The Radiological Accident in Soreq

IAEA

Editorial Note

The radiological accident described in this report occurred at an irradiation facility operated by Sor-Van Radiation Ltd, a commercial company. The facility, situated near the river Soreq, is on the premises of, but is independent of, the Soreq nuclear research centre. The name Soreq in the title of this report is employed solely as a geographical descriptor.

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THE RADIOLOGICAL ACCIDENT IN SOREQ

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FOREWORD
by the Director General

Industrial applications of ionizing radiation continue to spread around the world: millions of people benefit from these applications, especially in activities related to health care, for which the use of disposable medical supplies sterilized by radiation has been central to combating contagious diseases. There are currently more than 160 large gamma irradiation facilities and over 600 electron beam facilities in operation around the world, in almost every Member State of the IAEA.

Experience over more than 40 years in the field of radiation processing has shown that such technology is generally safely used. The steady improvement in the design of such facilities and careful selection and training of operators have contributed to a very good safety record. Nevertheless, there have been instances, as in Italy in 1975, in Norway in 1982 and in El Salvador in 1989, when safety systems have been circumvented and serious radiological accidents have ensued.

On 21 June 1990, one such accident occurred at an industrial irradiation facility in Israel when an operator entered the irradiation room and was acutely exposed to radiation, with fatal consequences. This accident was the result, as was the earlier one in San Salvador, of a violation of established operating procedures. The accident in Israel, a country with a comparatively good infrastructure for radiation protection, demonstrated that it is necessary to maintain close supervision over the operation of such facilites and the training of operators, and indicated the need for further research into the contribution of human factors to such accidents.

An international review was undertaken by the IAEA to document the causes and circumstances of the accident and to draw general lessons for the benefit of those people with responsibilities for the safety of such facilities and for physicians responsible for the treatment of patients after such accidents.

EDITORIAL NOTE

CONTENTS

1. INTRODUCTION

1.1. SUMMARY

On 21 June 1990 there was a radiological accident in a commercial irradiation facility at Soreq, Israel. Prepackaged medical products and spices are sterilized at the facility by irradiation by means of an intensely radioactive cobalt-60 source in a movable source rack. The accident happened after the source rack became stuck in the irradiation position owing to obstruction by cartons on the internal conveyor. The operator, having misinterpreted two conflicting warning signals, bypassed installed safety systems and contravened procedures in order to enter the irradiation room to free the blockage.

After a minute or so in the irradiation room, the operator felt a burning sensation in his eyes and pounding in his head. Frightened, he left the room and reported the incident to a superior. Shortly afterwards he felt sick and started to retch. He was immediately taken to a hospital where specialized care was provided. He presented signs and symptoms indicative of severe haematological and gastrointestinal phases of acute radiation syndrome (ARS). Localized skin injury due to irradiation also developed. It was estimated that he had received a whole body dose of between 10 Gy and 20 Gy.

Despite all medical efforts, including the use of new haematopoietic growth factor drugs, he died 36 days after the accident.

1.2. BACKGROUND TO THE 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. The use of intense radiation sources for purposes such as the sterilization of medical products or foodstuffs requires 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 being safely used, 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 may be highly case specific, review of the circumstances in which they arise may yield generally applicable lessons that can be of help in preventing further accidents or in improving the response to those that do occur. This was the motivation for reviews by the IAEA of two fatal accidents, in Goiânia, Brazil, in 1987 [1] and in San Salvador, El Salvador, in 1989 [2]. The latter accident also was

at an irradiation facility and it had a number of similarities with the accident in Israel reported here. Three other fatal accidents have occurred at irradiators: in Brescia, Italy, in 1975 [3]; in Kjeller, Norway, in 1982 [4]; and in Nesvizh, Byelorussian Republic, in 1991. The accident in Nesvizh happened while the present report was in preparation; an IAEA follow-up review has since taken place and a report is now in preparation on this accident also.

There are more than 600 industrial irradiation facilities of the gamma ray and electron beam type in use around the world. Many of these are in developing countries; however, as is evident, accidents are not confined to those irradiators in developing countries. The number of fatal accidents in irradiators has given impetus to the IAEA's programme of work in this area (see Section 5.3); one aspect of this work has been the post-accident review reported here.

1.3. FORMAT OF THE REPORT

Although the report is likely to be of general interest in the radiation protection community, it is aimed chiefly at two distinct and specific audiences, namely:

(i)   those responsible for the design, operation and regulation of irradiators; and
(ii) those concerned in the medical management of patients who have been subjected to acute whole body irradiation at high doses.

The report is presented in two separate parts. Sections 2 to 5 deal with the circumstances of the accident, its causes and the lessons to be learned. Sections 6 to 8 deal with the initial medical assessment and medical management of the patient, the post-mortem findings and the lessons to be learned from the case.

2. THE IRRADIATION FACILITY

Note: *Observations on factors contributory to the accident*
are presented in italic script

2.1. HISTORY AND GENERAL DESCRIPTION OF THE FACILITY

The irradiation facility at Soreq in Israel was built in the late 1960s and was licensed to operate in 1970. It was a joint venture between interests in the Netherlands and the Israeli Atomic Energy Commission. Because of the latter connection it is located within the Soreq nuclear research centre. However, it operates as a separate commercial concern under the name of Sor-Van Radiation Limited.

The facility uses a Model JS6500 gamma sterilizer designed, manufactured and installed by Atomic Energy of Canada Limited, which now trades as Nordion International Incorporated (hereinafter referred to as 'the supplier'). The irradiator is similar in design to one in San Salvador at which there was a fatal accident in 1989 [2]. In this design the product cartons either can be loaded into large product boxes or, if they are large enough, can be taped together. They are then moved by pneumatic cylinders (pistons) around a centrally located vertical source rack. The source rack holds cobalt-60 gamma source elements in the form of source pencils. The source is shielded when not in use by lowering it into a pool of water, making it a Category IV irradiator under the international classification [5]. The irradiation room has massive concrete walls and ceiling for protection; entry is through a maze.

In the remainder of Section 2, the facility and its operation are described in more detail, as it is intended to function and as it was at the time of the accident. For clarity, the differences between the two and other observations are shown in italic type. To supplement the description of the design and layout of the facility, three detailed drawings have been included at the end of the report (Figs 1–3: *see inside back cover*).

2.2. THE RADIOACTIVE SOURCE

Radioactive cobalt-60 metal is the radiation source in the JS6500 gamma sterilizer. The cobalt-60 source elements are contained in doubly encapsulated stainless steel source pencils approximately 45 cm long, with solid stainless steel end caps approximately 1 cm in diameter (see Fig. 4). Each source pencil is identified by a serial number engraved on an end cap.

The source pencils, together with dummy (non-radioactive) source pencils, are loaded into source modules in such a way as to give a uniform distribution of activity and the desired isodose rate distributions at the irradiation positions. The source pencils and dummy pencils are held in place by channels at the top and bottom of the source modules. In the JS6500 sterilizer, six modules in a 3 by 2 flat array form the source rack. At the time of the accident the total activity of the cobalt-60 source elements was 12.6 PBq (340 kCi).

In this accident, unlike in the one in San Salvador, none of the sources were dislodged from the source rack. However, the potential for this was recognized by the Israeli authorities in their post-accident review, and a number of recommendations consistent with those of the supplier were made.

2.3. THE SOURCE HOIST MECHANISM

The source rack, when not in use, is stored near the bottom of a 5.5 m deep storage water pool. It is raised from the pool to the irradiation position by a pneu-

Hoist cable

20.96 cm

0.81 cm

1.11 cm

49.5 cm

47.5 cm

45.2 cm

Guide cables

Source rack holding six
source modules

Source module containing
42 source pencils

Source pencil
containing
two standard
source elements
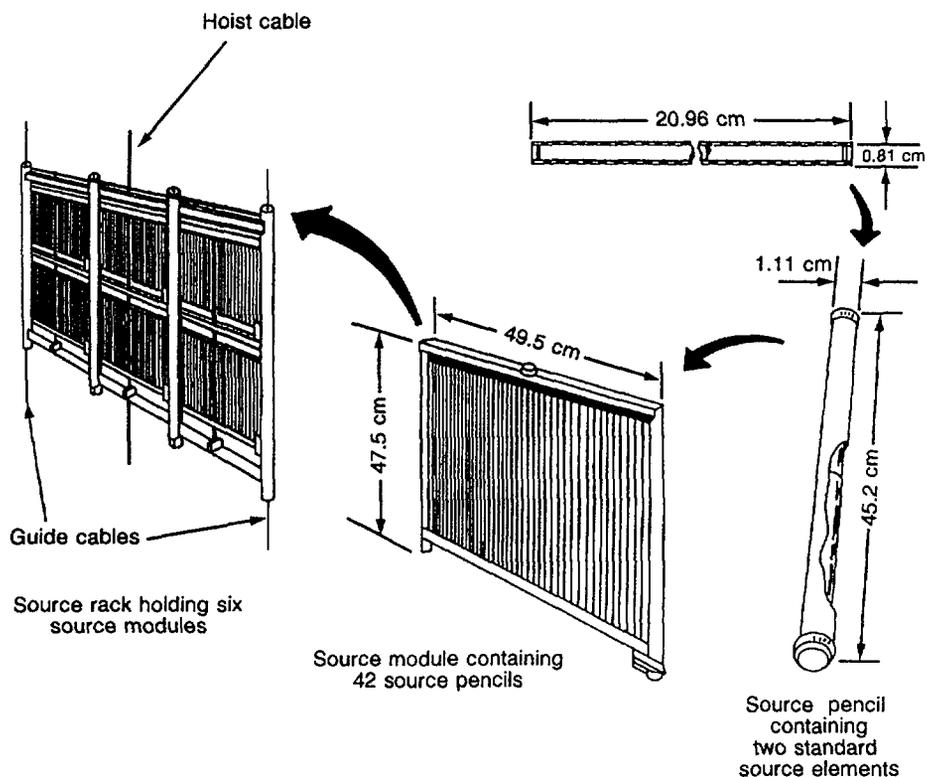
FIG. 4. The source rack with six source modules, each containing up to 42 source pencils with two standard source elements in each pencil. (By courtesy of Nordion International Inc.)

matic hoist mounted on the roof of the facility above the radiation shield (see Figs 2 and 3). A stainless steel hoist cable attached to the source rack passes through the shield and the roof to two sets of sheaves in the hoist cylinder that are moved by the pneumatic piston. The movement of the source rack is guided by two taut guide cables, one at each end of the rack (see Fig. 5). On being raised, the piston guide of the hoist cylinder actuates a microswitch (LS-109) mounted on the hoist cylinder to indicate that the source rack is no longer down; thus for any other position of the source rack than fully down, the microswitch should indicate that the source rack is up.

When air is exhausted from the source hoist, the source rack is returned under gravity to the safe storage position in the water pool. The weight of the source rack pulls the sheaves in the hoist cylinder back together, and the microswitch is deactuated to indicate that the source rack is down.
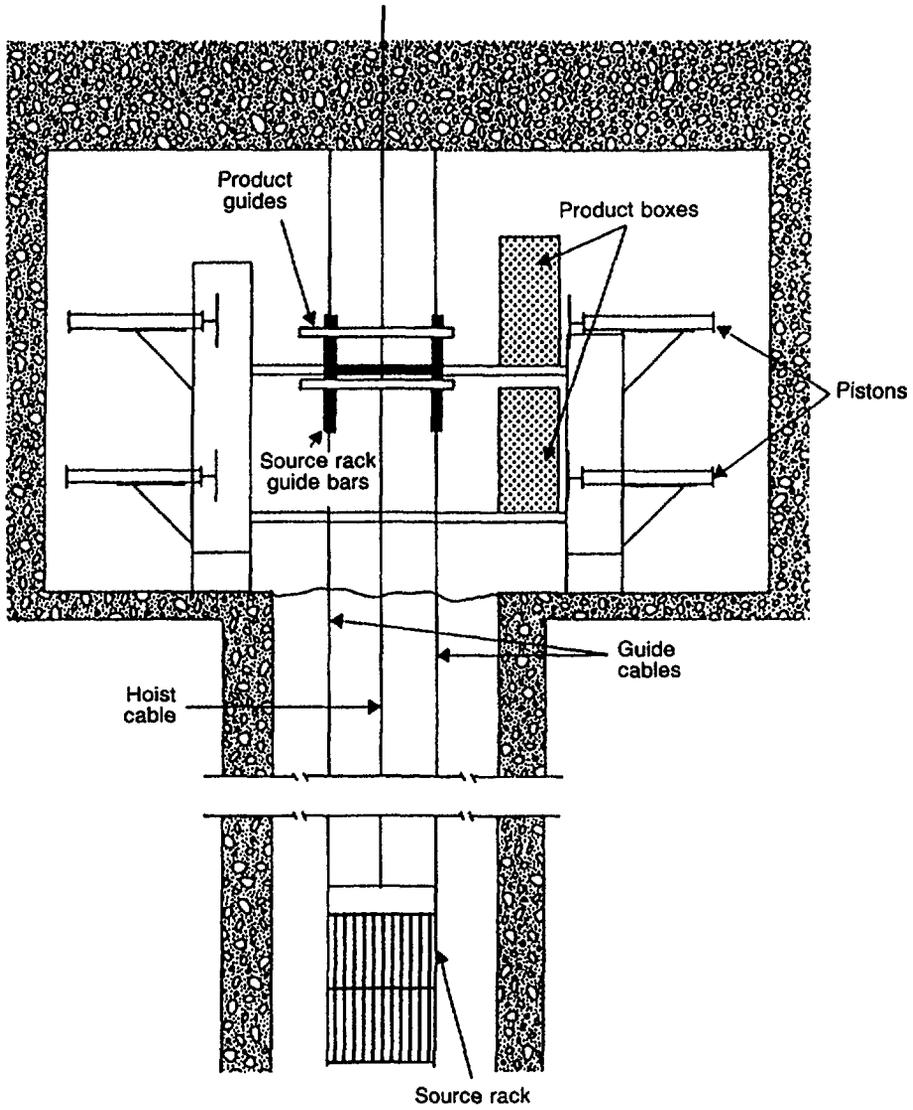
FIG. 5. Cross-sectional diagram of the source rack, hoist mechanism and transport mechanism. (By courtesy of Nordion International Inc.)

Source down position

Mounting bracket (with adjustment slots)

Piston guide
Indent
Actuator
Microswitch

Piston movement

Source up or moving

Switch movement

Travel arc

Switch positions

Operating position

Differential travel

Overtravel
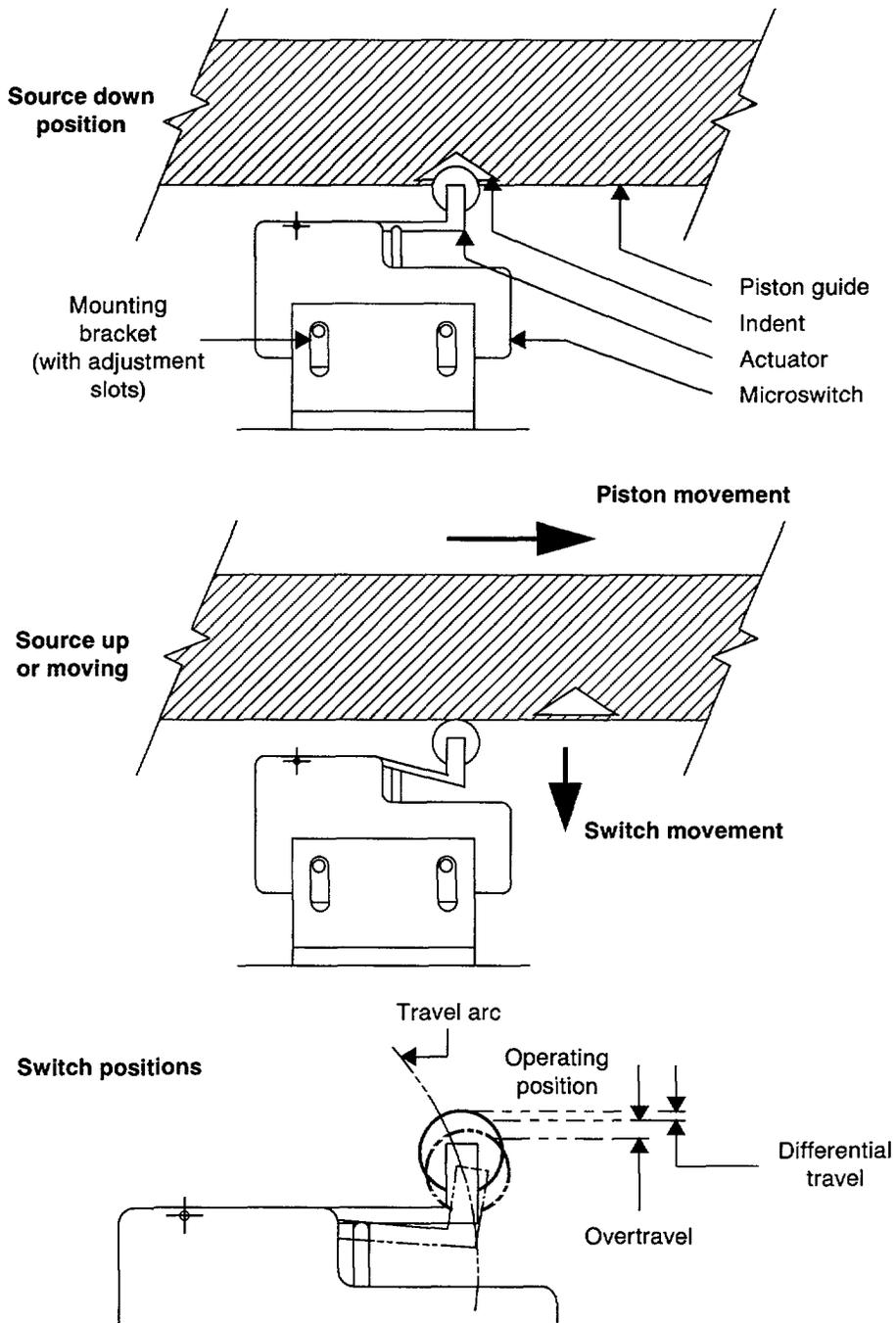
FIG. 6. *Diagram showing the working of the LS-109 limit microswitch mounted on the hoist cylinder to indicate when the source is down. (By courtesy of Nordion International Inc.)*

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Figure 6 illustrates the operation of the limit microswitch. When the source rack is in the down position a roller on the actuator of the limit microswitch drops into an indent on one of the guides for the piston of the hoist cylinder. This is clearly visible through a window opening on the cylinder barrel. As the hoist piston moves to raise the source, the roller is pushed out of the indent and rides on the surface of the piston guide, causing the switch to actuate (i.e. one set of switch contacts opens and another set of contacts closes).

When installing or replacing the microswitch it is necessary to adjust its position on the mounting bracket so that it is positively actuated when the cylinder moves and is clearly deactuated when the roller drops into the indent. This is done by ensuring that the actuator over-travels past the point of actuation, as illustrated in Fig. 6.

It seems that at the time of the accident the microswitch was out of adjustment and did not actuate reliably when the roller moved out of the indent. It was concluded that the adjustment of the microswitch did not allow sufficient over-travel when the source rack was raised, and the switch consequently continued to indicate that the source rack was down. As is discussed in subsequent sections, there are other safety systems to prevent access while the source is exposed, and these would have called into question the validity of the source down indication from the microswitch. In such a situation, a technician with knowledge of maintenance procedures could go to the roof to check whether the roller was in its indent. That the roller was not in the indent would indicate that the source rack was not safely down.

2.4. THE PRODUCT TRANSPORT MECHANISM

The packages to be irradiated are generally packed in cartons and often two or three cartons are stacked and taped together for passage through the irradiator. These cartons, moving on roller conveyors, are irradiated in 57 steps, between which they are moved by pistons of the product transport mechanism (see Fig. 7). The cartons are moved back and forth past the source rack along four rows, two on each side of the source rack, on each of two levels (shown schematically in Fig. 8), and are lowered from the upper to the lower level by a pneumatic elevator. Steel product guides restrict the movement of the cartons to the path around the source and provide some protection to the source rack. Limit switches monitor the locations of the pistons that move the cartons and control the sequence by means of a relay logic panel.

The length of time for which a carton remains in each irradiation position is controlled by a master timer. When the time set on the master timer has elapsed, a sequential movement of the pistons is initiated. This advances each carton by one position and shifts one fully processed carton to the lower shelf of a product carrier
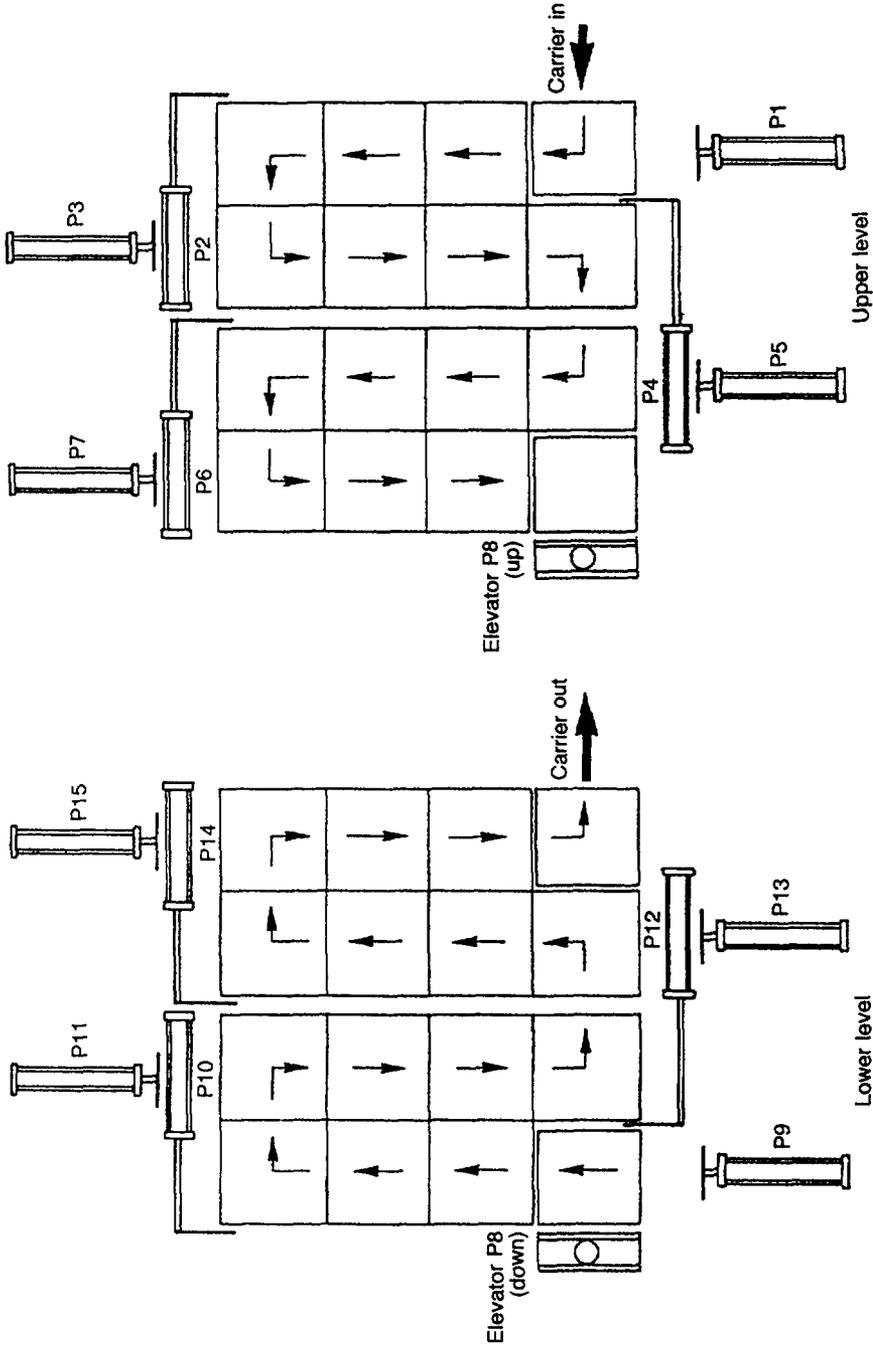
FIG. 7. Plan of the two levels of the transport mechanism of the JS6500 irradiator. (By courtesy of Nordion International Inc.)

