GMCSF	0.4×10^{-3}			0.8×10^{-3}	28.10.1991	29.10.1991
	GMCSF	0.4×10^{-3}			1.6×10^{-3}	30.10.1991	02.11.1991
	GMCSF	0.2×10^{-3}			0.2×10^{-3}	03.11.1991	03.11.1991
	GMCSF	0.6×10^{-3}			1.8×10^{-3}	11.11.1991	13.11.1991
	GMCSF	0.4×10^{-3}			8.8×10^{-3}	14.11.1991	04.12.1991
21	Heparin		$(5–24) \times 10^{3}$		424×10^{3}	26.10.1991	03.12.1991
22	IL-3	0.3×10^{-3}			6.75×10^{-3}	03.11.1991	25.11.1991
	IL-3	0.3×10^{-3}			2.1×10^{-3}	03.11.1991	09.11.1991
	IL-3	0.15×10^{-3}			0.15×10^{-3}	10.11.1991	10.11.1991
	IL-3	0.3×10^{-3}			0.3×10^{-3}	11.11.1991	11.11.1991
	IL-3	0.3×10^{-3}			0.6×10^{-3}	12.11.1991	13.11.1991
	IL-3	0.3×10^{-3}			1.2×10^{-3}	14.11.1991	17.11.1991
	IL-3	0.3×10^{-3}			2.4×10^{-3}	18.11.1991	25.11.1991
23	Imipenem	2.0			26.0	28.11.1991	10.12.1991
24	Immunoglobulin[a, e, f]	7.5–30.0			170.0	28.10.1991	07.02.1992
25	Ketocanazole	0.4			21.6	27.10.1991	19.12.1991
26	Methylprednisolone	0.06–1.00			2.05	29.10.1991	10.02.1992
27	Metronidazole	1.0–2.0			47.5	19.11.1991	23.11.1991
28	Nandrolone	0.025			0.025	29.01.1992	29.01.1992
29	Nituroxazide	0.8			10.4	07.12.1991	19.12.1991
30	Norfloxacin	0.4			12.0	05.11.1991	04.12.1991

No.	International non-proprietary name (INN)	Daily dose or range (g)	Daily dose or range (IU)	Daily dose or range (L)	Total dose	Start of administration (date)	End of administration (date)
31	Ofloxacin	0.4			6.4	26.10.1991	20.12.1991
32	Paracetamol	0.4–0.8			5.6	20.01.1992	27.01.1992
33	Pentaglobulin[a, g]	10.0			10.0	10.11.1991	10.11.1991
34	Polygeline 6%			0.4	1.2	02.12.1991	08.02.1992
35	Polymyxin B	1.0			14.0	11.12.1991	25.12.1991
36	Polyvidone 6%			0.4	0.4	06.02.1992	06.02.1992
37	Potassium chloride 5%			0.3–0.5	1.7	20.12.1991	20.12.1991
38	Potassium carbonate[h]	0.2–0.4			3.4	06.11.1991	28.12.1991
39	Prednisolone	0.03–0.06			0.33	28.10.1991	31.12.1991
40	Roboxin	0.2			0.4	20.12.1991	30.12.1991
41	Sodium bicarbonate 4%			0.15–0.6	1.25	06.02.1992	09.02.1992
42	Trimethoprime 80, Sulphamethaxasole 400	0.96–3.96			36.20	05.12.1991	05.02.1992
43	Vamin[a, b]			0.5–1.0	13.5	01.11.1991	25.11.1991
44	Vancomycin	2.0			28.0	05.11.1991	18.11.1991

[a] Non-INN.
[b] Amino acid mixture for parenteral nutrition.
[c] Anti-CMV immunoglobulin intravenous.
[d] Voltaren.
[e] Immunoglobulin intravenous (IGIV) G (Gammagard).
[f] Immunoglobulin intravenous (IGIV) G (Glovelin).
[g] Immunoglobulin intravenous (IGIV) M.
[h] Aldactone.

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