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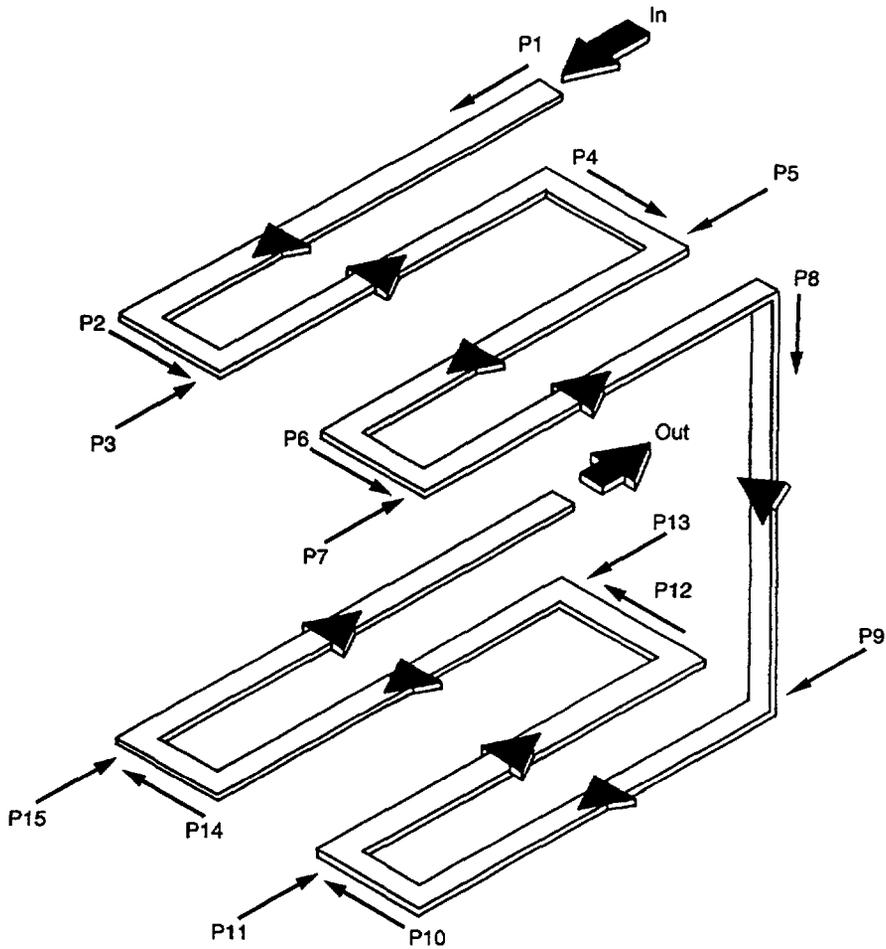
FIG. 8. Schematic diagram of the transport of product boxes in the irradiator. (By courtesy of Nordion International Inc.)

which transports it from the irradiator. At the time of the accident, each irradiation step lasted approximately 12 minutes and the total irradiation time for each carton was approximately 11 hours. The dose to the product was approximately 25 kGy.

Between 1975 and 1981 a number of incidents occurred at irradiators in the United States of America and elsewhere (including an earlier incident in San Salvador in 1975) when damaged product boxes obstructed the source rack and caused it to jam. Consequently, in 1981 the supplier distributed Warning Notice IND-81-1, in which it was recommended that a steel shroud be fitted around the

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irradiation position to prevent such obstruction. It also recommended that product boxes, where used, be routinely checked and those in poor condition replaced.

The plant had received Warning Notice IND-81-1 but had never put its recommendations into effect. The reasons for this are unclear, although it is understood that the company had taken the warning notice as advice rather than as a requirement and in response had indicated that they would not accept used cartons from customers. Subsequently, during a source replenishment in July 1988, the supplier had insisted that during the next replenishment a shroud must be fitted. Drawings for this had been procured in February 1990 and arrangements had been made to have the shroud fitted during the next source replenishment later in 1990. It is also relevant to note that the regulatory authorities were not aware of the existence of Warning Notice IND-81-1 concerning the shroud. It was reported that at the time of the accident all the cartons in use were new and intact.

2.5. SAFETY INTERLOCKS AND ACCESS CONTROL

2.5.1. Control console

The entire irradiation programme is run from a free standing control console outside the irradiation room (see Fig. 9 and Photograph 1). There are three key switches for power on, source raise and machine on. The first two control movement of the source and the third permits movement of the transport mechanism while the source is raised. There are warning lights in the form of illuminated legends to indicate source up and source down. The first of these is linked to limit switches at the irradiation position; the latter is linked to the microswitch mentioned previously on the hoist mechanism.

The irradiation programme is interrupted and the source automatically lowered if tripped by a safety interlock or if sensors detect high temperatures in the irradiation room, low pressure in the pneumatic hoist system or misaligned cartons jamming the transport mechanism (detected by a timer if not all pneumatic pistons have successfully completed their motions within a preset time). These failure modes have their own warning lights. A source rack warning light is illuminated if the source rack does not complete its upwards or downwards motion within the preset time. The systems for automatic lowering of the source rack had operated without faults over the lifetime of the plant.

If a product jam interferes with the movement of the source rack and prevents its return to the safe down position, the source rack light and source moving bell provide a warning. However, these would not be the only warnings of such an occur-
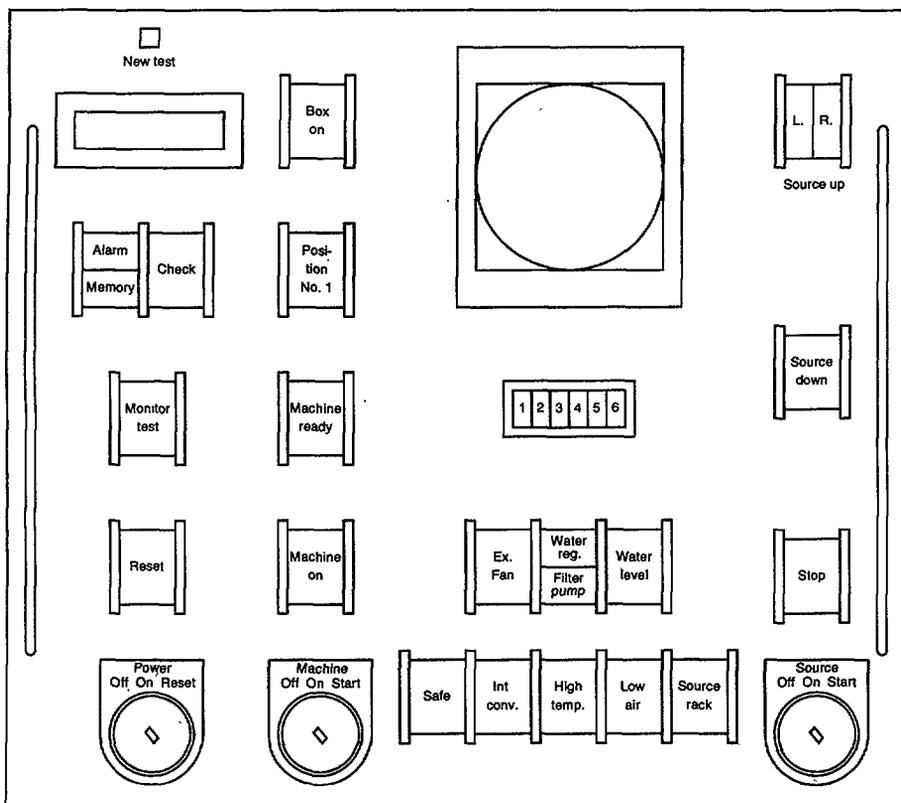
FIG. 9. The control panel of the JS6500 irradiator. (By courtesy of Nordion International Inc.)

rence; warning would also be given by an installed radiation monitor, as described in the following.

Inside the control console there is a backup timer for product overdose which occasionally needs adjustment. This timer was added after the original installation, and for quicker access to it the door panels of the control console were left unlocked. This made it easier to tamper with the console's internals.

2.5.2. Installed radiation monitor

A fixed radiation monitor Type L-118 (see Fig. 10) connected to circuitry in the control console is mounted on the wall at the inner end of the entrance maze.

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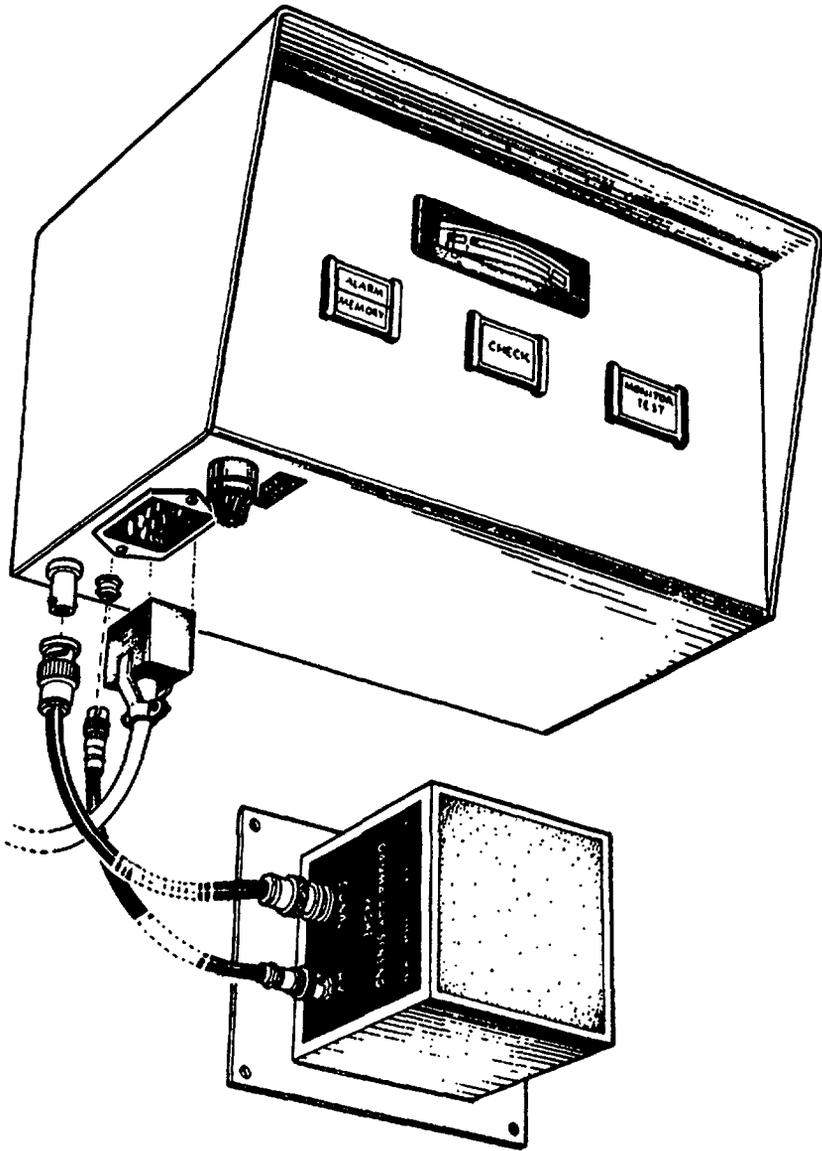
FIG. 10. The L-118 wall mounted single probe monitor system. (By courtesy of Nordion International Inc.)

Dose rate indicator

Alarm

Memory

Check

Monitor test

Pulsating DC
(detected radiation level)

1 amp

Source down switch

Source hoist mechanism

Alarm signal

Alarm horn

AC power input

Door interlock switch

Guide cables

Monitor

Door interlock

Sensor probe

Hoist cable

Source

Source pool
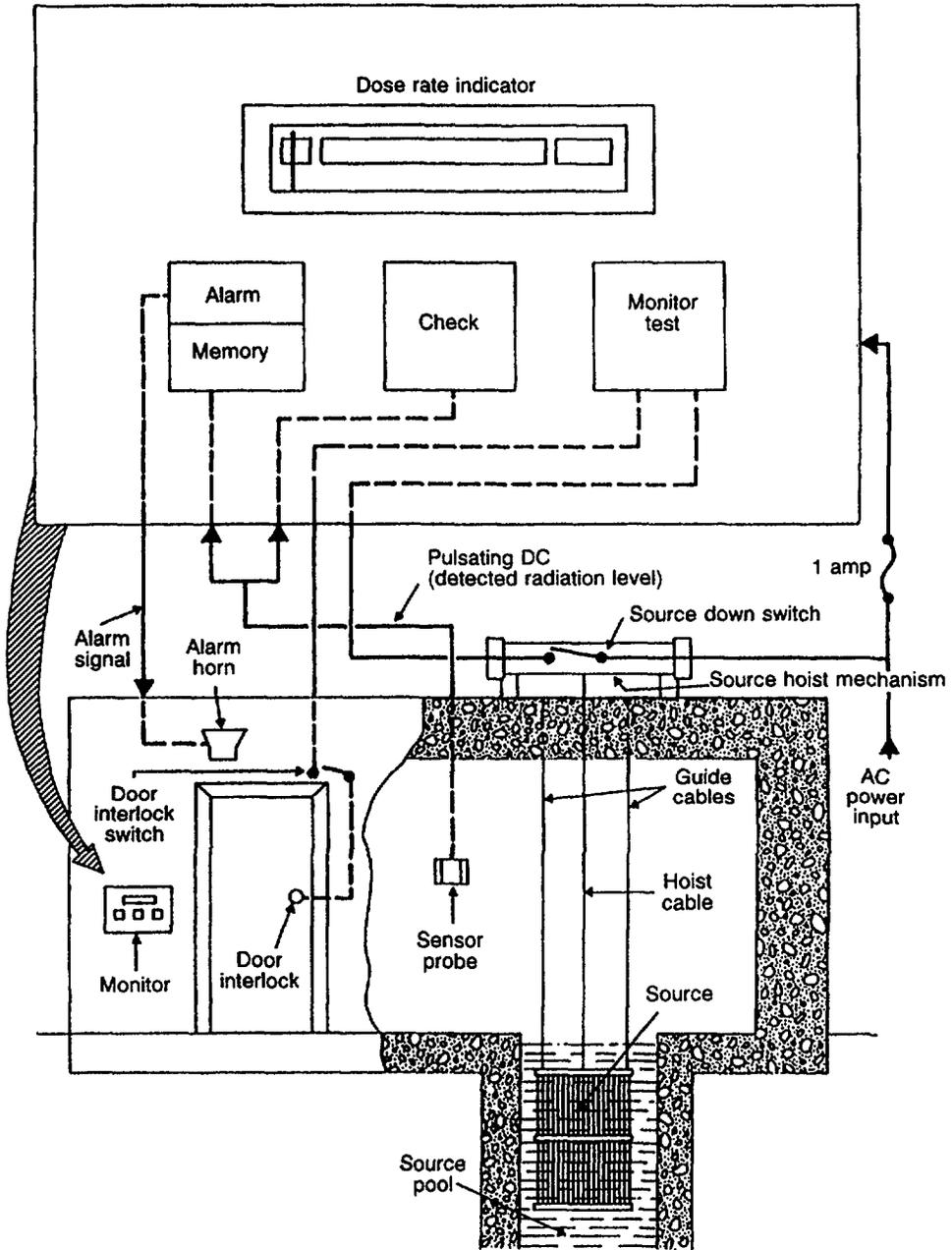
FIG. 11. Schematic diagram of the circuits for the radiation monitor in the radiation room and the interlock system. (By courtesy of Nordion International Inc.)

The fixed monitor is interlocked to the key switch that operates the door lock solenoid, and if dose rates are abnormally high when the source is supposed to be in the safe position, access is prevented and auditory and visual alarms are given. The monitor has an array of nine Geiger–Müller tubes and is designed to give an alarm condition for dose rates in the range of about eight times background levels to greater than 10 000 Sv/h. Figure 11 is a schematic representation of the monitor's main features and shows how they are integrated with other safety features.

In order to enter the irradiation room, the operator must first press the monitor test button. The counting circuitry in the monitor then counts pulses from the monitor probe as it registers natural background radiation to give a test alarm indication. The test cannot be performed if the monitor is already showing the alarm condition. When the monitor test button is released, the monitor must again indicate normal levels of background radiation before power can be supplied to the key switch that operates the door lock solenoid.

The radiation monitor and the source rack down microswitch are also interlocked. When the source rack is not fully down (i.e. is not in the safe position), power to the monitor is shut off. This also cuts off power to the key switch for the door lock solenoid, thereby disabling the access control system and preventing access to the irradiation room.

The monitor and its associated circuitry are the same as those in the irradiator in San Salvador at which there was a fatal accident in 1989, but the display and the test button are integrated into the control console rather than separate.

There was testimony after the accident to the effect that the monitor test procedure would occasionally cause the operators trouble in that it failed to release the interlock, and the operator had to repeat the test several times until the interlock mechanism yielded. At some stage a 'trick' to simulate the test procedure had been discovered. The origins of the trick are uncertain but there was speculation that it had been discovered three years previously during maintenance. The trick was to remove the key from the machine switch, insert it into the adjacent power switch and then cycle it on and off several times while depressing the test button. This power cycling generated electromagnetic pulses which were picked up by the monitor circuitry and which simulated pulses from the radiation monitor. This trick had been learned by the operators without their having appreciated its safety significance, and had been used in ignorance to bypass the interlock mechanism. Importantly, the management was not aware of the use of this unauthorized procedure.

Over time the Geiger–Müller tubes degrade owing to radiation damage, causing a loss of sensitivity. The supplier took account of this by providing for compensatory sensitivity adjustment in the monitor circuits. Eventually further adjustment was no longer possible, whereupon the tubes should have been replaced.

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The installed monitor had given a false alarm on one occasion some three years before the accident. The circumstances of this false alarm are not documented, but the fact that a false alarm had occurred was relevant to the course of the accident.

2.5.3. Other safety features

If the source rack down microswitch is actuated and no abnormal levels of radiation are detected by the installed monitor, power to the door solenoid releases a lock on the door. However, the operator is still required to test the monitor as described in Section 2.5.2 and to take the machine key out of the console (it can only be removed from the off position) and unlock the entrance door.

In the irradiation room there is a key switch with a delay timer which must be operated with the machine key to oblige the operator to enter the room. The operator is then to make an inspection to ensure that there is no one in the room and that the transport mechanism is in order before leaving the room to raise the source. When the delay timer is set, a buzzer sounds to warn personnel that the source rack is about to be raised. The operator then has approximately 90 seconds to leave the irradiation room, close the door and start the operation of the irradiator from the control console. In the irradiation room there is also an emergency pull cord running along the walls that returns the source to the safe position.

Turning the machine key switch to the off position or pressing the stop button on the control console will also stop the irradiator and lower the source.

In addition to the automatic safety features, there should be administrative controls to ensure that the facility is operated only by trained, authorized operators in accordance with the procedures in the instruction manual. In particular, attached to the key by a chain is a small portable Geiger–Müller dose rate meter that should be used inside the irradiation room to confirm that radiation levels are normal. Prior to entry a functional check of the instrument should be made using a small check source installed in the door frame. An additional portable monitor was available in the next room.

The last formal calibration of the portable dose rate meter was in November 1989, some seven months before the accident and therefore within the normal annual frequency. The meter has two dose rate ranges. It was subsequently found that at the time of the accident the meter was not responding to radiation on the more sensitive low dose rate range owing to a broken internal electrical connection.

2.6. MAINTENANCE

A regular preventive maintenance programme is prescribed in the instruction manual for the irradiator. The number of shutdowns of the irradiator can be kept to

a minimum by following this preventive maintenance programme. It includes a monthly test of all emergency shutdown devices.

Although most of the equipment was found to be in satisfactory condition after the accident, no written records had been kept on preventive maintenance, and it could not be determined whether the preventive maintenance programme had been rigorously implemented.

2.7. OPERATION, SUPERVISION AND RADIOLOGICAL TRAINING

The facility had a heavy work-load and the irradiator was often in operation for 24 hours a day, but it was only staffed on the regular day shift. For this reason the external input and output conveyors had been lengthened to hold enough cartons for 5 to 7 hours (depending on the irradiation programme). Before leaving at the end of the day shift the staff would load the input conveyor to its full capacity and completely unload the output conveyor. At around midnight an operator would go to the facility to reload and unload the conveyors for the night. In anticipation of possible malfunctions that would stop the irradiation process, the source rack down indicator is hard wired to the emergency control centre of the Soreq nuclear research centre, which is always staffed. In the event of a malfunction, the signal would be relayed to the Soreq duty officer who would call out a Sor-Van operator.

Of a total workforce of about 20 at Sor-Van, there were four operating staff: a senior technician who had worked at the plant since it was built in the late 1960s and three technicians (one with 9 years' experience and two with more than 3 years' experience). All four were trained locally at the plant and were certified by the supplier after an examination. Only staff who had been certified and had had one year's practical experience were allowed to operate the facility. In addition each operator had attended a four day basic course on radiation protection, as required by the Israeli authorities. Each operator had passed an examination at the end of the course, which was run by the Soreq nuclear research centre.

The training courses had been given in Hebrew (the working language of the operators), but the lecture notes were in English. Similarly, the operating manual and safety instructions (parts of the instruction manual) were only available in the original English. A short list of routine operating and safety instructions, including the procedure for entering the irradiator, had been issued in Hebrew and was posted in the facility.

The senior technician had a good knowledge of English but the other three technicians had only an elementary knowledge. It was concluded after the accident that the lack of a translation into Hebrew of the operating manual and safety instructions had contributed to the operators' inability to cope with unusual events. The same applies to the lecture notes from the training courses,

which were also available in English only. In other respects the training was considered to have been correctly done.

There was a prevailing (oral) instruction that if the normal entry procedure could not be followed and particularly if the radiation alarm sounded, the operator must not act alone but must call a supervisor. The only written instruction to this effect was in English.

Also of relevance was the fact that no warning notices (which were recommended by the supplier and the Israeli authorities) had been posted.

The senior technician had been appointed many years earlier as Radiation Safety Officer (RSO), with the most experienced operator appointed his deputy. Professional advice on health physics was available from the Soreq nuclear research centre. In the facility's early years, when it was more closely associated with the nuclear research centre, there had been routine inspections by health physics staff, but these had been discontinued after a few years of operation. Advice was available on request and some 'external' inspections were still made by the health physics staff at Soreq, but these were infrequent and were not overseen by the administration of the Soreq centre. Staff are routinely monitored using thermoluminescent dosimeters (TLDs), but do not wear personal alarm monitors.

3. REGULATORY CONTROL

Responsibilities for safety in irradiation facilities must rest primarily with those who supply and use them; however, regulatory authorities can greatly influence how those responsibilities are discharged.

The authorities in Israel responsible for regulating the use of radioactive substances and radiation sources are:

(1) The Officer in Charge in the Ministry of Health (responsibility is being transferred to the Ministry of the Environment), who is responsible for issuing licences for facilities using radioactive materials and for inspection and enforcement.

(2) The Director, who in this case is the Director General of the Israeli Atomic Energy Commission and who must be consulted in certain cases before a licence can be issued.

(3) The regional Safety Inspector of the Ministry of Labour and Welfare, who has responsibilities for inspections in relation to safety in the workplace, and to whom radiation exposures and accidents must be reported.

The Officer in Charge at the Ministry of Health had hired the services of the radiological protection department of the Soreq nuclear research centre to perform most of the inspections for the Ministry and to advise the Officer in Charge.

Subsequent to the accident, the Ministry of Labour and Welfare appointed a committee of experts to investigate its causes and circumstances. The committee of inquiry studied the documentary records relating to the licensing and inspection of the Sor-Van facility. It found that these lacked depth and that the enforcement had been placable and inadequate.

4. THE ACCIDENT

4.1. INITIATING EVENTS

Shortly after 17:00 on 21 June 1990 a jam occurred in the transport mechanism of the irradiator. The cartons undergoing irradiation were reported to have been in good condition, and the exact cause of the jam is unknown. The pressure caused cartons on the outer lower conveyor to bulge and burst (see Photograph 2). This also disrupted cartons on the adjacent inner lower conveyor, causing one carton to protrude towards the source rack. The overdose timer detected the jam and the control system automatically caused the source rack to begin to descend. However, before it had descended one metre it was blocked by a carton on the inner lower conveyor (see Photograph 3) which was protruding under the upper edge of the source rack. (The carton on the inner lower conveyor that hindered the descent of the source rack was torn later in the action of releasing the rack. Photograph 3 also shows the steel guide bar into which the upper edge of the source rack fits and the source hoist cable.)

The microswitch on the source hoist is now known to have been malfunctioning and to have indicated incorrectly that the source rack was fully down. It seems that at the time of the accident the microswitch (Fig. 6) was out of adjustment and did not actuate when the roller moved out of the indent (see Section 2.3). It was concluded that the adjustment of the switch did not allow sufficient over-travel in the source moving/up position. As a result, the source down light on the control console (Photograph 1) was illuminated (together with the product jam warning light) and power was supplied to the installed radiation monitor. This registered very high dose rates, causing the gamma radiation alarm horn to sound.

The product jam (without any details) was registered at the emergency centre of the Soreq nuclear research centre, and the Sor-Van duty operator was informed at home by telephone. He was also telephoned by several staff members who were

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at the facility and heard the alarm. One of these was a senior staff member who on his way out switched off the power to the unit to silence the alarm. He was not familiar with the equipment and left it to the qualified operator to deal with. He in fact met the operator outside and told him that he had turned the power off and about the contradictory indications on the control console. He also suggested that the operator contact the RSO for instructions.

4.2. ENTRY AND EXPOSURE

The operator arrived at approximately 17:35 and switched the power back on at the control console. The previous signals resumed, namely the product jam warning light, the source down signal and, importantly, the gamma radiation alarm horn. Although the written (English) operating instructions and the oral (Hebrew) standing orders forbade operators to deal with such cases by themselves, he did not inform the RSO as he should have done but decided to deal with the matter alone. There are indications that he was in a hurry.

A series of mistakes in reasoning and unauthorized actions followed this decision.

The operator was faced with two conflicting signals, one indicating that the source was safe and one that it was not. He chose to believe that the source down signal was correct and that the radiation alarm was false. Subsequently he said that his reasoning was that the movement of the source rack and the source down signal had never failed but that there had been a false gamma alarm from the radiation monitor about three years previously. Had the operator been in less of a hurry he could have called for assistance from a technician with more knowledge of maintenance procedures who could have gone to the roof to check the position of the indent on the guide of the source hoist piston. This would have indicated that the rack was not down.

On the basis of his reasoning he decided to enter the irradiation room. There were, however, several safety features designed to prevent this. First of all, in order to silence the horn and possibly, according to his logic, to terminate a false signal from the radiation monitor, he went behind the console, opened the unlocked doors and disconnected the cable from the radiation monitor to the alarm and control circuitry (see Photograph 4). The alarm stopped.

The intention of the design of the safety systems was that disconnecting the monitor cable would have prevented the door from being opened, because the monitor test could not be made and hence power would not be supplied to the door lock solenoid. However, as described in Section 2.5.2, there was an established trick to simulate the monitor test. The operator removed the key from the machine switch and inserted it into the power switch, which he cycled on and off several times while

|			143 cm	
2.35	7.5	12.3		12.0
		14.5	123 cm	
			100 cm	
2.3	7.5	14.1		14.0

200 cm   100 cm

Left   Right
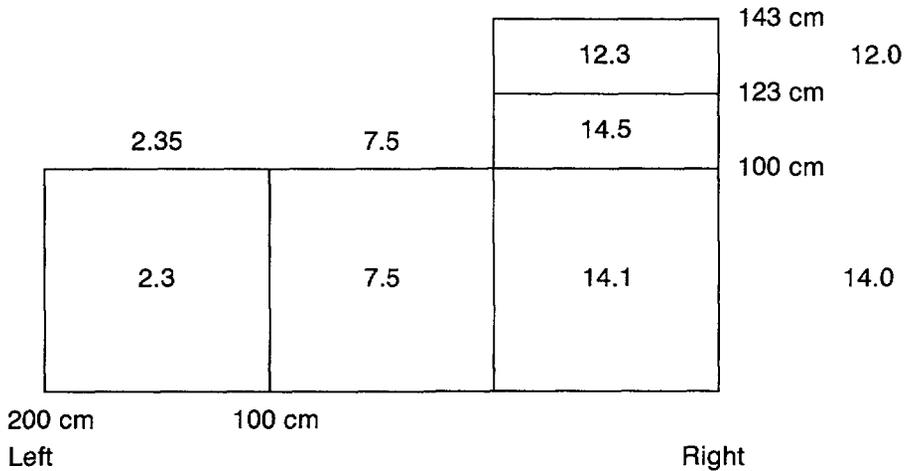
FIG. 12. Evaluation of dose rates where the operator stood in the plane of the source rack: for 10–20 seconds in front of the source, then to the left, then further to the left, with a total duration of exposure of 1–2 min. Dose rates are in Gy/min.

pressing the test button, thereby inducing pulses similar to those due to background radiation. This trick works irrespective of whether or not the radiation monitor is connected; however, the radiation monitor, had it not been disconnected, would have detected the high dose rate and the interlocked key switch for the door lock solenoid could still not have been powered.

Once the door interlock had been defeated, the operator proceeded to open the door in the normal way, using the key with the attached radiation monitor. He switched on the instrument but crucially *he did not check it against the small check source mounted on the door*. The instrument did not function on the low dose rate range to which he had switched (on the high dose rate range it was functional). A spare monitor was available in the RSO's room.

The operator then went down the maze and into the irradiation room. At this point he was already committed to receiving a very large dose of radiation, but he could perhaps have escaped receiving a fatal dose had he noticed (and appreciated the significance of) the absence of the intense blue light due to Cerenkov radiation visible in the storage pool under the conveyor when the source rack is submerged. However, he did not notice its absence, his concern being the damaged cartons on the lower outer conveyor. The cartons concealed the source rack from view.

The operator left the irradiation room to fetch a cart, then re-entered the room with one and began to remove the damaged cartons from the conveyor (Fig. 12 shows an evaluation of dose rates in the positions in which he worked). After working for about a minute or so, he began to feel a burning in his eyes and a pounding

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sensation in his head. (Ionizing radiation acts as a non-specific irritant.) He took fright and left the room. He had not been wearing a TLD badge.

At this point, at about 17:45, he telephoned his superior, the senior technician, and explained what had happened. Shortly after this he felt sick and started to retch. The senior technician telephoned the emergency centre of the Soreq nuclear research centre and an RSO was immediately despatched to the plant. The operator related to the RSO what had happened and at the RSO's request demonstrated how he had opened the door by 'playing with the console'. With his own radiation monitor switched on, the RSO went into the maze. After a few steps he encountered dose rates of the order of 0.5 Sv/h. He immediately left the maze and locked the door.

The operator was taken to the Ichilov medical centre in Tel Aviv where he was examined by a physician (an oncologist). Later that night he was transferred to the bone marrow transplantation unit at the Hadassah medical centre in Jerusalem.

Despite intensive medical care the patient died 36 days later. Sections 6 to 8 of this report describe the medical management of the patient.

4.3. SUBSEQUENT ACTIONS

The source rack was returned to its safe position later that evening in accordance with advice requested by telephone from the supplier's headquarters in Canada. Firstly the pressure to the actuating pistons of the transport mechanism was released, leaving the cartons free to move. Secondly, the source rack was raised to its maximum height by pulling up the hoist cable on the roof and then released. It fell free between the obstructing cartons to its safe position under water. Photograph 3 shows the torn carton after the source had been returned to the pool. The carton had protruded under the horizontal steel guide bar intended to prevent contact between the cartons and the rack, an early design feature. Had a source shroud been fitted, obstruction of the source rack could have been prevented.

The accident was reported to the authorities which initiated an immediate investigation. The facility was shut down until the investigation had been completed and recommendations had been made for immediate implementation. The actions arising from this and other initiatives are described in Section 5.

5. ACTIONS AND LESSONS

On 24 June 1990, three days after the accident, the Ministry of Labour and Welfare appointed a committee of experts to investigate its causes and circumstances and to recommend remedial measures that should be taken at Sor-Van and elsewhere

in Israel to prevent the recurrence of similar accidents. The report of that investigation was the major input to Sections 2 to 5 of this report and its conclusions and recommendations are summarized in Section 5.1. For each recommendation, the actions taken in response, as reported at an IAEA Technical Committee meeting in August 1991 (see Section 5.3), are presented in italics. Section 5.2 reviews general lessons to be learned from this accident and from the similar one in San Salvador in 1989.

5.1. FINDINGS OF THE INVESTIGATION BY ISRAELI AUTHORITIES

5.1.1. Conclusions

The committee concluded that the direct cause of the accident was a combination of equipment malfunctions and misjudgements and unauthorized actions by the operator. The important features were:

(1) the transport jam that prevented the descent of the source rack into the pool;
(2) the false indication by the limit microswitch LS-109 that the source rack was down;
(3) the grave misjudgement by the operator who assumed that the source down signal was correct and disregarded the radiation alarm;
(4) the unauthorized action by the operator who failed to consult his superior and defeated the safety interlock mechanism in order to enter the irradiation room;
(5) the malfunctioning of the portable dose rate meter;
(6) *the failure of the operator to check the portable dose rate meter before entering* the irradiation room, notwithstanding the fact (of which he was aware) that the radiation alarm was on.

It is noteworthy that the operator could perhaps have escaped receiving such a high dose had he noticed, and appreciated the significance of, the absence of the intense blue light due to Cerenkov radiation that is visible in the storage pool when the source rack is submerged, or the sharp smell of ozone, and left the room earlier.

The committee concluded that the operator had had adequate knowledge of the plant and the basic principles of radiation protection, and that it was predominantly his contravention of the entry procedures in his haste that caused the fatal accident.

The committee also concluded that several factors may have contributed to the conditions that made this accident possible, namely:

(1) A less than adequate design of the limit switch LS-109 (or its assembly).
(2) A reliability problem with the room monitor test procedure.
(3) Inadequate tamper proofing of the door interlock mechanism against simple bypassing devices.
(4) The omission on the part of the plant management to install the protective shroud.

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(5) The omission on the part of the plant management to enforce by means of clear written instructions and warnings the strict precautionary procedures recommended by the supplier.

(6) The use of damaged cartons that caused frequent transport jams.

(7) The inadequacy of the inspection and enforcement programme of the authorities.

The committee made several recommendations, some for immediate and some for later implementation (the latest to be completed within a year).

5.1.2. Recommendations and actions

The committee's recommendations and comments are summarized here, with reported subsequent actions in italics.

Operating organization

(1) A protective shroud should be fitted at the source rack irradiation position, as recommended by the supplier.

A shroud has now been fitted. As a result of this accident and the accident in San Salvador, the supplier has sent a second warning notice to all customers advising that a shroud should be fitted. Those that did not confirm already having installed the protective source shroud were either sent a second letter or telephoned and urged to comply. All but one customer have now either already installed or agreed to install a shroud.

(2) The control circuitry must be modified so that the door interlock safety systems cannot be bypassed by means of the keys, buttons or cables (see point (13)).

(3) A complete edition of the operating manual, warning posters and the training manual must be provided in Hebrew. As soon as these are available, there should be a refresher course for operators. *Implemented.*

(4) Unstaffed operation of the irradiation facility should not be permitted until additional alarm signals have been relayed to the emergency control centre of the Soreq nuclear research centre. These extra signals should include the radiation and fire alarm signals.

A later recommendation required that:

(a) the extra gamma alarm (see point (8)) be repeated at the emergency control centre, so that the officer on duty would be able to tell at a glance whether the source was up or down;

(b) the Soreq nuclear research centre should be equipped with a means to stop the irradiation process and to lower the source rack into its storage position.

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The facility is currently being operated with staffed shifts.

(5) Operators should be explicitly forbidden to tamper with the internals of the control console or with any other components of the plant that they are not specifically authorized to handle. *Implemented.*

(6) The periodic test and preventive maintenance programme should be updated and records kept. These records should be available for review in internal audits and audits by inspecting authorities. *Implemented.*

(7) A gamma alarm monitor should be installed inside the maze near the product exit port to ensure that any source pencil falling out of a source rack cannot be transported out of the facility without detection. If a pencil is detected, an alarm should sound at the plant and at the Soreq nuclear research centre and the conveyor should automatically stop.

This recommendation is not directly related to this accident, but reflects the current standard of installed safety systems recommended by the supplier and the IAEA [5]. In the accident in San Salvador source pencils fell out of the source rack and might have fallen into a product box and been lost.

As well as implementing this specific recommendation, the company also installed an earthquake detector and an additional microswitch on the door, both of which, if actuated, would cause the source rack to descend to the safe storage position. Again, these switches are recommended by the supplier and by the IAEA.

(8) An additional gamma alarm monitor should be installed in the maze entrance to indicate high dose rates, due to either a stuck source rack or a spilt source pencil. This monitor should have circuitry independent of the control console circuitry and should provide clear warnings both outside the irradiation room and in the maze entrance. *Implemented.*

(9) The operating company and the competent authority were required to assess the potential consequences of fire within the irradiation room and to take appropriate measures. *The fire detection system has been improved and extended and is now linked to an extinguishing system.*

(10) When an operator enters the irradiation room, there should also be another person present on the spot. *This is now company policy.*

(11) In addition to TLD badges, operators should be provided with personal alarm monitors that should be worn at all times within the plant. *Implemented.*

The supplier

(12) The design of the limit switch (LS-109) that provides the source down indication should be improved.

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For all new irradiators the supplier will fit a source down switch actuated by the physical presence of the source rack under water. A retrofit model suitable for 90% of existing irradiators has been tested. The relevant companies are being advised by letter of its availability for purchase. The remaining irradiator operators are being consulted individually to determine suitable configurations for their irradiators.

(13) The test procedure for checking the performance of the gamma alarm (in the door opening sequence) should be reviewed and improved. Also, appropriate instructions for its periodic testing should be prepared.

The efficiency of Geiger–Müller tubes decreases with time. This means that after a time the number of pulses generated by background radiation in the test procedure could fall below the minimum number that the circuitry recognizes as an acceptable detection rate. This was the reason why the operators found the test procedure to be 'obstinate' and used unauthorized means to speed things up. The sensitivity of the system can be adjusted to overcome this problem.

The supplier has designed a new power supply circuit board which will filter out pulses from any source other than the L-118 Geiger–Müller tubes. This has been installed at Sor Van and has also been made available to all existing customers.

(14) The source rack and modules should be inspected for damage and for any possible ejection of a source pencil.

This was done by the supplier shortly after the accident. No damage was found.

Competent authorities

(15) For facilities using large radiation sources, the competent authorities should have thorough inspection programmes and procedures.

The various authorities involved have revised their relevant inspection programme, both in content and in method of execution. In addition, an Israeli parliamentary committee on Labour and Welfare has reviewed and made recommendations on the organization of radiological protection and its regulation in Israel.

5.2. GENERIC LESSONS

The findings of the Israeli authorities clearly identify the causes of the accident, and their recommendations cover the necessary remedial action for the Sor-Van

facility; many of them have already been implemented. However, the broader context needs to be considered in order to derive generic lessons. Observations and (in italic type) recommendations that follow from them are presented under a number of topic headings relevant to irradiator safety. Many of the recommendations cover procedures and practices essential to safe operation. Action on others would enhance and reinforce present safety practices. Although it will be clear from the text where the prime responsibilities for implementation of some of the recommendations lie, many if not all have implications for all concerned: suppliers, operating organizations, competent authorities and international bodies.

5.2.1. Priorities

(1)   The circumstances and causes of this accident were the same as those dealt with in the recommendations of the IAEA report on the radiological accident in San Salvador [2]. The lessons from that accident have yet to be fully learned. An appropriate means of communication must be found for this purpose. The prompt exchange of information after events of this type must have a high priority in order to alert users and regulators to circumstances that may give rise to an accident.

Further serious irradiator accidents have occurred since the accident in Israel. At an electron beam irradiation facility in France in August 1991, three people were exposed to an electron beam at an energy of 2.4 MeV; two received localized doses of the order of several tens of grays, resulting in extensive skin lesions.

There was a fatal accident at a Soviet designed Category IV type irradiator (panoramic wet source storage irradiator) with a 29.6 PBq (800 kCi) cobalt-60 source in the Byelorussian Republic in October 1991. One person entered the irradiation room while the source was raised and received a whole body dose of approximately 15 Gy. He died 113 days later.

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

(2)   The report on the accident in San Salvador stated that "Many of the recommendations cover procedures and practices already widely considered to be essential to safe operation" (Ref. [2], p. 40). This statement is equally valid for the accident in Israel. The IAEA has recently published guidance in this area [5] and this is commended to those with responsibilities for irradiator safety. Further:

It is strongly recommended that a thorough review of radiation safety be carried out at each irradiator, to take account of:

(a) lessons from this report and from the report on the accident in San Salvador;

(b) current guidance from the IAEA, suppliers and competent authorities.

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

In planning their work programmes, suppliers, 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 less well developed.

5.2.2. Obstruction of the source rack

(4) In this and other accidents, a product jam that obstructed the free movement of the source rack has been the initiating event.

(a) *As recommended by the supplier, a source shroud should be fitted in all similar irradiators as soon as possible;*

(b) *Product boxes and packaging should be inspected regularly and boxes or packaging in poor condition should be replaced.*

5.2.3. Installed safety systems

(5) IAEA Safety Series No. 107 [5] on installed safety systems adopts a safety philosophy that is based on the concept of defence in depth. The components of the safety system should provide:

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

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

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

The investigation by the Israeli authorities identified improvements that could be made to achieve defence in depth.

(a) *The need for defence in depth should be a special feature of the review advocated in recommendation (2). It will be particularly important for those irradiators that have been in use for some time.*

(b) *Where improved safety designs such as for the source down interlock are available, they should be installed as soon as possible.*

(6) In the accidents in both Israel and San Salvador, tricks were used to circumvent the installed safety systems.

(a) *Redesigned power circuit boards that prevent the use of the power cycling trick should be installed in all units as soon as possible.*

(b) *To achieve appropriate defence in depth and help eliminate possible methods of circumvention, suppliers should review their safety systems using a technique such as probabilistic safety analysis.*

(7) Preventive maintenance was not carried out as rigorously as it should have been. Indeed, had the appropriate checks recommended by the manufacturer been made, the reduced sensitivity of the radiation monitor would have been noticed and compensated for, thus reducing the incentive for staff to seek to speed up the process.

Preventive maintenance schedules, as recommended by the supplier, should be observed rigorously. Records should be kept and these should be inspected, both in routine internal safety audits and by competent authorities.

5.2.4. Instruction and training of staff

(8) A contributory cause of the accident in Israel and of that in San Salvador was the lack of an accurate local language version of the instruction manual, training notes and warning notices.

The instruction manual, operating rules, emergency procedures, training material and warning notices must be available in an accurately translated local language version.

The supplier and the operating organization have a joint responsibility in this matter, and the competent authority should insist on that responsibility being discharged.

(9) Although the original operator training was considered appropriate, the actual actions of the operator at the time of the accident indicated a lack of understanding of what could go wrong and the potential consequences. This suggests the need for routine refresher training.

(a) *Training should be reinforced regularly and updated when necessary.*

(b) *Staff training should be given annually.*

(c) *Arrangements should be made to ensure that all new staff receive the required training and that the training needs of staff affected by any internal reorganization are reviewed.*

5.2.5. Personal monitoring

(10) Failure to follow procedures for the use of a dose rate meter on entering the irradiation room after the termination of irradiation was a contributory cause in this and in previous fatal accidents. An additional line of defence should be provided by the use of personal alarm monitors.

(a) *Personal alarm monitors should be routinely worn by operators throughout the working day.*

(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 replacement of, hand held monitors on entry into the irradiation room.*

5.2.6. Inspections and audits

(11) The test procedure that the operators found to be tedious and the trick to speed up access to the irradiation room were contributory causes of the accident, of which the management was unaware. Routine auditing can help to bring such matters to light. Also, audits are 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 in such facilities. A formal report should be presented to the management and any appropriate action should be taken.

(12) One conclusion of the post-accident investigation was that the authorities had an insufficient inspection and enforcement programme. The primary responsibilities for safety rest with the supplier and the operating organization; nevertheless, the regulatory programme enforced by the competent authority can affect how well those 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.

5.3. INITIATIVES BY THE IAEA

. Following the irradiator accident in San Salvador, the IAEA enhanced its work related to radiological protection in irradiation facilities. This was given impetus by the accident in Soreq and it would be relevant to note some aspects.

5.3.1. Training

Experience from the accidents in San Salvador and in Soreq was given prominence in the existing programme of regional training courses in radiological protection. In addition a series of two week regional training courses specifically on irradiator safety for senior staff was commenced in 1991. At the time of this report, five such courses had been given in three different world regions (in Latin America, in the Middle East and Europe, and in Asia and the Pacific).

A feature of all fatal accidents at irradiators has been ignorance or negligence on the part of the operators of the consequences of not following the procedures. Clearly there is a need to provide simple but effective training supplements for the operators. A training video is a good way of reaching a wide audience, and the IAEA, in consultation with suppliers, operating organizations and national bodies, has produced a training video which is available to Member States. This should be used to supplement normal training regimes and should not be regarded as a substitute.

5.3.2. Dissemination of information

Information disseminated on accidents and incidents necessarily takes many forms. The IAEA post-accident review reports, such as this one, necessarily take some time to complete, since it is sought to compile information on all aspects and to analyse it and report in depth. To ensure that there was early dissemination of the key points in the present case, a summary based on the findings of the Israeli authorities was prepared and distributed within a month of the accident. Distribution of this summary was on an informal basis, primarily to those known to have a specific interest in this area or who had previously asked advice.

In order 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 facilities and their implications for competent authorities, designers and manufacturers (Vienna, 19–22 August 1991). The meeting heard presentations on fatal accidents in Italy, Norway [4], El Salvador [2] and Israel. These presentations prompted some thinking and ideas on the problems of disseminating information, particularly in developing countries. For example, suppliers often have difficulty in identifying competent authorities with

regard to either 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 be made, and the IAEA is keeping the matter under review.

6. OVERVIEW OF THE MEDICAL ASPECTS

6.1. RADIATION EFFECTS AND THEIR TREATMENT

Acute exposure to high doses of penetrating ionizing radiation leads to well defined signs and symptoms, as evidenced by previous radiation accidents. Medical practitioners may be called upon to treat such cases of accidental irradiation with localized, partial or whole body exposure. The accidental exposure may be non-uniform and the dose not precisely known.

Localized exposure (e.g. to fingers, hands or feet) can lead to erythema and epilation at doses of up to about 10 Gy, and to dry or wet epidermitis at doses of 10 to 20 Gy of penetrating radiation. Necrosis of the skin and underlying tissue may result from doses in excess of 25 Gy. The timing for expression of skin insult is similar to that for patients undergoing external beam radiotherapy; the effects are accelerated at doses exceeding 50–100 Gy of acute radiation.

Whole body exposure at doses in excess of 1 to 2 Gy leads to a characteristic set of signs and symptoms commonly called acute radiation syndrome (ARS). ARS is characterized by early nausea and/or vomiting (prodromal phase); haematopoietic depression leading to infection characteristic of the neutropenic and immuno-suppressed patient; and bleeding due to thrombocytopenia (haematopoietic phase). At doses in excess of about 8 Gy, gastrointestinal distress (gastrointestinal phase) may be severe due to sloughing of the intestinal epithelium. Following doses in excess of about 50 Gy neurological disturbances can occur owing to direct or indirect (vascular) cell effects (cerebrovascular phase).

The clinical experience following accidental acute whole body exposure is limited. Before 1986, therapy for acute whole body exposure was directed towards prevention of infection and bleeding using appropriate antibiotics/antiviral agents, transfusion and isolation techniques.

Bone marrow transplantation was attempted with some success in two cases before 1986 (at Vinca, Yugoslavia in 1958; and at Pittsburgh, USA in 1967). More recent accidents (in Chernobyl, USSR in 1986; in Goiânia, Brazil in 1987; and in San Salvador, El Salvador in 1989), however, led to a new therapeutic approach
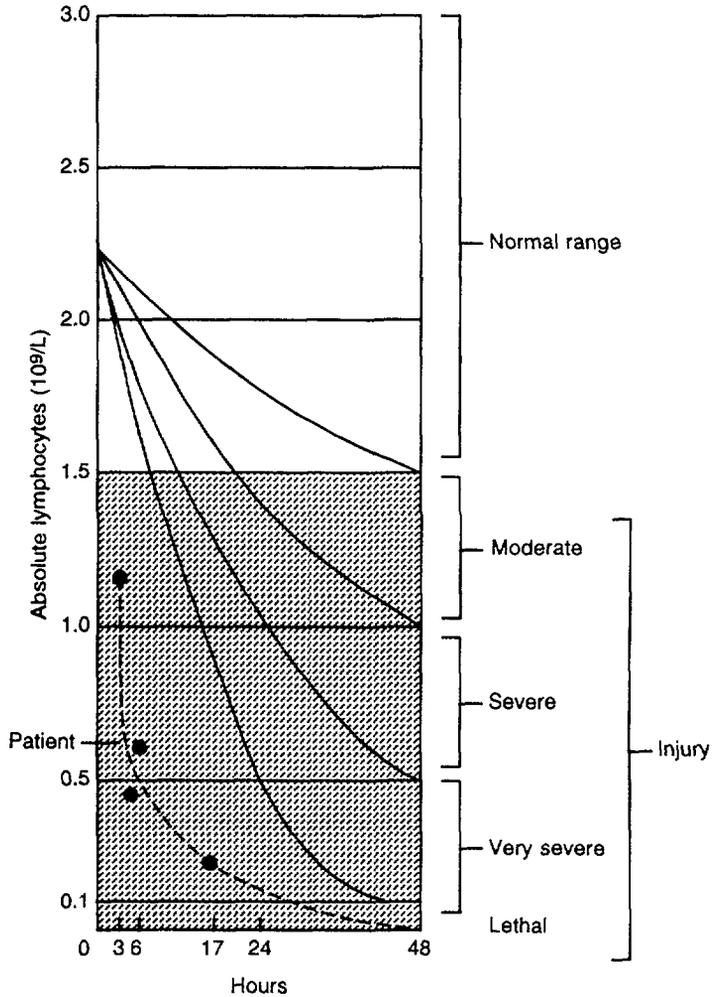
FIG. 13. Schematic relations between lymphocyte levels and dose.

using the haematopoietic growth factor, granulocyte macrophage colony stimulating factor (GMCSF), produced through advances in recombinant technology with deoxyribonucleic acid (DNA) [1, 2, 6]. This growth factor was used in selected patients after the aforementioned three accidents. Its effect could not be entirely satisfactorily evaluated, however, owing to its late administration, at a time when patients may already have been in early stages of haematopoietic recovery. Nevertheless, early recovery of granulocyte count was evidenced in some patients, which gave encouragement for its usefulness after subsequent accidents.
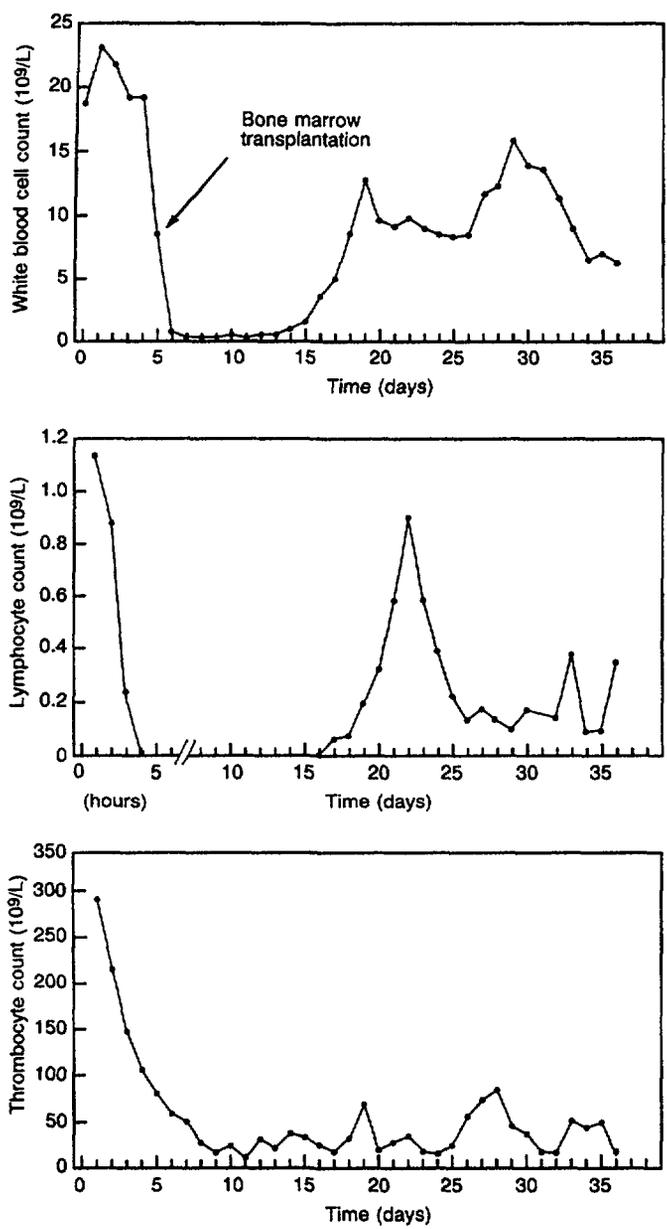
FIG. 14. Time variation of white blood cell count, lymphocyte count and thrombocyte count.
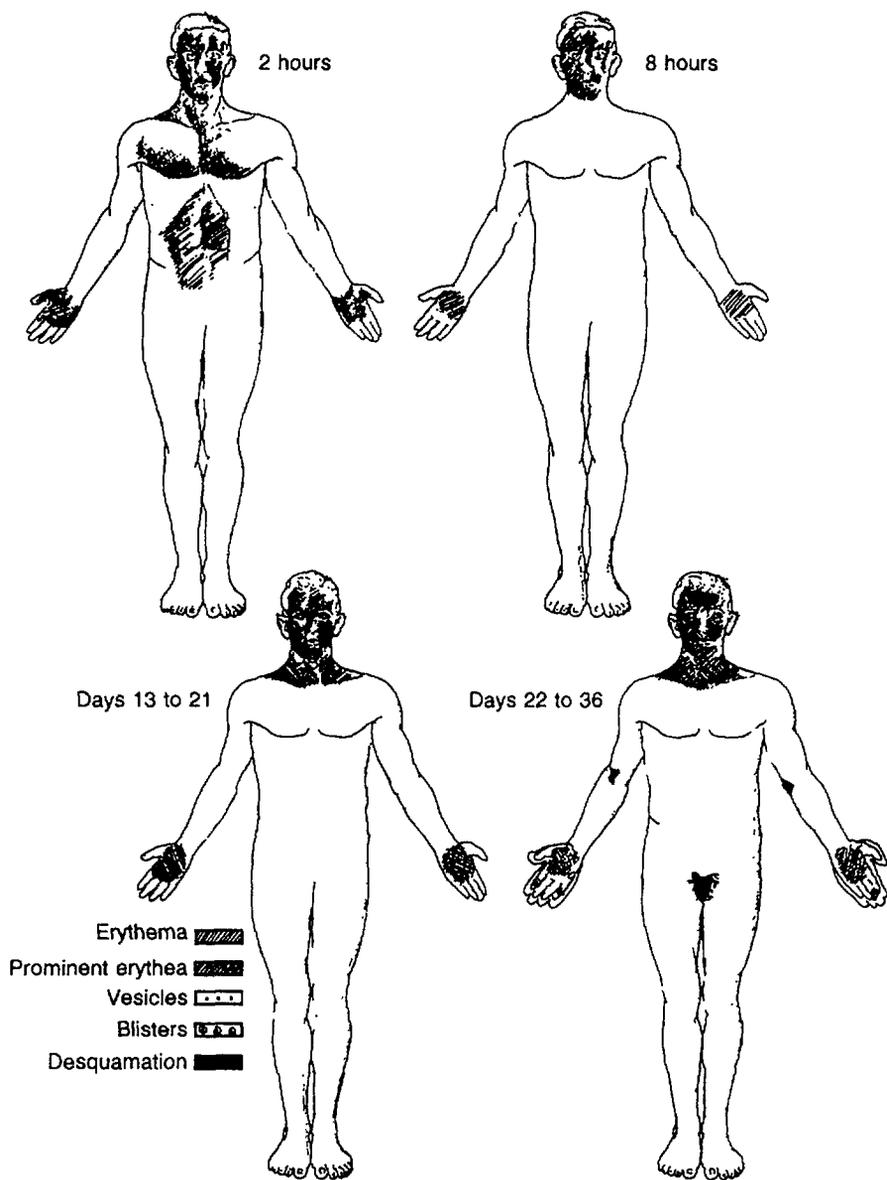
FIG. 15. Corporal distribution of the effects on the patient's skin of the radiation dose: (a) two hours after exposure; (b) eight hours after exposure; (c) 13–21 days after exposure; (d) 22–36 days after exposure.

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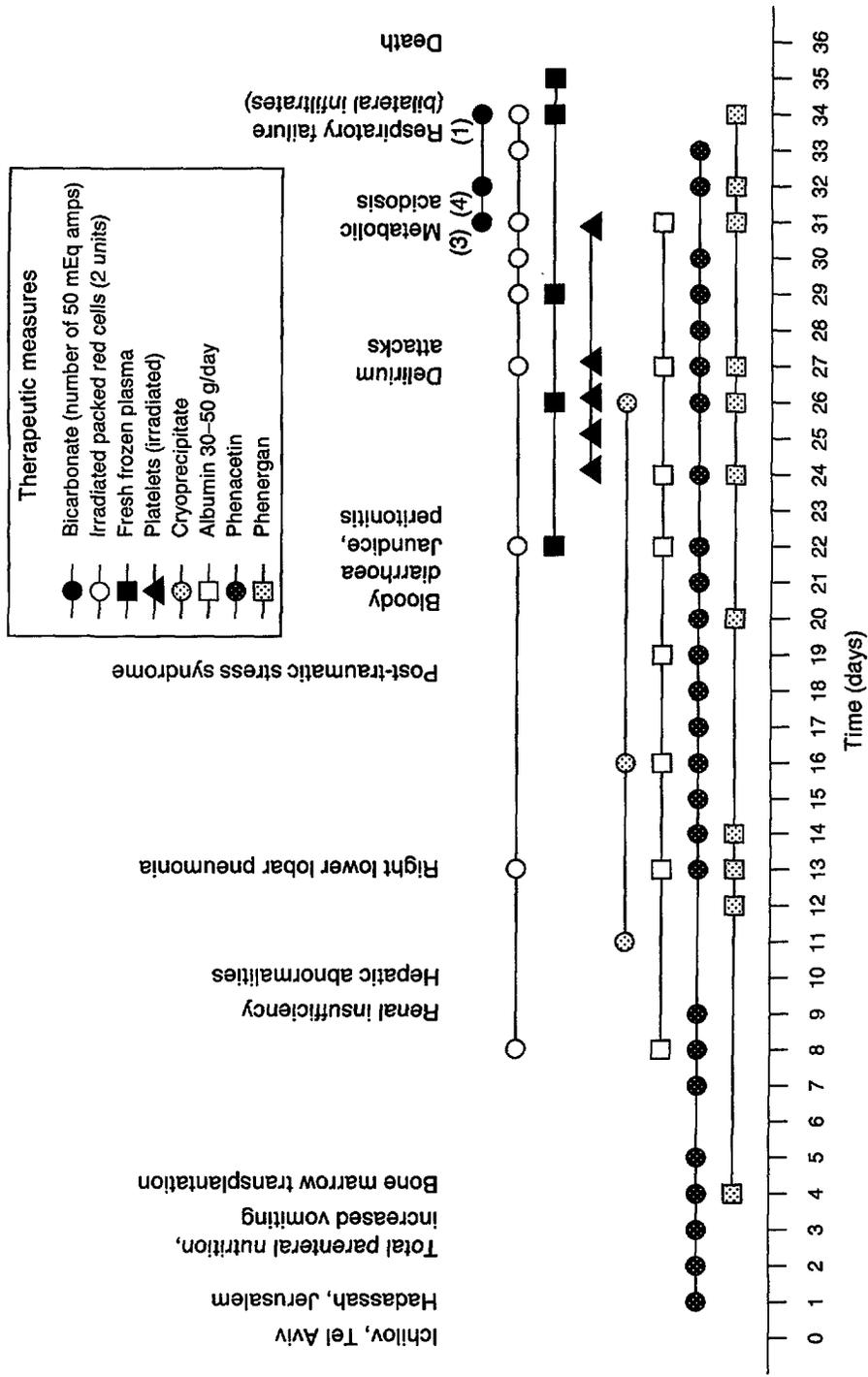
FIG. 16. Chronology of significant medical events. Source: Radiation Emergency Assistance Center/Training Site (REAC/TS), United States Department of Energy, Oak Ridge.
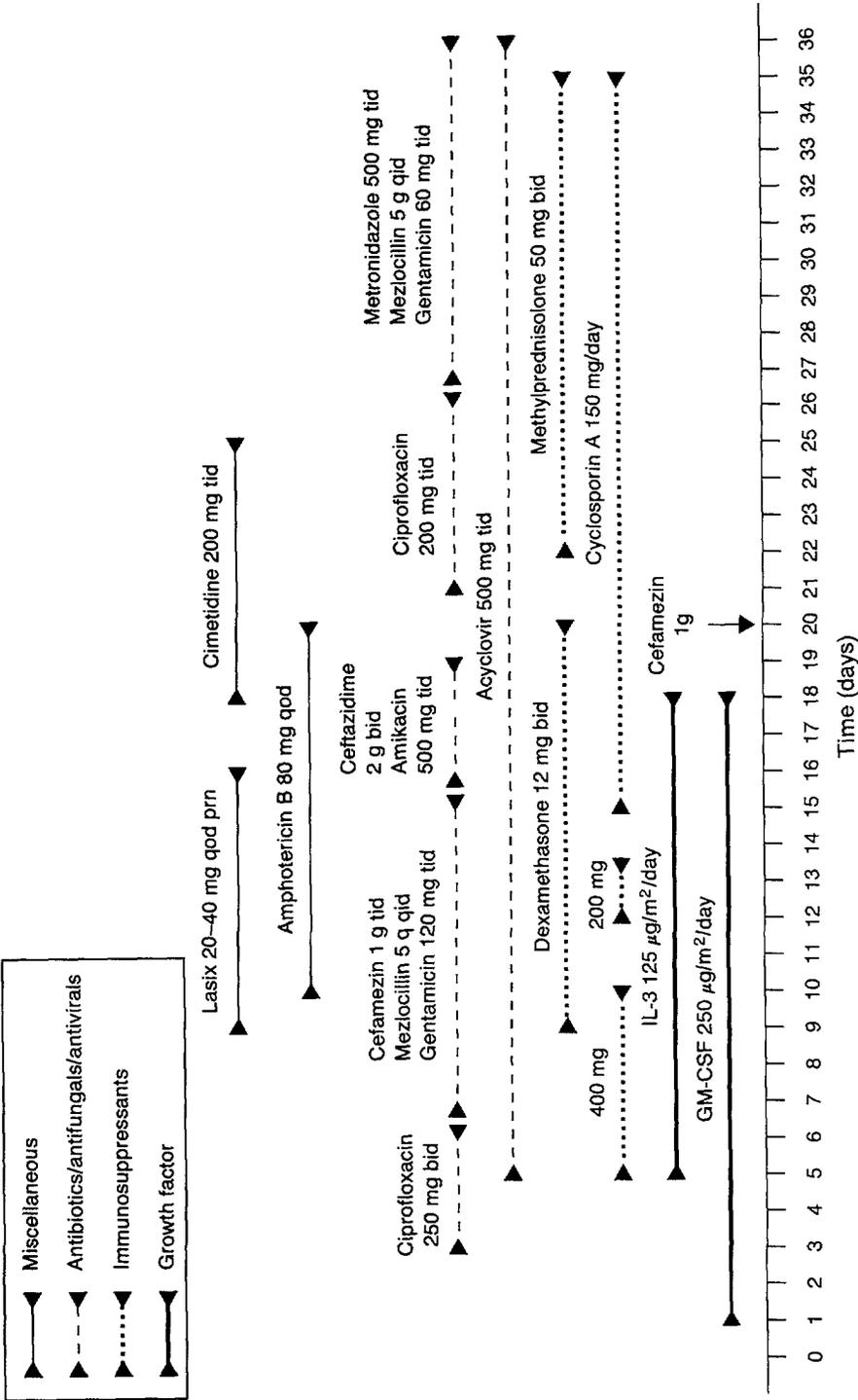
FIG. 17. Chronology of therapeutic measures taken. Source: REAC/TS.

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6.2. RADIATION EFFECTS IN THE PRESENT CASE

In the case presented here the patient was admitted to hospital a few hours after suffering accidental whole body exposure to an acute dose of between 10 and 20 Gy. The patient presented signs and symptoms indicative of severe haematological and gastrointestinal phases of ARS (see Photographs 5–8). The prognosis for survival was poor and indicated the need for heroic treatment. GMCSF was administered soon after the exposure, followed by allogenic bone marrow transplantation. Following the bone marrow transplant, the patient received a combination of GMCSF and Interleukin-3 (IL-3), in an attempt to maximize the potential for haematopoietic recovery.

The patient was treated until his death five weeks later. Localized skin injury evolved over time, as did neuropsychological manifestation, but these were not major complicating factors at the time of death.

The following sections of the report describe: the general clinical course; management of the haematological and gastrointestinal phases; localized radiation injuries; and neuropsychological phases. Key parameters and treatment regimes are covered in the text, but where possible these have also been presented in graphical or schematic form (see Figs 13–17).

Experience from the medical management of the patient and from post-mortem findings is drawn upon in Section 9 to identify lessons to be learned for such cases in the future.

7. MEDICAL MANAGEMENT OF THE PATIENT

7.1. INITIAL ASSESSMENT

Since in this case there was no doubt that an acute radiation exposure had occurred, the RSO at the Soreq nuclear research centre contacted a physician (oncologist) known to him. The oncologist examined the operator (from here on referred to as the patient) in the Emergency Department at Ichilov medical centre in Tel Aviv, one of the major referral centres for the Tel Aviv area. The patient was seen 2 hours and 15 minutes after exposure. The information about the radiation exposure that was available to the oncologist was that the patient had been estimated to have received a dose of between 10 and 20 Gy to the whole body and that he had been exposed for 1 to 2 minutes. The patient was a 32 year old man, married with two children, and had one brother. He smoked 40 cigarettes per day and had no significant medical history except for a traumatic rib fracture followed by a pneumothorax three years earlier.

The patient told the oncologist that he had left the irradiation room because of a sensation of burning in the eyes. Five minutes later he experienced nausea, one large emesis and some soft stool. He complained of subjective fever, severe abdominal pain and thirst. On physical examination, the vital signs were: rectal temperature 40.7°C; pulse rate 126/min; regular respiration rate 16/min; blood pressure 130/60. The oncologist found the man to be robust, with generalized erythema that was most prominent on his face and neck. There was a slight eyelid oedema and some conjunctival injection. The patient complained of a retrosternal burning sensation and diffuse moderate abdominal pain with defence (rigidity). In addition, the oncologist found rebound tenderness and suspected peritonitis. The oncologist initiated treatment with intravenous hydration and aspirin for fever and obtained the following laboratory data:

Arterial blood gases: pH 7.433
O_2 saturation: 88.6%
pCO_2: 31.5
pO_2: 54.1

Serial studies of sodium, potassium, blood urea nitrogen and glucose were normal and the results of serial blood counts are given in Table I.

Approximately 2 hours and 45 minutes after exposure the oncologist obtained two consultations (almost simultaneously) with a local surgeon and with a bone marrow specialist in Jerusalem. The consultation with the surgeon revealed no evidence of peritonitis, abdominal tenderness had lessened, and there was now no defence. The surgeon recommended antibiotics, cimetidine, abdominal X rays and continuous observation. The bone marrow specialist recommended drawing blood samples immediately for human leucocyte antigen (HLA) typing and for cytogenetic dosimetry. He advised urgent location of all family members in order to obtain blood for HLA typing as possible bone marrow donors. He recommended no surgical intervention and advised that the patient be transferred to Hadassah medical centre in

TABLE I. RESULTS OF SERIAL BLOOD COUNT ON ADMISSION

Time after exposure (h)	White blood cells (10^9/L)	Lymphocytes (%)	Haemoglobin (g/dL)	Haematocrit (%)
3	19.1	6	15.0	45.1
5	23.4	2	13.9	43.2
6	20.2	3	12.1	34.2

Jerusalem which has facilities for bone marrow transplantation. The patient was transferred by ambulance directly to the bone marrow transplantation unit at Hadassah medical centre, where he arrived 8 hours post-exposure. The patient's brother had already been located and was flown to Jerusalem, where he was available for HLA typing shortly after the patient arrived.

Blood for cytogenetic evaluation was drawn 4 hours post-exposure. Standard culture techniques were used and the results were available four days later. Prepared slides were screened and only 9 metaphases or partial metaphases were observed, all of poor quality. The poor yield of metaphases was partly due to interphase death and mitotic delay of the cells in culture. One ring was observed, but almost all the chromosomes were abnormal, with many translocations and fragments. The results were not sufficient for accurate dose estimation, although it could be inferred that a very high radiation exposure had occurred.

A plot of the patient's absolute lymphocyte count on the schematic Andrews nomogram [7] over the first 48 hours post-exposure is shown in Fig. 13. The rate of lymphocyte decrease appeared to predict a lethal outcome, as indicated in the figure.

7.2. GENERAL CLINICAL COURSE

Days 1 to 4

Physical examination of the patient on his arrival at the Hadassah medical centre in Jerusalem showed that he was confused but in good general condition. His vital signs were: pulse rate 130/min and regular; respiration rate 16/min; blood pressure 130/60; and rectal temperature 40.7°C. He demonstrated isolated facial and palmar erythema, diffuse abdominal tenderness and slight corneal injection with mild swelling of the lower eyelids. The results of the physical examination were otherwise unremarkable.

The patient was placed in an isolated room under sterile laminar flow conditions. On the night of admission, a central intravenous line (Hickman catheter) was inserted under Cefamezin (cephazolin sodium) antibiotic coverage and fluid support was begun. Acyclovir (500 mg three times a day) was given for prophylaxis against herpetic infections. Stimulation of possible residual host progenitor cells was attempted using recombinant human GMCSF (rhGMCSF). In the first 24 hours after exposure the patient vomited eight times. Results of initial laboratory tests are shown in Table II.

Over the next few days (Days 1–3) the patient's general condition did not change. He complained of headache, fatigue and weakness. His body temperature was around 37.5°C, peaking once to 38.5°C, with no documented infection. Blood cultures were taken daily and whenever a rise in his temperature was noted.

TABLE II. LABORATORY RESULTS ON ADMISSION

Parameter	Value		Parameter	Value	
White blood cells	22.0	10^9/L	Prothrombin time (PT)	67 %	
Lymphocytes at 17 h at 60 h	1% 0%		Partial thromboplastin time (PTT)	29	s
Platelets	205	10^9/L	Thrombin time	11	s
Haemoglobin	13.8	g/dL	Fibrinogen	206	mg/L
Glucose	6.3	mMol/L	Serum		
Sodium	144	mEq/L	LDH (Lactic dehydrogenase)	236	IU/L
Potassium	3.4	mEq/L	CPK CPK (8 h later) (creatinine phosphokinase)	167 348	IU/L IU/L
Urea	8.6	mMol/L	Urinalysis	normal	
			Chest X ray	normal	
Uric acid	516	mMol/L			
Creatinine	159	μMol/L			

Administration of ciprofloxacin was commenced on Day 3. There were no new findings in physical examinations. The blood level of creatinine phosphokinase (CPK) was 301 IU/L and that of amylase had dropped to 334 IU/L. Vomiting occurred on the evening of Day 3. Total parenteral nutrition (TPN) was started.

On Day 4 the white blood cell count dropped to 8.5 × 10^9/L. No lymphocytes were observed in the peripheral blood smear and the platelet count dropped to 80 × 10^9/L. The haemoglobin level was 11.3 g/dL with 33.1% haematocrit. Results for blood chemistry and biochemistry were unremarkable. The CPK level was 288 IU/L and for amylase 92 IU/L.

On Day 4 the decision was made to perform a bone marrow transplant. This was done the same day with haploidentical bone marrow, T lymphocyte depleted, from the patient's brother, followed by cyclosporin A (6 mg/kg/d) as additional prophylaxis against graft versus host disease (GVHD). Haematopoietic reconstitution was supported by recombinant human haematopoietic growth factors, including

PHOTOGRAPHS

Note: *All medical photographs are by courtesy of Hadassah medical centre, Jerusalem.*
Further information on the medical photographs,
and in particular the computerized tomography scans, may be obtained from
Dr. S. Slavin, Unit for Bone Marrow Transplantation, Hadassah medical centre,
*Kiryat Hadassah, P.O. Box 12000, IL-91120 Jerusalem, Israel.*

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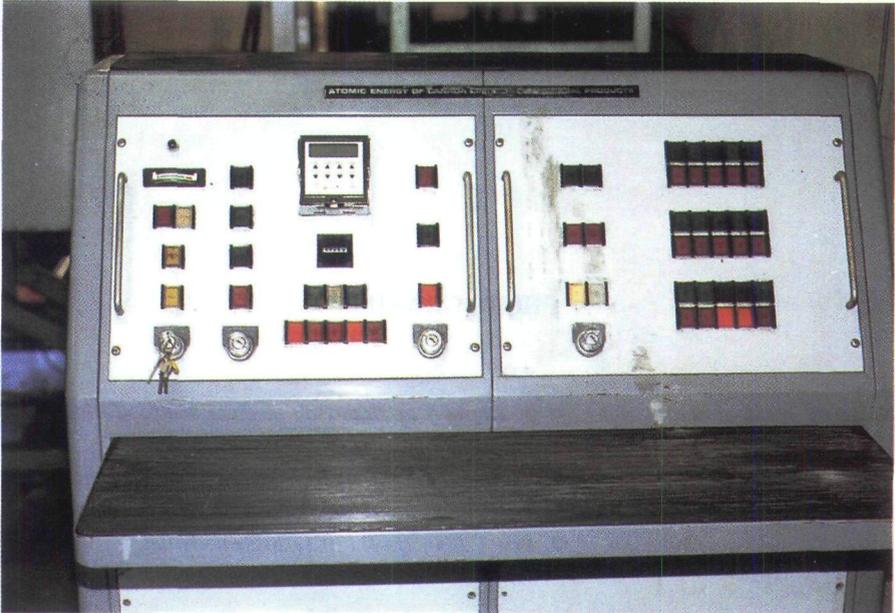
1.   The control console.

2.   The carton on the outer lower conveyor that caused the jam and which the operator worked to free.

3. The carton on the inner lower conveyor that obstructed the source rack. Also shown are the steel guide bar and the source hoist cable.
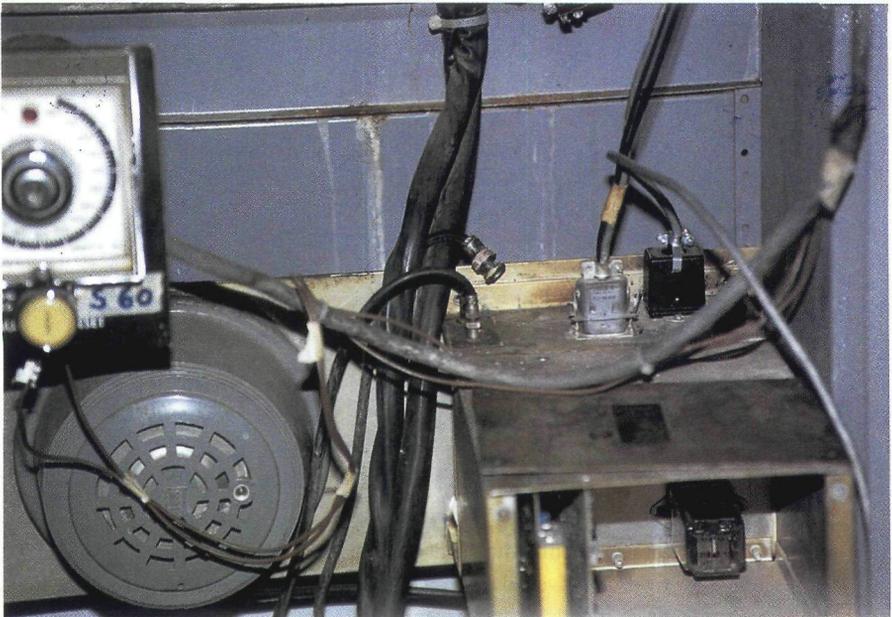
4. The inside of the control console showing the disconnected cable from the installed radiation monitor.

5. Skin erythema with slight oedema; dilation of conjunctival blood vessels with haemorrhage; severe mucositis in mouth. (After seven days.)
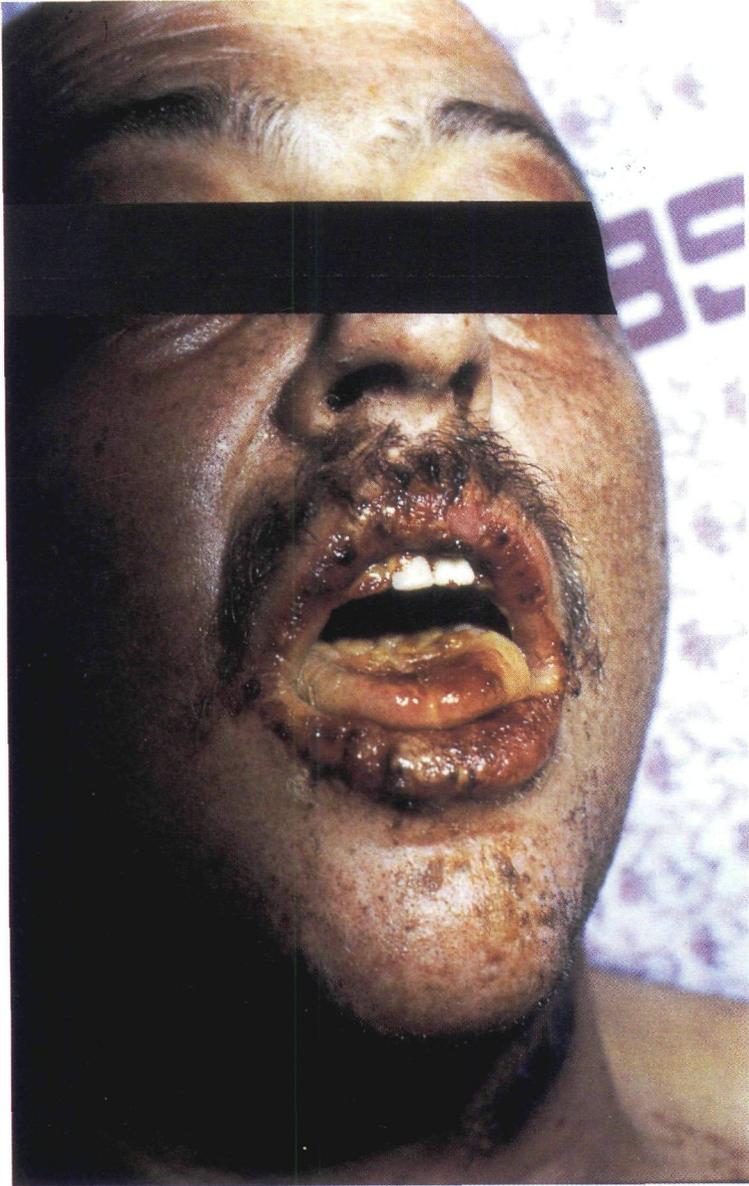
6. Radiation injury to the skin of the face; onset of epilation; severe radiation induced mucositis. (Third week.)
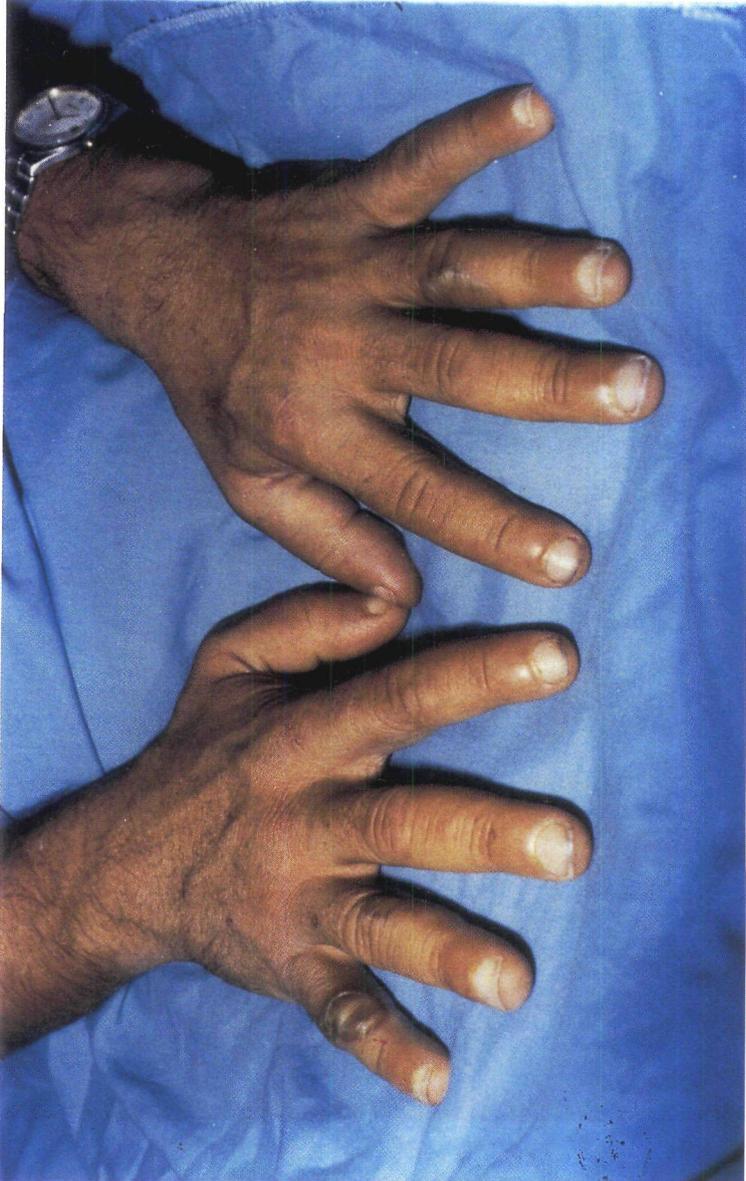
7. Appearance of blisters on an area of skin erythema and oedema. (Third week.)

8. Radiation injury to the skin of the left elbow.
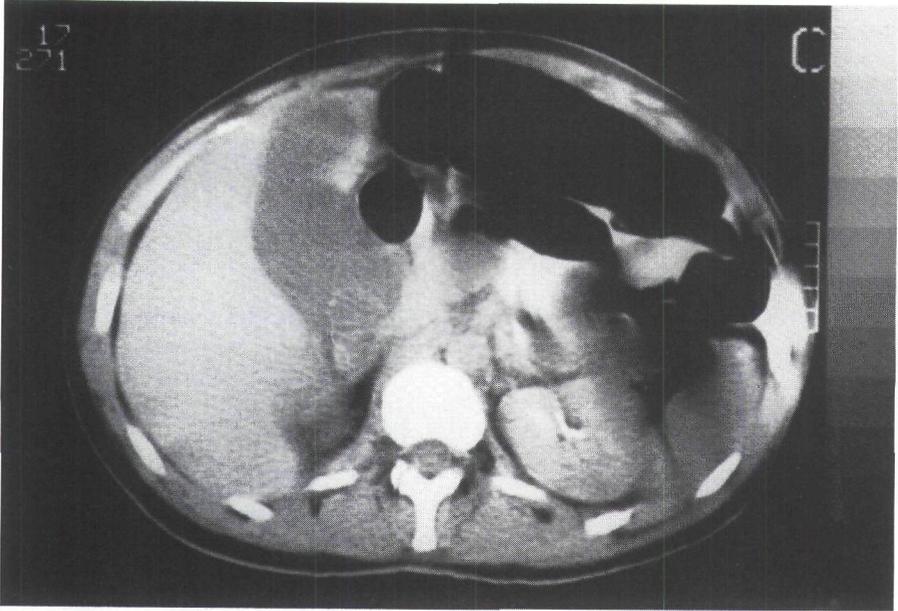
9. Intravenous enhanced contrast tomograph of the abdomen: gall bladder markedly enlarged.
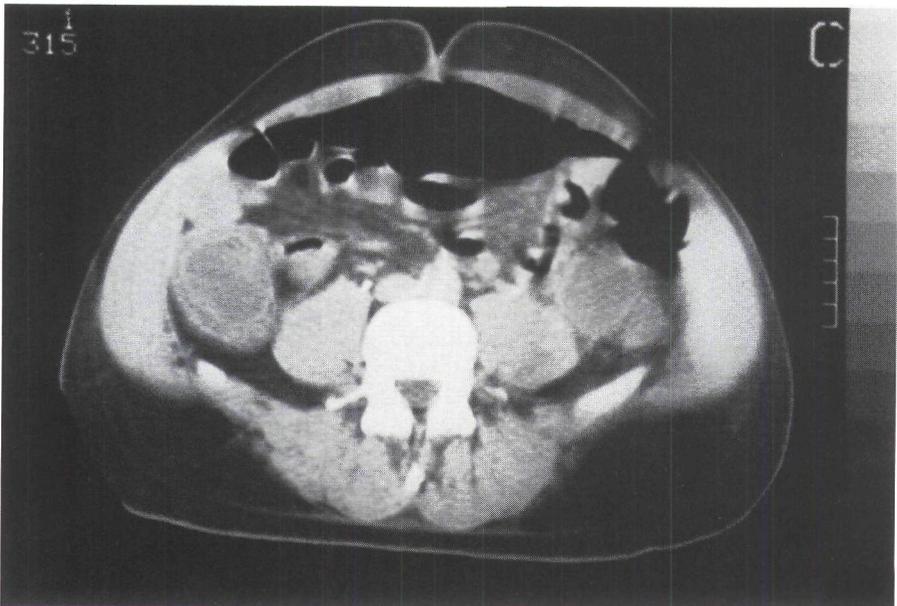

10. Dilatation of the ascending and descending colon; submucosal oedema in the ascending colon; thickening of the mesenterium.
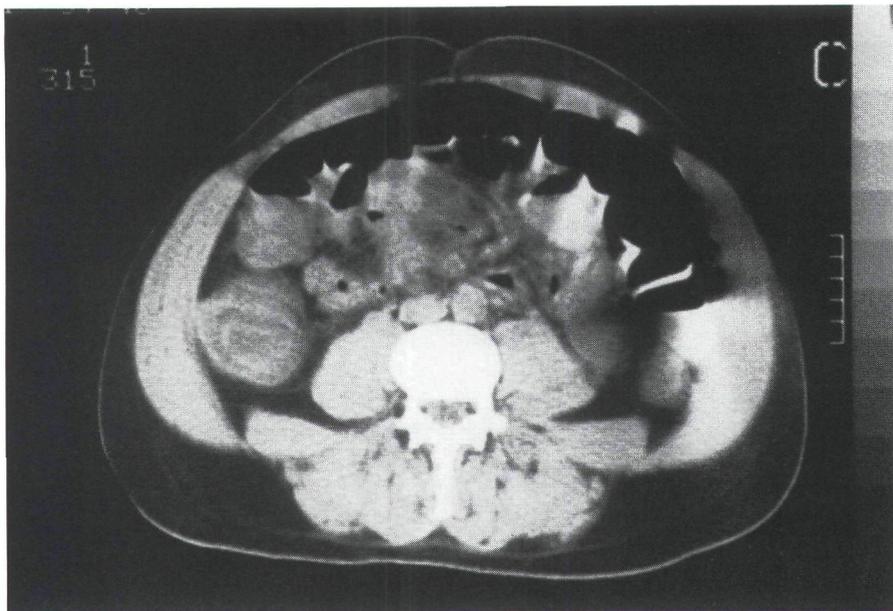
11.   Thickening and oedema of the caecum walls.
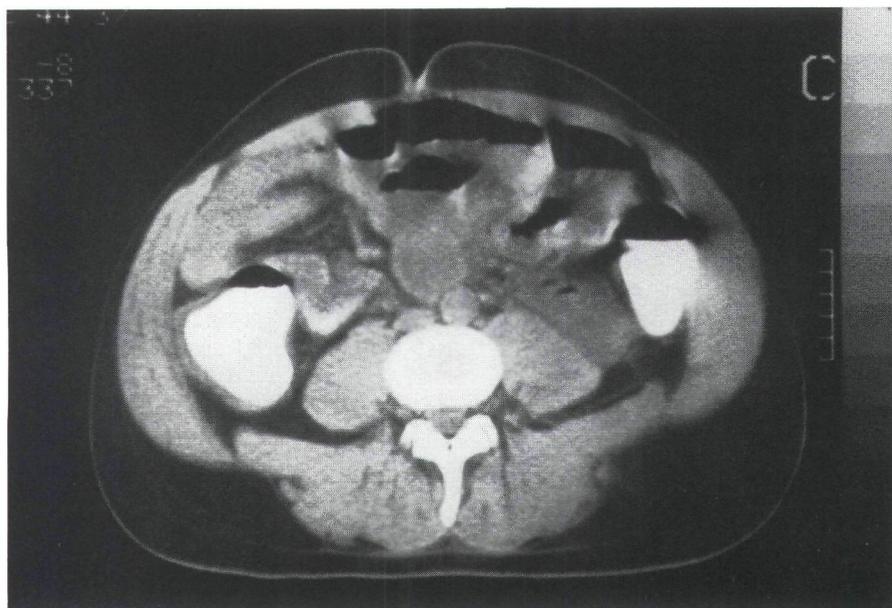
12.   Abdomen following gastrographin enema; marked thickening of the walls and submucosal oedema; thickening of the mesenterium also evident.
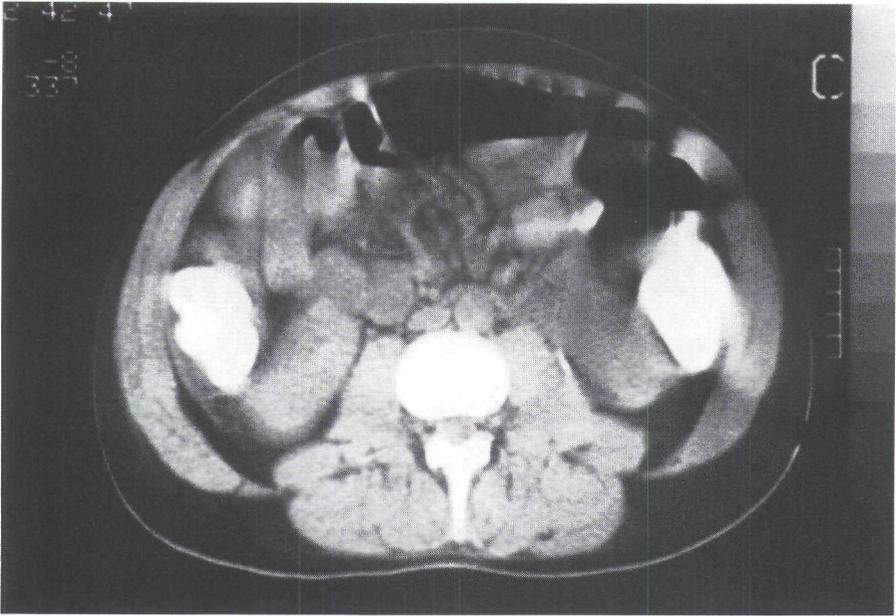
13. Abdomen following gastrographin enema; marked thickening of the walls and submucosal oedema; thickening of the mesenterium also evident.
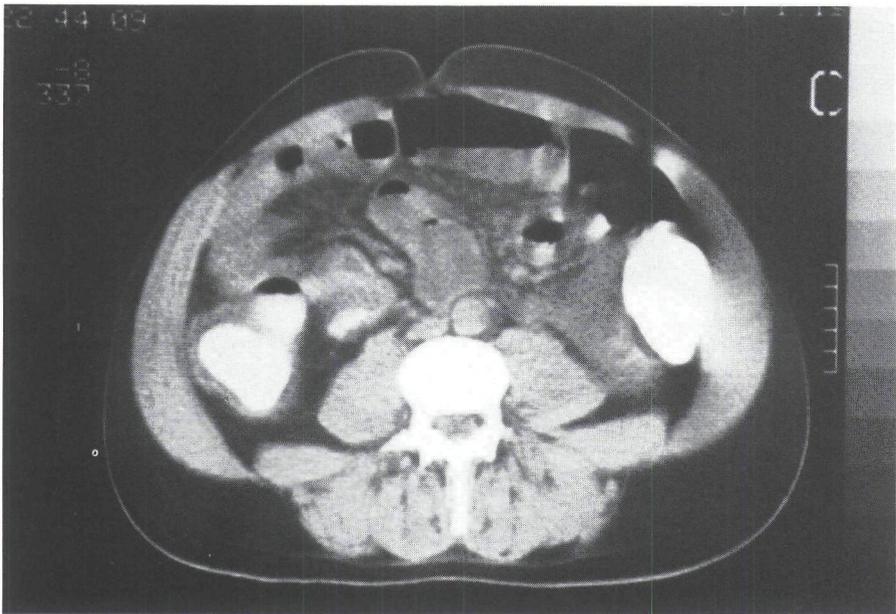

14. Abdomen following gastrographin enema; marked thickening of the walls and submucosal oedema; thickening of the mesenterium also evident.
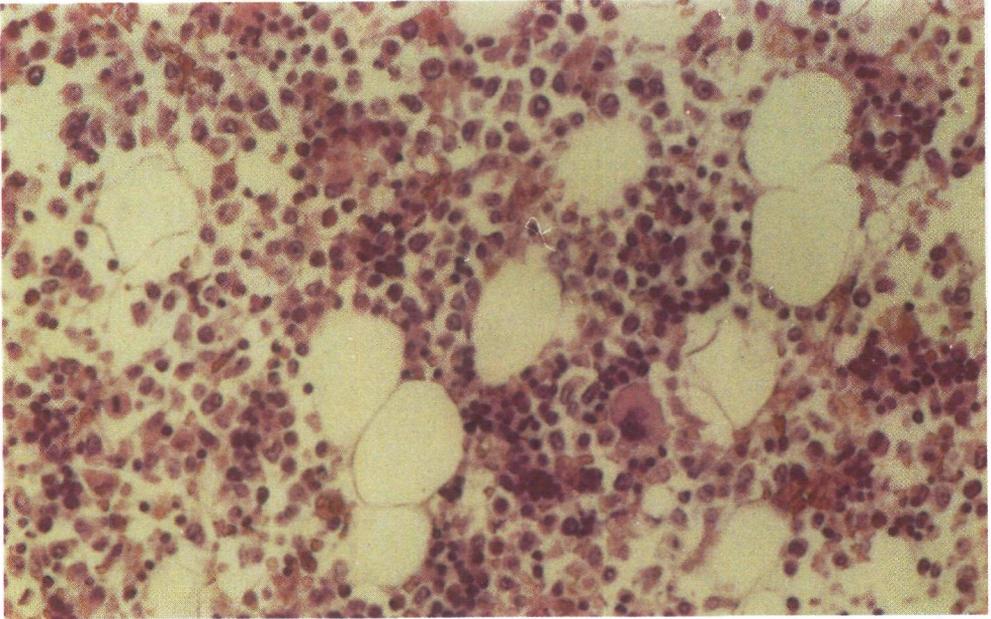
15. Bone marrow, post-mortem examination: plasmacytoid infiltration standing out against cellular bone marrow with almost normal cell differentiation.
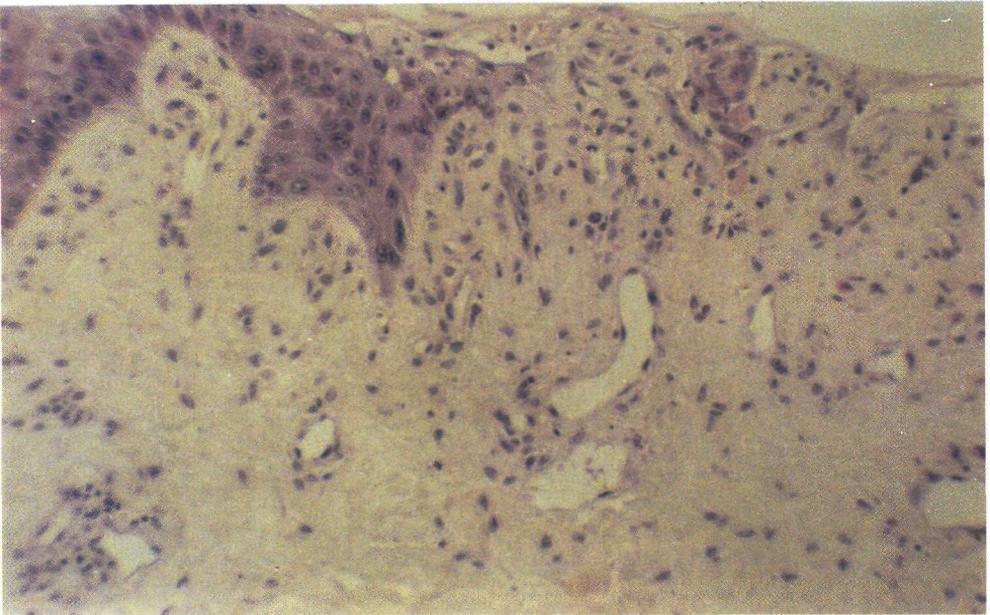
16. Skin, blister on ankle: partially recovered epidermis in left part; disintegration of epidermis in right part. Also oedema in the dermis with dilation of capillaries.
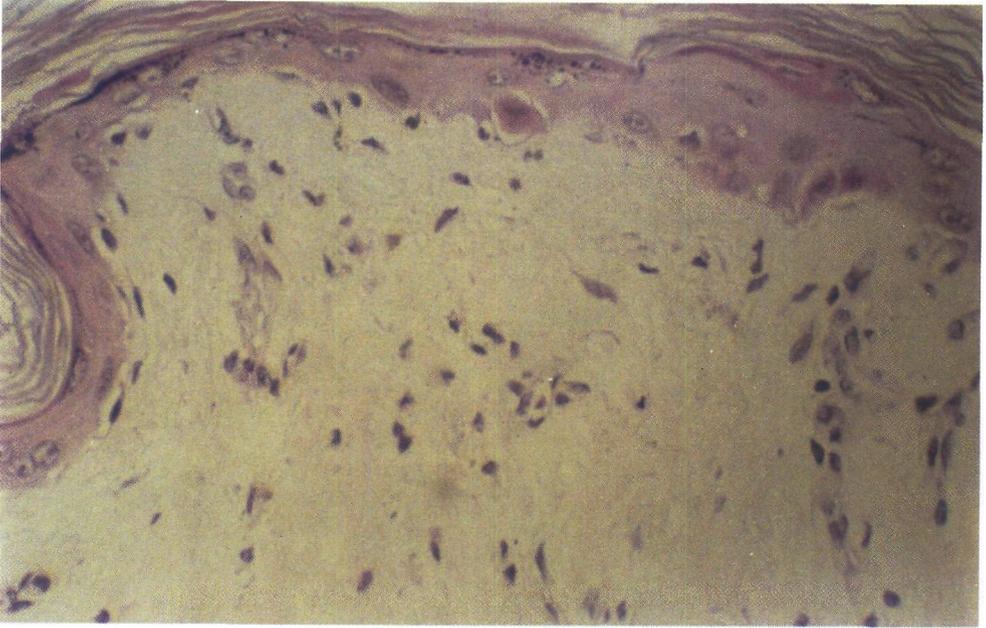
17. Skin: complete disorder of epidermal layers and some disintegration of dermis.
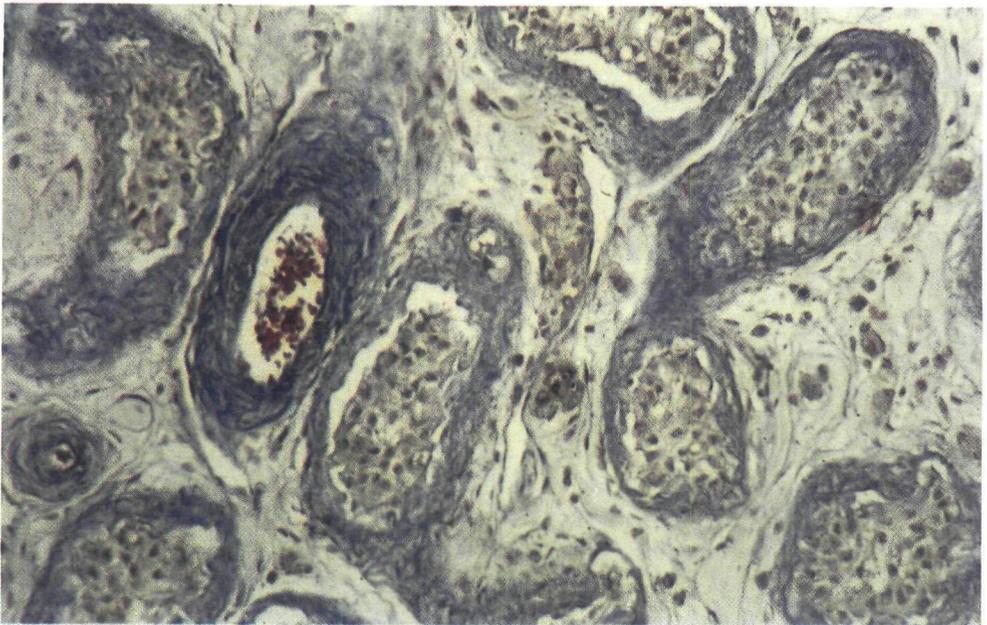
18. Testis: complete disintegration of testicular epithelium.
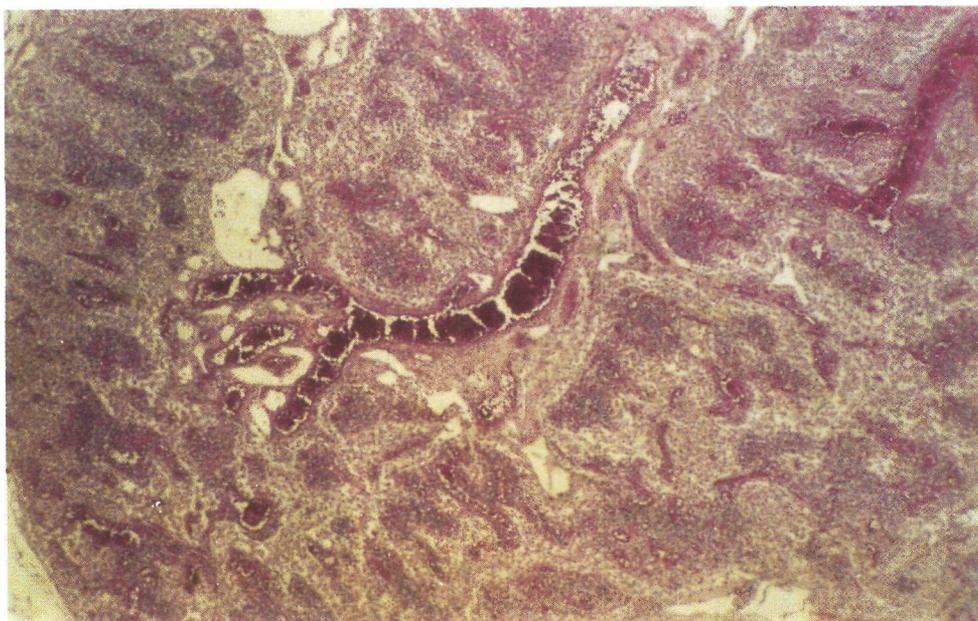
19. Lymph nodule: cell depletion with abnormal (significantly changed) blood vessels.
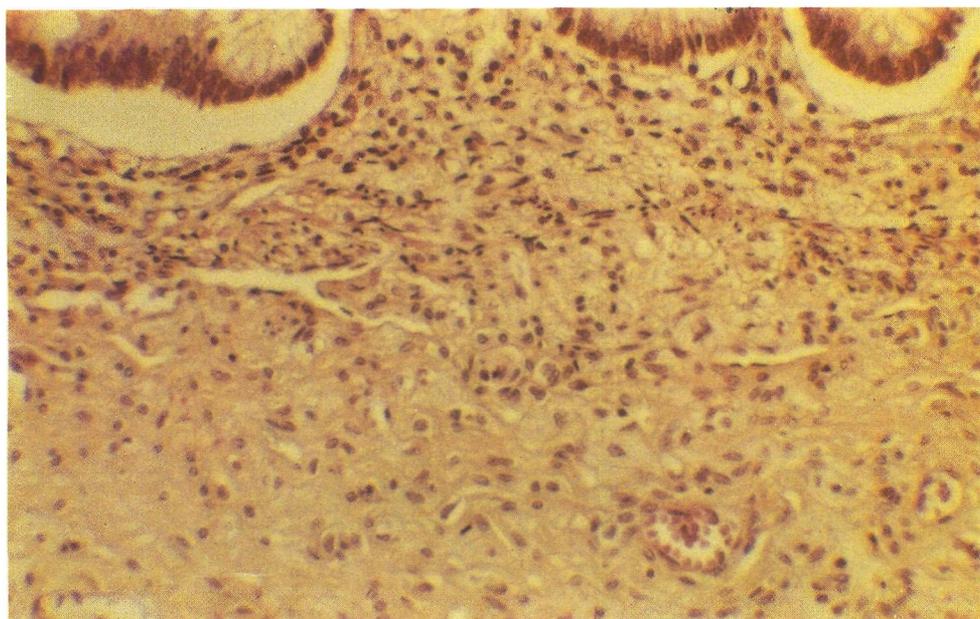
20. Appendix: depletion of lymphoid elements.
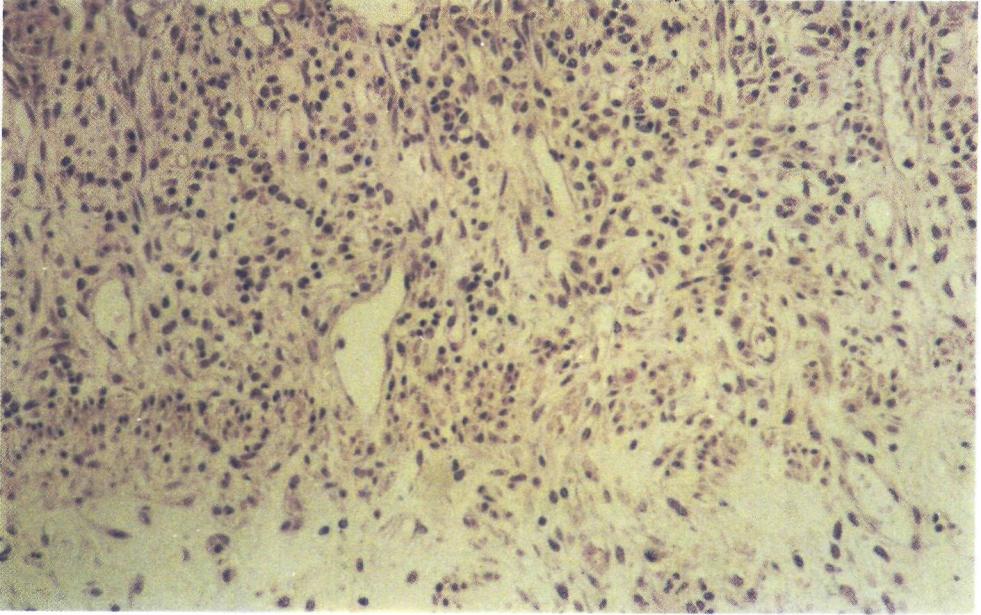
21. Intestine: depletion of lymphoid elements and disintegration of mucosae.
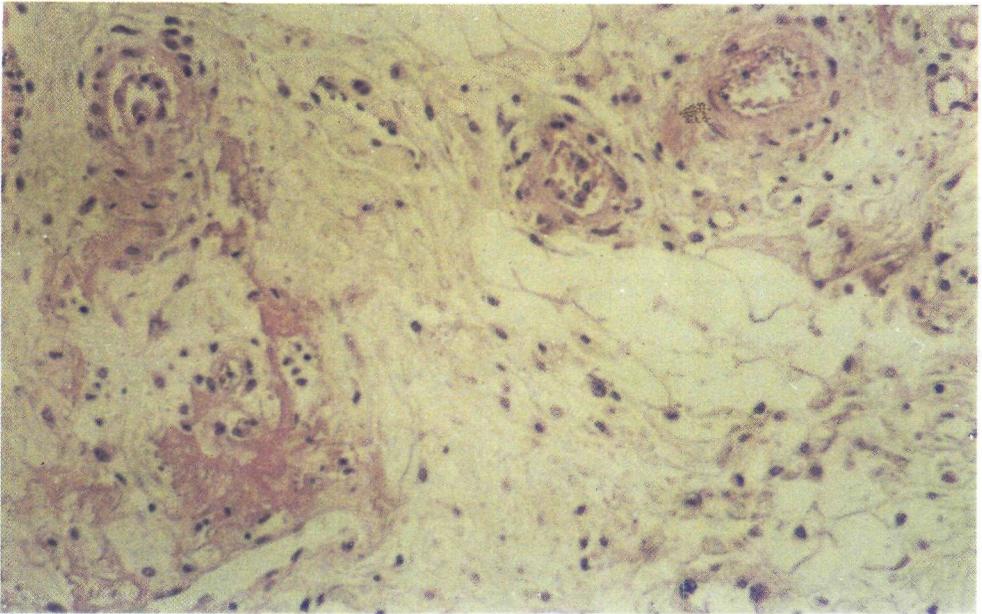
22. Intestinal submucosa: marked oedema and disrupted blood vessels.
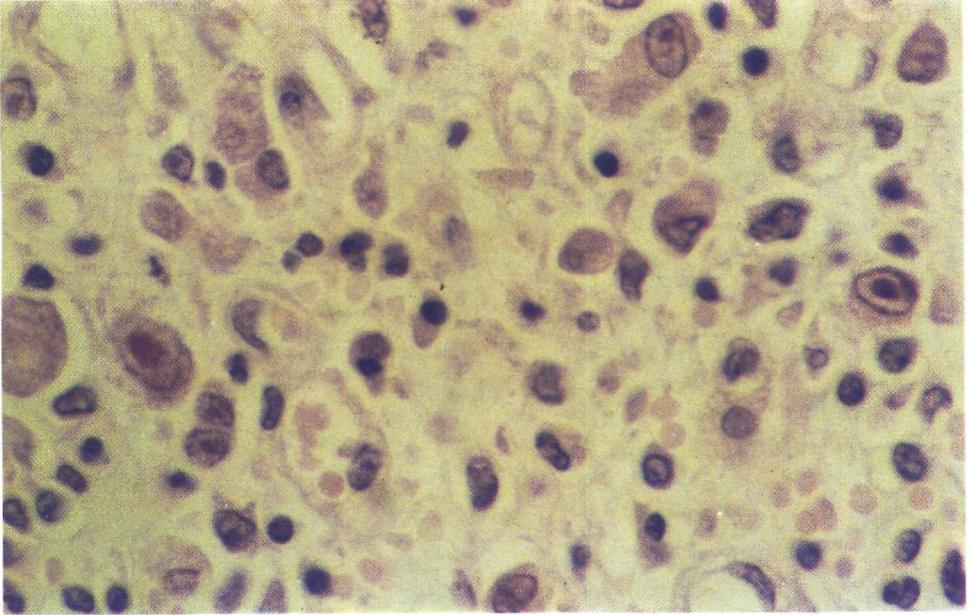
23.   Cytomegalovirus bodies in intestinal submucosa.
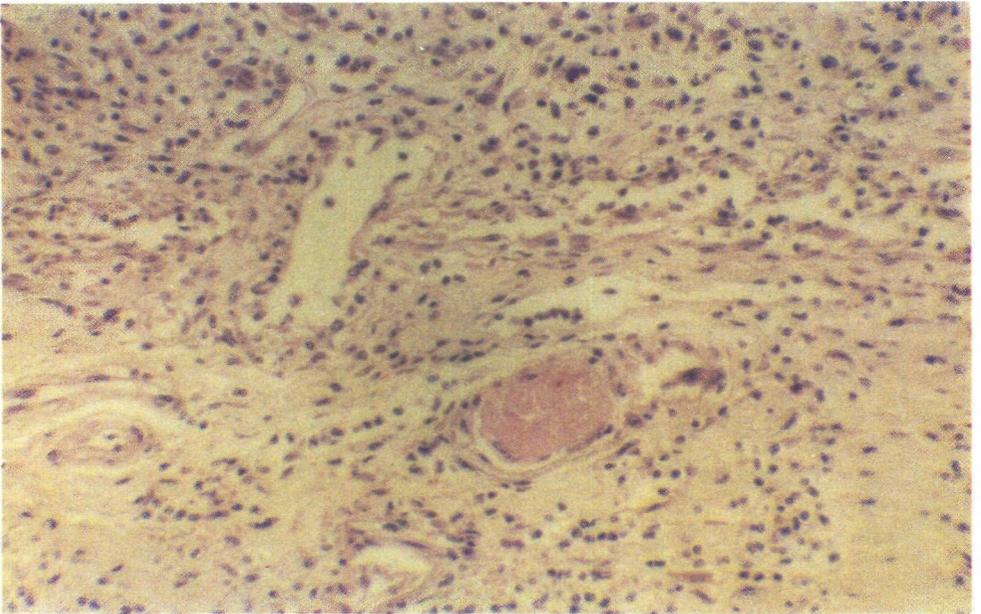
24.   Colon: significant disorder in epithelium and submucosa with oedema and disrupted blood vessels; some thrombosis.
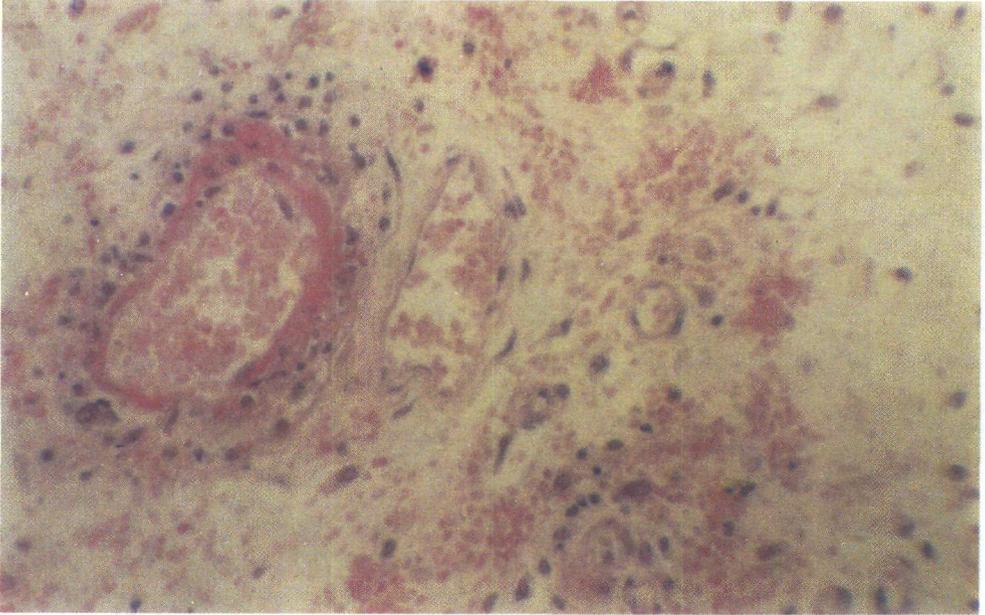
25.   Colon: significant disorder in epithelium and submucosa with oedema and disrupted blood vessels; some thrombosis.
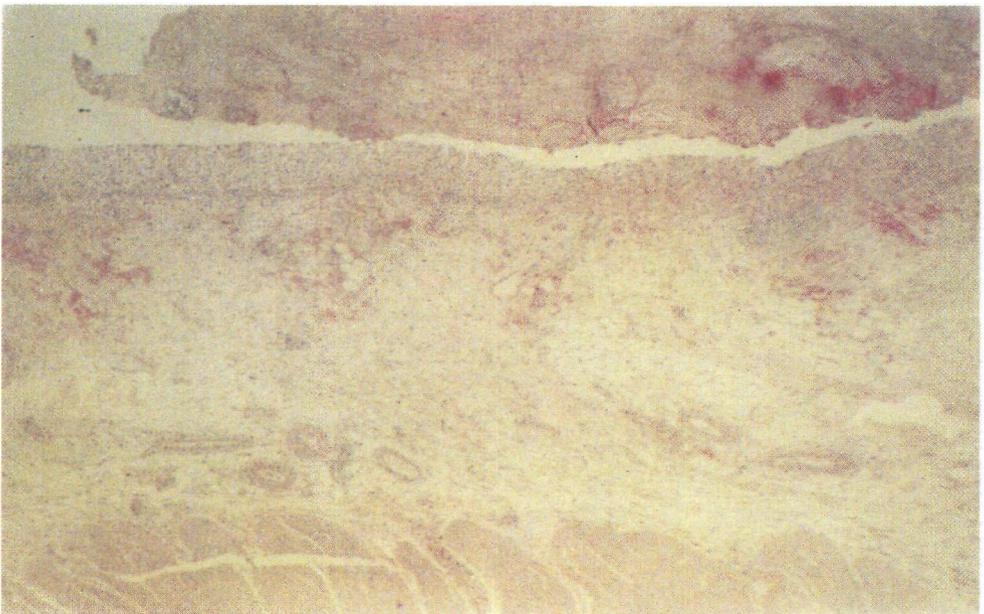
26.   Colon: 'pseudomembranes' in the lumen part of the colon.
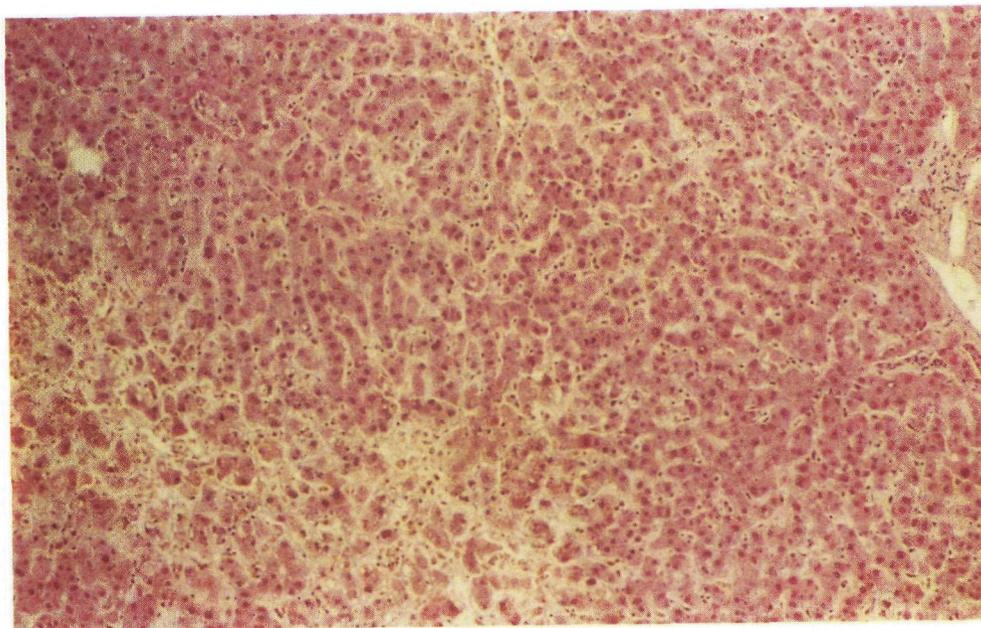
27. Liver: oedema of parenchyma with occasional extravasation of red blood cells and acidophilic bodies indicating necrosis of hepatocytes (seen better in 28).
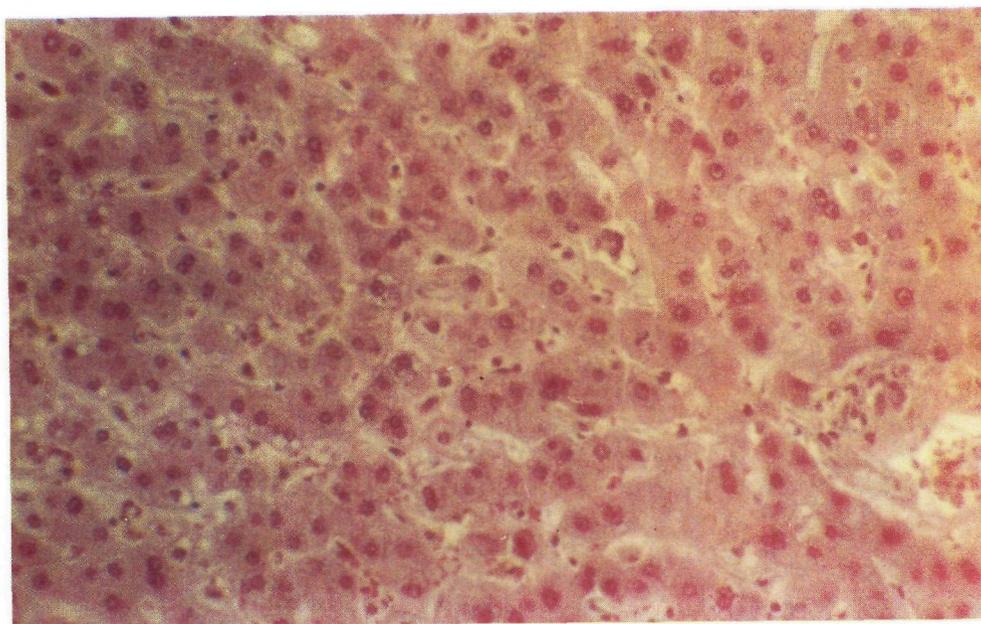
28. Liver: oedema of parenchyma with occasional extravasation of red blood cells and acidophilic bodies indicating necrosis of hepatocytes.
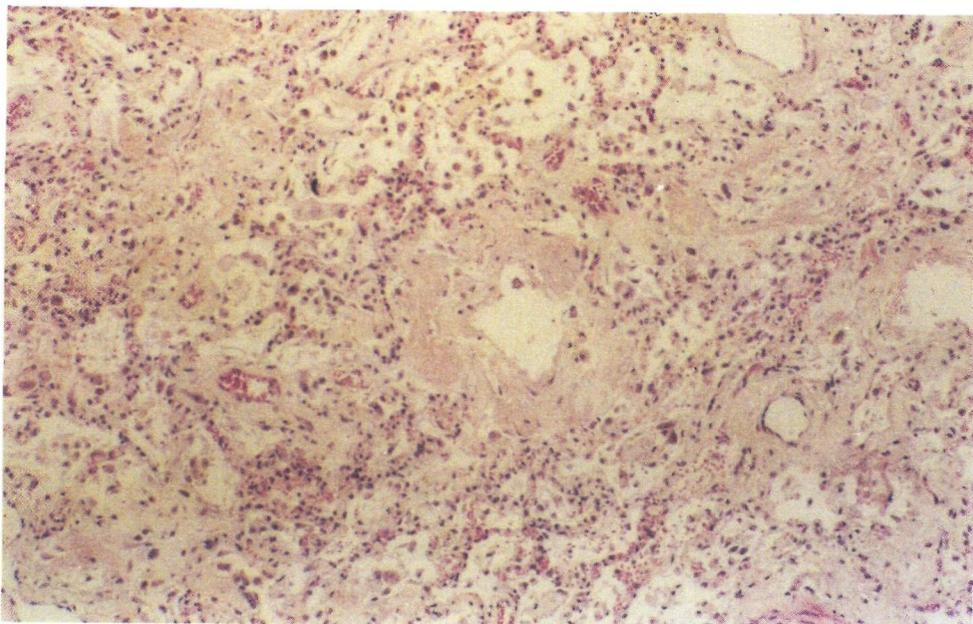
29. Lung: marked thickening of alveolar septa and interstitial oedema with inflammatory infiltrates and fibrosis.
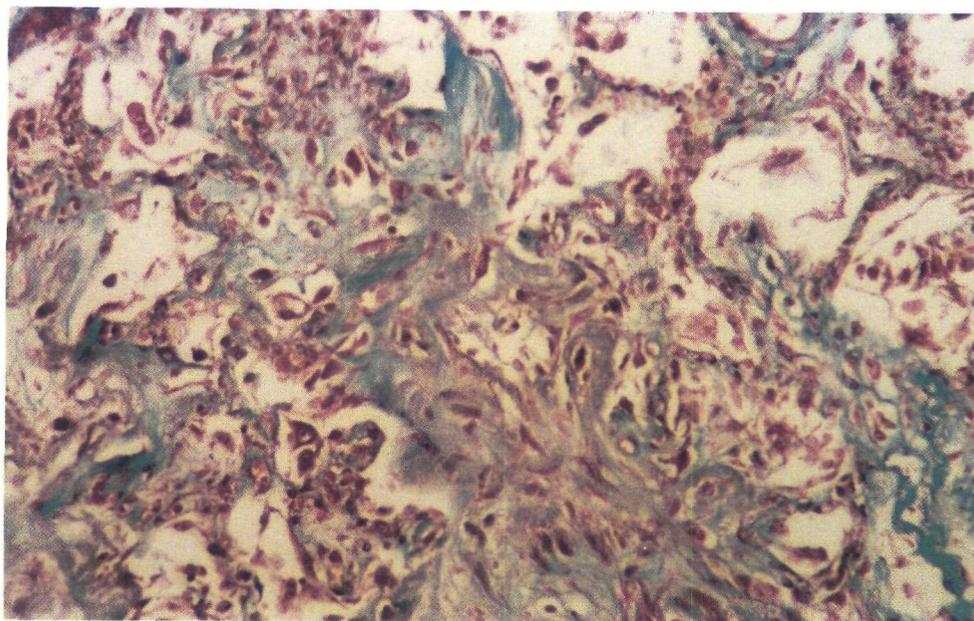
30. Lung: marked thickening of alveolar septa and interstitial oedema with inflammatory infiltrates and fibrosis.
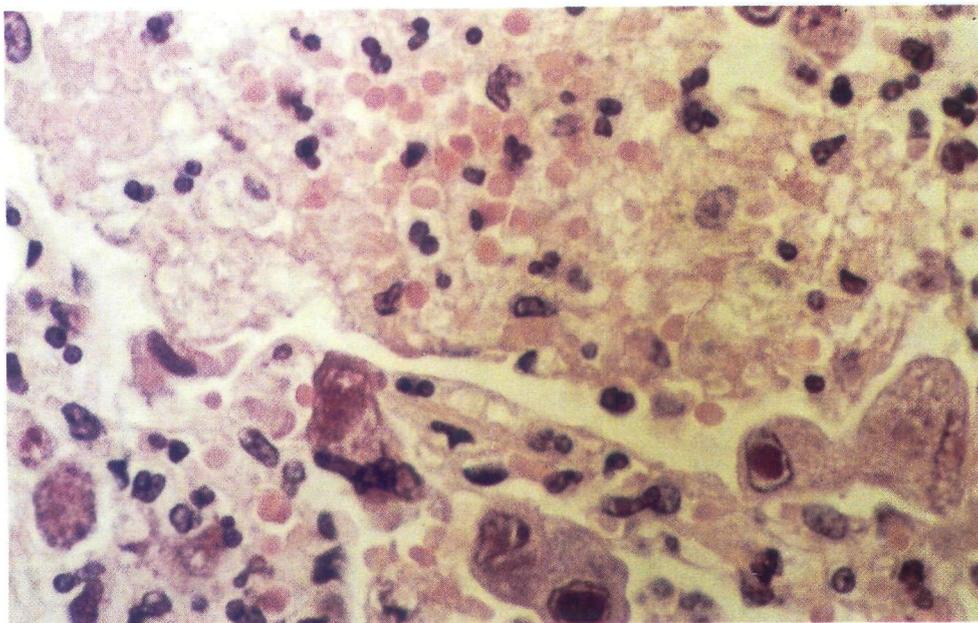
31. Lung: cytomegalovirus bodies in zone of inflammation.
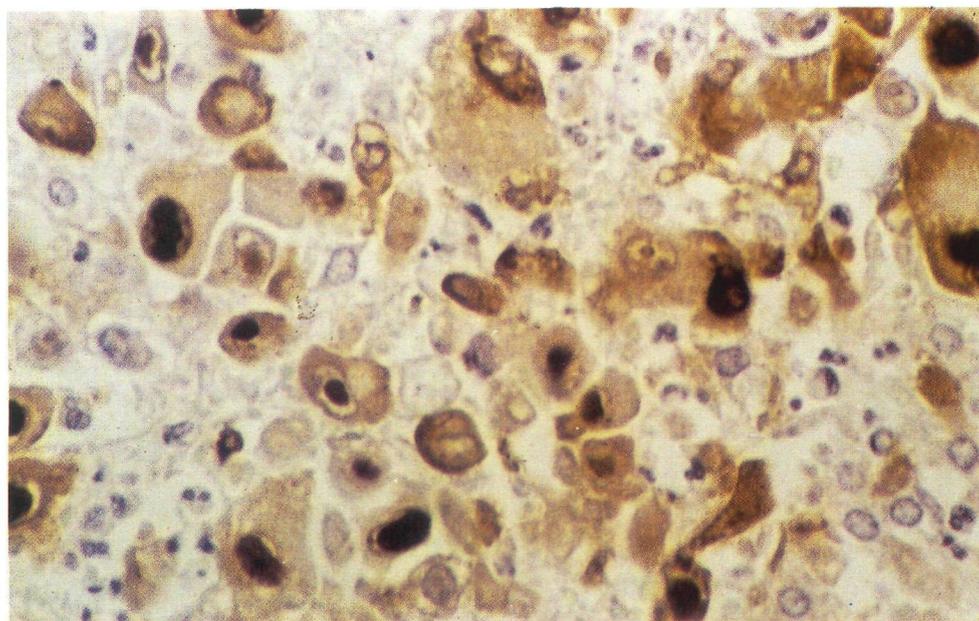
32. Adrenal gland: cytomegalovirus bodies in adrenal parenchyma.

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rhGMCSF and Interleukin-3 (rhIL-3) (see Section 7.3). The patient continued to complain of fatigue and weakness. He felt nauseous, was vomiting twice or three times per day and had watery stools (twice daily). His body temperature rose to 39°C with no documented source of infection. There was a slight tenderness over the parotid glands.

Days 5 to 12

On Days 5–12 (the first week after the bone marrow transplant), the patient continued to vomit once or twice a day and had watery stools (up to 1 L/d), with some days without bowel movement. He developed severe grade III mucositis. His body temperature rose to 40°C despite a broad spectrum antibiotic treatment. Blood cultures remained consistently negative.

On Day 9 (the fifth day after the bone marrow transplant), before engraftment was documented, he developed a maculopapular rash on his abdomen and hips; this disappeared spontaneously within two days without alteration of the therapeutic regimen.

The white blood cell count continued to drop rapidly on Day 5 and no white blood cells were observed in the peripheral blood smears until Day 14, 10 days after bone marrow transplantation (see Fig. 14). The patient's condition did not improve and he gradually developed renal insufficiency, with blood urea level rising to 15.2 mMol/L and creatinine rising to 165 μMol/L. Liver function started to deteriorate with total bilirubin rising to 51 mMol/L and gamma glutamine transpeptidose (γGT) to 145 IU/L, consistent with veno-occlusive disease of the liver. The CPK level declined to 46 IU/L and the amylase level to 16 IU/L. Results of chest X rays were normal. Despite the negative blood cultures, normal results of chest X rays and no evident source of infection except severe mucositis, body temperature was persistently high, and therefore ciprofloxacin was replaced with gentamicin, mezlocillin and Cefazolin (cephazolin sodium) on Day 6. One day later amphotericin B was added.

Days 13 to 21

On Days 13 to 21 (the second week after bone marrow transplantation on Day 4), the patient continued to suffer from nausea, vomiting and watery stools (up to 1.5 L/d). High body temperature persisted despite the empiric antibiotic regimen, and overt jaundice developed. Erythema on the palmar aspect of distant phalanxes, the entire head and upper thorax became more marked (see Fig. 15). Small vesicles typical of radiation injury (rather than acute GVHD) appeared on the ears and particularly on the dorsolateral aspects of the middle phalanges of the fourth and fifth fingers of the right hand and the fourth finger of the left hand. Patchy hair loss became apparent on the skull, face and pubis. On Day 13 (nine days after bone

marrow transplantation) engraftment was documented. The patient's clinical condition did not improve. There was an increase in liver size together with abdominal distention. Liver function was tested and continued to deteriorate with the bilirubin level rising to 143 mMol/L and γGT to 222 IU/L, and with hypoalbuminaemia of 20 g/L which necessitated albumin administration. Chest X rays revealed a right lobar infiltrate. The antibiotic regimen was replaced with amikacin and ceftazidime.

Days 22 to 34

On Days 22 to 34 (the third and fourth weeks after bone marrow transplantation), fever persisted up to 40°C but all blood cultures remained negative. There were signs of superficial and deep partial thickness burn injuries. Jaundice persisted, with right upper abdominal tenderness and hepatomegaly (10 cm below the right costal margin) and marked aggravation of the gastrointestinal phase of ARS. The white blood cell count was stable and within the normal range but thrombocytopenia and anaemia developed gradually. Liver function continued to deteriorate in tests. The bilirubin level rose to 120 mMol/L, alkaline phosphatase to 226 IU/L, aspartate aminotransferase (AST) was 88 IU/L, γGT was 192 IU/L, prothrombin (blood clotting factor II) time was 45% (normal 70%–80%) and partial thromboplastin time was 67 s (normal 25–37 s). The blood level of urea increased to 27 mMol/L and creatinine to 213 μMol/L. The findings were suggestive of veno-occlusive disease of the liver.

Days 35 and 36

On Days 35 and 36 (four and a half weeks after bone marrow transplantation) the patient became markedly confused and disoriented. He developed tachypnea of 48/min. Arterial blood gases disclosed respiratory failure and were manifested by severe hypoxia and metabolic acidosis. Chest X rays revealed massive bilateral interstitial infiltrates.

At 02:00 on 27 July 1990, Day 36, five weeks after the accident, the patient died. An autopsy was performed and is reported on in Section 8.

7.3. MANAGEMENT OF THE HAEMATOLOGICAL PHASE

The haematopoietic system is extremely sensitive to ionizing radiation. The degree of marrow aplasia expected following exposure to gamma irradiation is a function of the total cumulative dose as well as the dose rate and the dimensions of the radiation field. Upon the patient's arrival in the bone marrow transplantation unit, the information available indicated that the patient had been exposed over the entire body with no part shielded; however, no details of dosimetry were available.

In the absence of results of early complete physical dosimetry in order initially to assess the severity of the radiation exposure, only biological dosimetry seemed of use. Rapid onset of the gastrointestinal symptoms of the prodromal phase, including nausea, vomiting and soft bowel movement (within 5 minutes of the exposure to radiation) seemed to indicate a poor prognosis. The burning sensation of the eyes, the symptom that caused the operator to leave the irradiation room, also seemed to be indicative of high radiation exposure (above 10 Gy).

The most important parameters were the haematological findings observed over the subsequent few hours (see Figs 13, 14). These included initial leucocytosis, up to 23.4×10^9/L, with 6% lymphocytes 3 hours after exposure dropping to 2–3% within 6 hours. Follow-up of peripheral blood counts revealed a further steep drop of the lymphocyte count to zero at 60 hours after exposure, which again was a poor prognostic sign that alerted the medical team towards an absolute indication for bone marrow rescue.

A more detailed dose assessment was made on the basis of the known intensity of the source, the exposure geometry and the estimated period of time for which the patient remained near the source. A simulation of his actions during his two periods in the radiation room suggested a high whole body exposure of 10–20 Gy. The dose would have been higher if the amount of time he spent near the source rack had been even slightly underestimated. In view of the data obtained from the physicists and the agreement between the data and the results of biological dosimetry, especially the rapid drop in the lymphocyte count, it was concluded that the patient had probably received a lethal radiation dose and that heroic measures were required.

In view of the uncertainty in the dose estimation, it was considered that it would be beneficial to seek to aid the haematopoietic reconstruction of marrow cells that might have escaped irreversible radiation injury by the use of rhGMCSF. Recombinant GMCSF has previously been shown to facilitate the recovery of granulocytes following chemoradiotherapy and autologous bone marrow transplantation. Hence within one hour of his admission and within 9 hours of the exposure, the patient began receiving continuous infusion of GMCSF (supplied by Behringwerke AG, Marburg, Federal Republic of Germany) at doses of 250 μg/m2/d (skin surface area). Because of experience with herpetic infection in the clinical bone marrow transplantation programme, acyclovir (500 mg three times a day) was given prophylactically.

In anticipation of the option of allogeneic bone marrow transplantation, the patient's parents and brother were brought to the medical centre for an HLA typing. The conclusions were as follows:

Patient's genotype	Brother's genotype
A2	A28
B14	BW55
DR1	DRW11

Patient's genotype	Brother's genotype
DQW5/A2	DQW7/A2
B17	B17
DR3	DR3
DQW2	DQW2

These results indicated a haploidentical mismatch in three loci. Results of one way mixed lymphocyte reaction obtained one week later indicated a strongly positive reaction when cells from the patient's brother reacted against irradiated lymphocytes from the patient. The mixed lymphocyte reaction was negative when the patient's cells were mixed with irradiated lymphocytes from his brother; however, no response was observed by the patient's cells to unrelated controls either, owing to the unresponsiveness of the patient's lymphocytes induced by his radiation exposure. The patient's blood group was B+ and his brother's blood group was AB+. Both the patient and his brother were seropositive for cytomegalovirus (IgG), herpes simplex virus (IgG) and varicella zoster virus (IgG). The patient was seronegative for Epstein–Barr virus, while the brother was seropositive (IgG). Both the patient and his brother were seronegative for hepatitis B surface antigen.

In view of the potential need for bone marrow rescue, a search was initiated on the night of the patient's admission for a matched unrelated donor at the Israeli registry at the tissue typing laboratory of Hadassah medical centre and throughout the major international donor banks of Europe and the USA; no unrelated HLA compatible donor could be identified, however.

By Day 4 a decision to perform bone marrow transplantation seemed unavoidable in view of the following:

 (i) the rapidly falling white blood cell count, particularly the early disappearance of lymphocytes;
 (ii) the biological dosimetry by clinical signs and symptoms;
(iii) the official reports of the physicists' assessment of the patient's radiation dose.

On the basis of the foregoing, it became evident that the first limiting factor for the patient's survival would be complete marrow aplasia.

The bone marrow cells from the patient's brother were aspirated under epidural anaesthesia on Day 4 (the day of the bone marrow transplant). The mononuclear cell fraction was separated by gravity sedimentation at room temperature for 45 minutes following the addition of Volex (Hetastarch). The mononuclear cell fraction was resuspended at 10^8 cells/ml and a monoclonal rat anti-human lymphocyte antibody (IgM) recognizing cell surface CDW-52 (the antibody CAMPATH 1-M, provided by Drs G. Hale and H. Waldmann of the University of Cambridge, United Kingdom) was added at a final concentration of 100 μg/ml for 30 minutes at room temperature. Fresh donor's serum obtained on the morning of

the procedure was added at the final concentration of 20% for 30 minutes at 37°C as complement.

On the basis of previous experience this procedure was expected to deplete all recognizable immunocompetent donor T-lymphocytes without impairing the number or function of normal progenitor cells. Further blocking of potential residual T-lymphocytes was carried out by adding to the final cell preparation a similar monoclonal rat anti-human lymphocyte antibody of the IgG2b isotype (the antibody CAMPATH 1-G) at the final concentration of 0.15 μg per 10^6 cells for 15 minutes at room temperature. This antibody binds effectively to residual lymphocytes leading to their elimination in vivo through anti-body dependent cell mediated cytolysis. The patient received a total of 2.36 × 10^8 nucleated cells per kg with no complications.

On the day of the bone marrow transplant, cyclosporin A (6 mg/kg/d) was added as an additional prophylaxis against GVHD, while infusion of rhGMCSF was continued. On the day after the transplant (Day 5), rhIL-3 (provided by Dr. H.P. Krämer, Behringwerke AG, Marburg, Federal Republic of Germany) was added as a continuous infusion of 250 μg/d, consent having been obtained from the patient and after approval of the procedure by the Institutional Review Board for the first use of this combination. This use of rhGMCSF and rhIL-3 in combination was based on in vivo studies in mice and in vitro studies in human bone marrow cells, both of which suggested synergistic facilitation of haematopoiesis by these growth factors.

Following the bone marrow transplant, the white blood cell count dropped to zero and the platelet count dropped to 15.80 × 10^9/L eight days later. Platelet transfusions were initiated with a Travenol plasmapheresis unit using single donors in order to maintain the platelet count above 20.0 × 10^9/L. The infusion of growth factors (rhGMCSF and rhIL-3) was totally uneventful. On Day 13 (the ninth day after bone marrow transplantation) engraftment was documented and the neutrophil count was as shown in Table III.

Administration of both rhGMCSF and rhIL-3 was discontinued on Day 18 in view of the normalization of the white blood cell count. Engraftment rather than reconstitution of host cells was documented by analysis of DNA extracts of

TABLE III. NEUTROPHIL COUNT FROM DAY 13

Day	Neutrophil count (10^9/L)
Day 13[a]	>0.5
Day 14	>1.0
Day 15	3.2
Day 16 onwards	4.6 to 15.0

[a] Nine days after bone marrow transplantation.

peripheral white blood cells using donor specific DQ probes by polymerase chain reaction. Assays for chimerism disclosed donor to recipient ratios exceeding 10:1, confirming extremely rapid marrow engraftment. The white blood cell counts remained normal throughout hospitalization and did not drop after the cessation of administration of haematopoietic growth factors.

7.4. MANAGEMENT OF THE GASTROINTESTINAL PHASE

The prodromal phase of ARS was typical in that the patient vomited eight times in the first 24 hours after exposure, the first time being within 5 minutes of the exposure. In addition, the patient experienced abdominal pain and soft bowel movement. A central intravenous line was inserted approximately 10 hours after exposure (on Day 1) and total parenteral nutrition was commenced on Day 3 of 2 L/d with the addition of intralipid solutions on subsequent days. Fluid balance was carefully monitored each day by measuring intake (oral and intravenous) and output (urine, vomiting and diarrhoea), with daily control of body weight.

Manifestations of the gastrointestinal phase began on Day 3 with nausea, vomiting (two to three times a day), watery stools (twice daily) and elevated body temperature with no documented infection. Diarrhoea increased gradually, with a total volume of up to 1 L of watery stool daily over the next ten days, and with a continuous high temperature. On Days 13 to 21 the volume of watery stool increased to 1.5 L/d with concomitant deterioration of liver function in tests, which could be indicative of veno-occlusive disease of the liver. From Day 22 to Day 34 the intensity of diarrhoea increased from 2 L/d to 6 L/d. Stool content became bloody on Day 22. Over the same period, other signs diagnostic of veno-occlusive liver disease developed, including overt jaundice and tender hepatomegaly. On Day 23 the patient complained of severe pain in the right upper abdomen. Physical examination disclosed localized peritonitis in the right upper abdomen. Results of a barium enema and ultrasound and computerized tomography scans (see Photographs 9–14) were compatible with radiation enteritis, although intussusception could not be absolutely ruled out. The patient was treated conservatively and the right upper abdominal pain disappeared gradually. The administration of large volumes of intravenous fluids and parenteral nutrition were indicated to control fluid balance adequately.

On Day 24 endoscopy of the upper and lower gastrointestinal tract was performed and disclosed diffuse severe oedema, hyperaemia, inflammation and widespread ulcerations. The antibiotic regimen was changed to mezlocillin, gentamicin and metronidazole to better handle possible invasive gram negative bacteriaemia. L-glutamine (40 g/d) was added in parallel with the total parenteral nutrition solution in an attempt to facilitate regeneration of the gastrointestinal tract. However, despite adequate control of fluid balance, none of the therapeutic modalities seemed effective in controlling the massive bloody diarrhoea.

7.5. MANAGEMENT OF LOCALIZED RADIATION INJURIES

The first evidence of high dose localized radiation injury, a burning sensation in the eyes, was the cause of the patient's leaving the irradiation chamber. Indeed, when the patient was first seen by the physician in Tel Aviv, redness of the eyes was noted. Conjunctivitis persisted throughout hospitalization and conjunctival bleeding occurred together with thrombocytopenia.

Generalized transient cutaneous erythema was apparent two hours after exposure. Prominent erythema of the head and the neck with oedema of the eyelids persisted. Upon arrival at the bone marrow transplantation unit at Hadassah medical centre the patient was given a povidone iodine bath and placed in a laminar flow room under sterile conditions. The generalized erythema as noted earlier was localized to the head, neck, anterior chest and palms (see Fig. 15). On Day 9 (the fifth day after bone marrow transplantation), before marrow engraftment could be documented, a maculopapular rash was apparent on the abdomen and hips. This disappeared spontaneously within two days without alteration of the therapeutic regimen and without additional therapy.

Erythema on the palmar aspects of the tips of the fingers of both hands, the entire head and neck and the upper anterior trunk became more marked between Days 13 and 21. Small vesicles typical of radiation skin injury rather than acute GVHD became apparent on the dorsolateral aspects of the medial phalanges of the fourth and fifth fingers of the right hand and the fourth finger of the left hand. Erythema of the head and neck worsened and small vesicles were also apparent on the tips of the ears. Additional findings were: peeling of the brow; oedema and erosion of the lips; peeling of the skin of the elbows; erythema and blisters on the palms; erythema and large blisters on the dorsal aspects of the fingers of both hands; and moist desquamation of the scrotum. Erythema and vesicles on both soles were apparent on Days 22 to 34. All blisters with necrotic bases increased in size over time. There was no evidence of superimposed infection and no pus was seen in the vesicular sacs.

7.6. NEUROPSYCHOLOGICAL ASPECTS

The patient was a married man with two children and had an unremarkable past psychosocial history. Upon admission the patient appeared confused and tired with a tendency to somnolence and he complained of headache and weakness. Nevertheless, his behaviour appeared adequate with extreme optimism and even some denial of the severity of his condition. The patient and his family were fully co-operative. Initially the patient did not show any evidence of depression and he seemed to cope extremely well with matters by denying the potentially serious outcome of the accident. No psychiatric abnormality of any kind could be defined initially. A full neuro-

logical assessment was made, including cranial nerves, cerebellar functions, sensory and motor functions, and all were normal. All reflexes were normal.

On Day 3 somnolence increased. No major abnormalities were found in a detailed neurological examination except for mild end-point nystagmus. The result of the Romberg test (a clinical test for the degree of equilibrium of a patient) was defined as with a tendency to fall but the results of complete re-evaluation of the cranial nerves as well as sensory and motor functions and all reflexes were normal.

The patient's mental condition began to deteriorate on Day 15; the patient appeared restless during the daytime and also had difficulties in sleeping at night. He appeared distressed with a psychiatric condition compatible with post-traumatic stress reaction. He appeared to be bothered by repeated denial and guilt feelings, together with repeated visual recollections of his exposure episode. According to family members, the patient confused names and displayed changes in behaviour. Clonazepam was prescribed in an attempt to control his psychiatric disturbances. His psychiatric condition continued to deteriorate with the deterioration in his general condition. On Day 27 he was totally confused with labile behaviour, even talking about immediate discharge from the hospital. The patient became progressively anxious with dysphoric features and transient delirium attacks. Clonazepam was replaced with Haloperidol. No specific additional neuropsychiatric findings could be subsequently reported because of the gradual deterioration in his general condition, dictated primarily by the severe gastrointestinal phase of ARS and finally by his terminal respiratory failure.

8. FINDINGS OF THE POST-MORTEM INVESTIGATION

A detailed post-mortem examination was carried out with the written consent of the patient's family. Specimens were obtained for gross and histopathological studies, the results of which are described in the following (see Photographs 15–32).

Bone marrow. Adequate bone marrow engraftment was confirmed by histological evaluation of the adequate degree of cellularity and differentiation of bone marrow cells in the narrow spaces. Lymphoplasmacytoid infiltration of the marrow was also noted which could be part of mild GVHD or reaction to cytomegalovirus infection.

Evidence for acute GVHD. Detailed evaluation of histopathological findings compatible with GVHD was not possible owing to overlapping histopathological findings resulting from radiation injuries to all tissues. Morphology compatible with acute though not severe GVHD was documented in the skin. A typical cell necrosis at the dermoepidermal junction was seen with very mild inflammatory reaction. Changes

compatible with acute GVHD affecting the dermoepidermal junctions were also noted around hair follicles.

Skin. Severe radiation dermatitis was documented by histological evaluation of large areas of the skin. Typical radiation induced lesions were noted by discontinuation of a normal pattern of epidermis with blister formation and complete denudation of affected skin. Mild inflammatory reaction, oedema and thickening were noted in the dermis. Radiation induced abnormalities of the dermal blood vessels were noted.

Lymphoid system. Marked depletion of the lymphatic tissue was noted in all lymph nodes examined. Extreme depletion of all lymphoid elements was noted in the white pulp of the spleen. Complete disappearance of all lymphoid elements was noted along the entire gastrointestinal tract, as could be best seen from the small intestines and the appendix.

Testicles. Marked radiation induced changes were noted in both testicles. The findings were indicative of radiation induced testicular atrophy with complete aspermatogenesis.

Gastrointestinal system. The gastrointestinal system was severely affected, including severe erosive oesophagitis and erosive gastritis all along the mucosa. Marked specific pathology is indicated in the following.

Small intestine. In addition to marked lymphoid depletion the most striking finding was complete disappearance of the normal crypt anatomy with complete denudation of the epithelial layer. Marked pathology was also noted in submucosal areas including severe radiation induced inflammatory changes and marked oedema. Marked abnormalities were noted in the intima of the small blood vessels in submucosal spaces with secondary inflammatory changes. Secondary infection with cytomegalovirus was documented by typical inclusion bodies which were also confirmed by immunoperoxidase staining to have been caused by cytomegalovirus.

Colon. Major distortion of the morphology of the epithelium and submucosa of the colon was noted. Marked changes were found in submucosal blood vessels with distortion of the intima. Intimal thickening caused by oedema and thromboses occasionally occluding the diameter of the blood vessels with secondary fibrosis was observed. Formation of pseudomembranes in the lumen of the colon was also noted.

Liver. The architecture of the liver was preserved but marked oedema due to hepatic congestion was noted. Acidophilic bodies representing necrosis of hepatocytes were also noted with occasional extravasation of red blood cells. The findings were suggestive of radiation induced veno-occlusive liver disease with centrilobular necrosis.

Lungs. Severe radiation induced pneumonitis was noted with complete obliteration of the alveolar spaces in large areas of both lungs. Marked thickening of alveolar septa and the interstitial spaces was seen with marked oedema and secondary inflam-

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matory infiltrate. Radiation pneumonitis was further complicated by secondary infection with cytomegalovirus which could be easily detected by typical inclusion bodies, which were also confirmed by specific immunoperoxidase staining.

Central nervous system. No overt abnormalities could be documented in the brain tissue.

SUMMARY

The autopsy disclosed severe generalized radiation injuries including denudation of the gastrointestinal tract and radiation pneumonitis. Typical cytomegalovirus inclusion bodies were found in the lungs, liver and gastrointestinal tract (specificity was confirmed by immunohistology). Although some of the findings were compatible with acute GVHD, the specific role and severity of GVHD could not be fully assessed because of the overlapping severe multisystemic injuries that were attributed to radiation.

9. LESSONS TO BE LEARNED

The patient was exposed to an acute high uniform whole body dose (of the order of 10 to 20 Gy) and, importantly, this was immediately recognized. The exposure resulted in accelerated haematological depression complicated by the development of associated injury to the gastrointestinal tract, lungs and skin. The case demonstrates 'state of the art' haematological therapy, including emerging therapies, which temporarily rescued the patient, only to have him succumb to irreversible gastrointestinal and pulmonary complications for which treatment possibilities are limited. However, despite the fatal outcome the case history provides valuable information and important lessons for medical radiation specialists. As with the assessment of the causes of the accident, some lessons simply serve to underline accepted practice.

9.1. PHYSICAL/BIOLOGICAL DOSIMETRY AND EARLY RESPONSE

(1) This accident took place in circumstances that aided the immediate appreciation of the nature of the accident. In contrast, in the previous accidents in Goiânia and San Salvador [1, 2] several days passed before the nature and severity of the accident could be fully recognized and medical treatment

planned. As in other radiation accidents, a high whole body dose does not constitute a medical emergency, but it does present an urgent need for early medical decisions.

  (a) *This case underlines the need for medical preparedness to establish priorities and make an early choice of therapy protocols.*
  (b) *The decision to consult, as early as possible, medical specialists such as bone marrow transplant specialists is fundamental to timely decisions on therapy protocols.*

(2) This and other accidents indicate that medical decisions will be primarily based on clinical and biological indicators, including the early onset of nausea and vomiting and the rapid fall in lymphocyte count. Nevertheless, physical and biological estimates do provide a useful input.

  The need for early medical decisions points to the necessity for early biological sampling for standard blood counts, cell typing and lymphocytes for cytogenetics.

(3) The high dose and the short exposure time resulted in an associated division delay and interphase death of lymphocytes, making the cytogenetic results of limited value.

  (a) *Although not a routine procedure, it may be possible in future cases to use the premature chromosome condensation technique to rescue heavily damaged cells and thus to obtain an estimate of dose.*
  (b) *It would have been useful if the possibilities of using electron spin resonance techniques for dose estimation had been pursued. This may also be of value post-mortem by the use of tooth enamel.*

9.2. ASSOCIATED RADIATION INJURIES

(4) Although localized skin injury was not a major factor in this case, it should be noted that extensive radiation induced skin burns complicate the management of induced aplasia.

  Therapeutic decisions should be adopted in anticipation of the chronological expression of radiation injury.

9.3. THERAPEUTIC APPROACH

(5) The patients in the Goiânia and San Salvador accidents [1, 2] were treated with the growth factor GMCSF to stimulate any viable progenitor cells, but with

inconclusive results, since the treatment necessarily could only be commenced more than a week after exposure. The accident in Israel is the first in which GMCSF was administered early (about 9 hours after exposure). However, the therapeutic regime was necessarily wider than this. In view of the sharp drop in circulating lymphocytes, granulocytes and platelets, the results of bone biopsy, and the confirmation of high dose exposure with no known complicating factors, an early decision to perform an allogeneic bone marrow transplant was taken.

Overall, decisions on transplants should not be rushed into after accidental exposure, even when the whole body is exposed. Effective alternative therapies such as the use of haematopoietic growth factors (singly or particularly in combination, as in this case) combined with adequate clinical management may permit the survival of the patient until autologous haematopoietic reconstruction occurs. However, the availability of unequivocal data suggesting irreversible bone marrow aplasia may dictate an attempt at the earliest possible marrow reconstruction using the best available donor, provided that the consequences of acute GVHD can be prevented.

Although the role of growth factors alone in enhancing residual host stem cells cannot be judged on present findings, the data clearly indicate that a combination of GMCSF and IL-3 may lead to early and effective engraftment and maturation of donor marrow cells.

REFERENCES

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

[2] INTERNATIONAL ATOMIC ENERGY AGENCY, The Radiological Accident in San Salvador, IAEA, Vienna (1990).

[3] PARMENTIER, N., NENOT, J.C., JAMMET, H., "A dosimetric study of the Belgian (1965) and Italian (1975) accidents", The Medical Basis for Radiation Accident Preparedness (Proc. REAC/TS Int. Conf. Oak Ridge, TN, 1979) (HÜBNER, K.F., FRY, S.A., Eds), North-Holland, New York (1980).

[4] STATENS INSTITUTT FOR STRÅLEHYGIENE, Reports of the fatal radiation accident at the Institute for Energy Technology (Institutt for Energiteknikk), Kjeller in Norway in 1982, paper presented at an IAEA 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.

[5] INTERNATIONAL ATOMIC ENERGY AGENCY, Radiation Safety of Gamma and Electron Irradiation Facilities, Safety Series No. 107, IAEA, Vienna (1992).

[6] INTERNATIONAL NUCLEAR SAFETY ADVISORY GROUP, Summary Report on the Post-Accident Review Meeting on the Chernobyl Accident, Safety Series No. 75-INSAG-1, IAEA, Vienna (1986).

[7] ANDREWS, G.A., AUXIER, J.A., LUSHBAUGH, C.C., "The importance of dosimetry to the medical management of persons accidentally exposed to high levels of radiation", Personnel Dosimetry for Radiation Accidents (Proc. IAEA/WHO Symp. Vienna, 1965), IAEA, Vienna (1965) pp. 3–16.

LIST OF ABBREVIATIONS

ALT	Alamine aminotransferase (hepatic enzyme)
ARS	Acute radiation syndrome
AST	Aspartate aminotransferase (hepatic enzyme)
bid	Twice daily
BMT	Bone marrow transplantation
CPK	Creatinine phosphokinase
DNA	Deoxyribonucleic acid
GVHD	Graft versus host disease
GMCSF	Granulocyte macrophage colony stimulating factor
Hb	Haemoglobin
Hct	Haematocrit
HLA	Human leucocyte antigen
IL-1	Interleukin-1
IL-3	Interleukin-3
IU	International units
LDH	Lactic dehydrogenase
PT	Prothrombin time
PTT	Partial thromboplastin time
qod	Every other day
rhGMCSF	Recombinant human granulocyte macrophage colony stimulating factor
rhIL-3	Recombinant human Interleukin-3
RLL	Right lower lobar
RSO	Radiation Safety Officer
tid	Three times daily
TLD	Thermoluminescent dosimeter
TPN	Total parenteral nutrition
VOD	Veno-occlusive disease (liver)
γGT	Gamma glutamine transpeptidase (hepatic enzyme)

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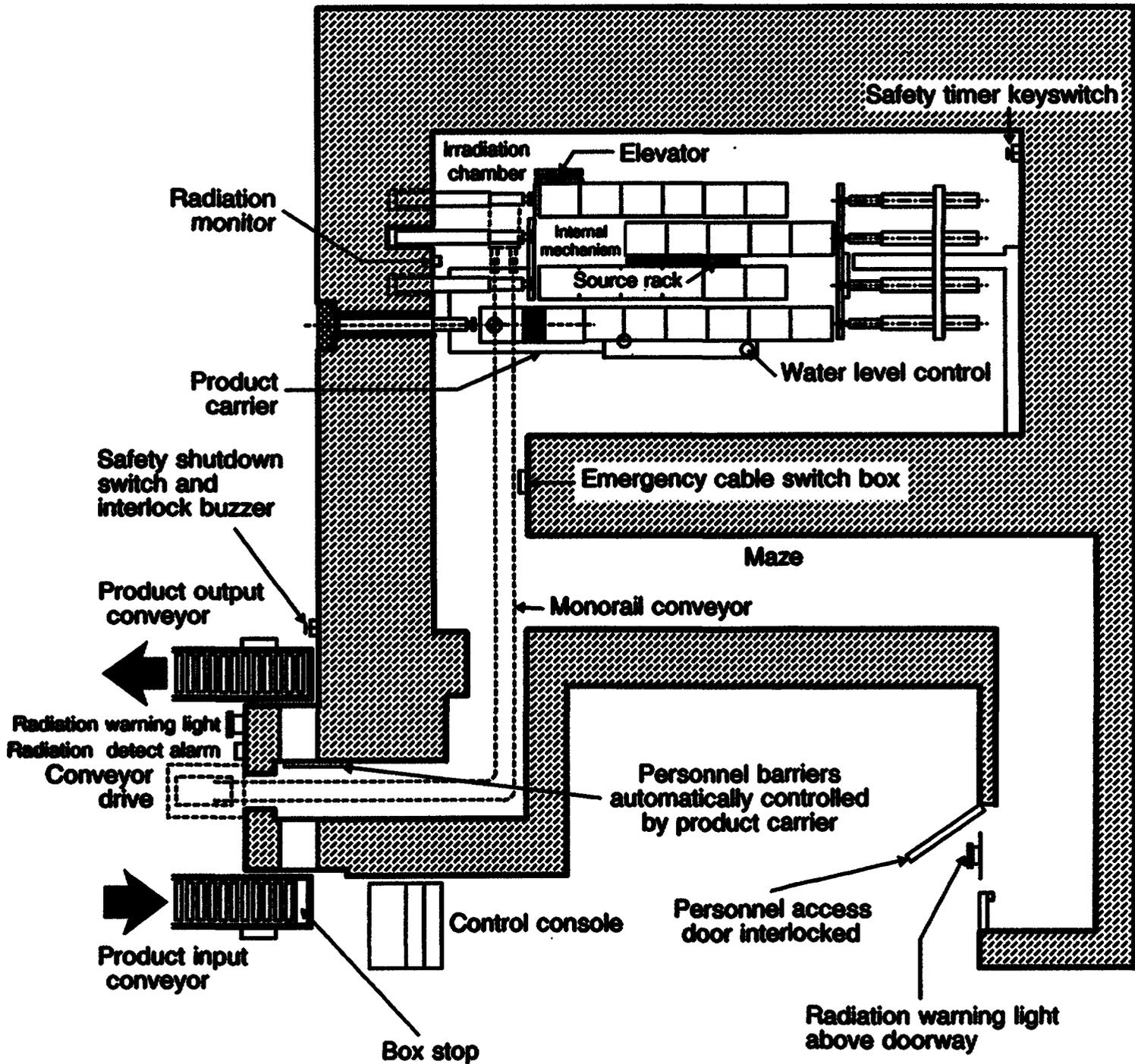
FIG. 1. A floor plan of the irradiation facility and JS6500 irradiator. (By courtesy of Nordion International Inc.)

Source hoist valve board

Source hoist and emergency return

5 ton hand operated hoist

Product boxes

Source in irradiation position

Hand rail

Floor line

Water level

Pool

Ceramic tile lining of pool

Hoist and guide cables

Source in safe or down position
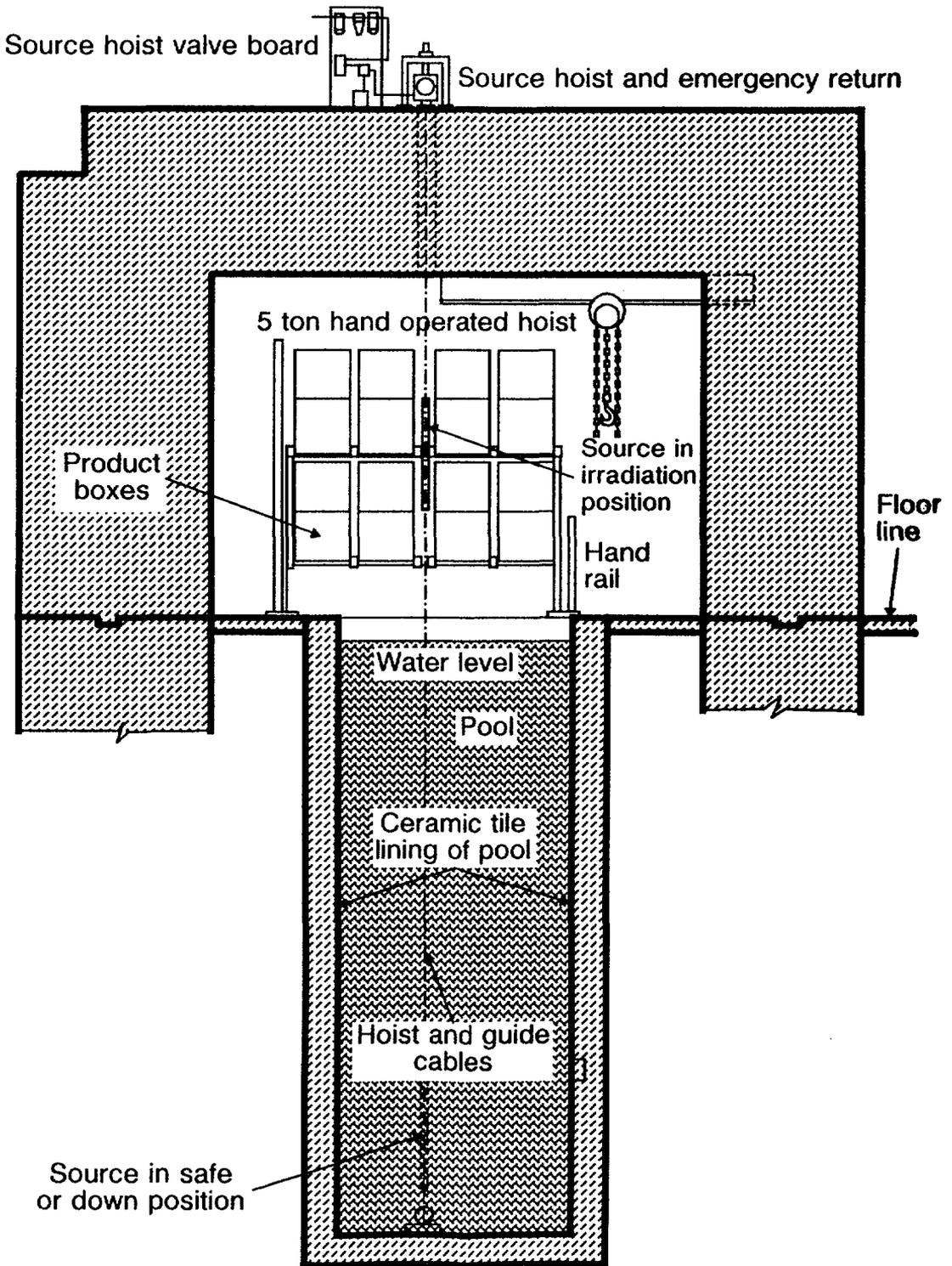
FIG. 2. *A cross-sectional elevation of the irradiation facility. (By courtesy of Nordion International Inc.)*
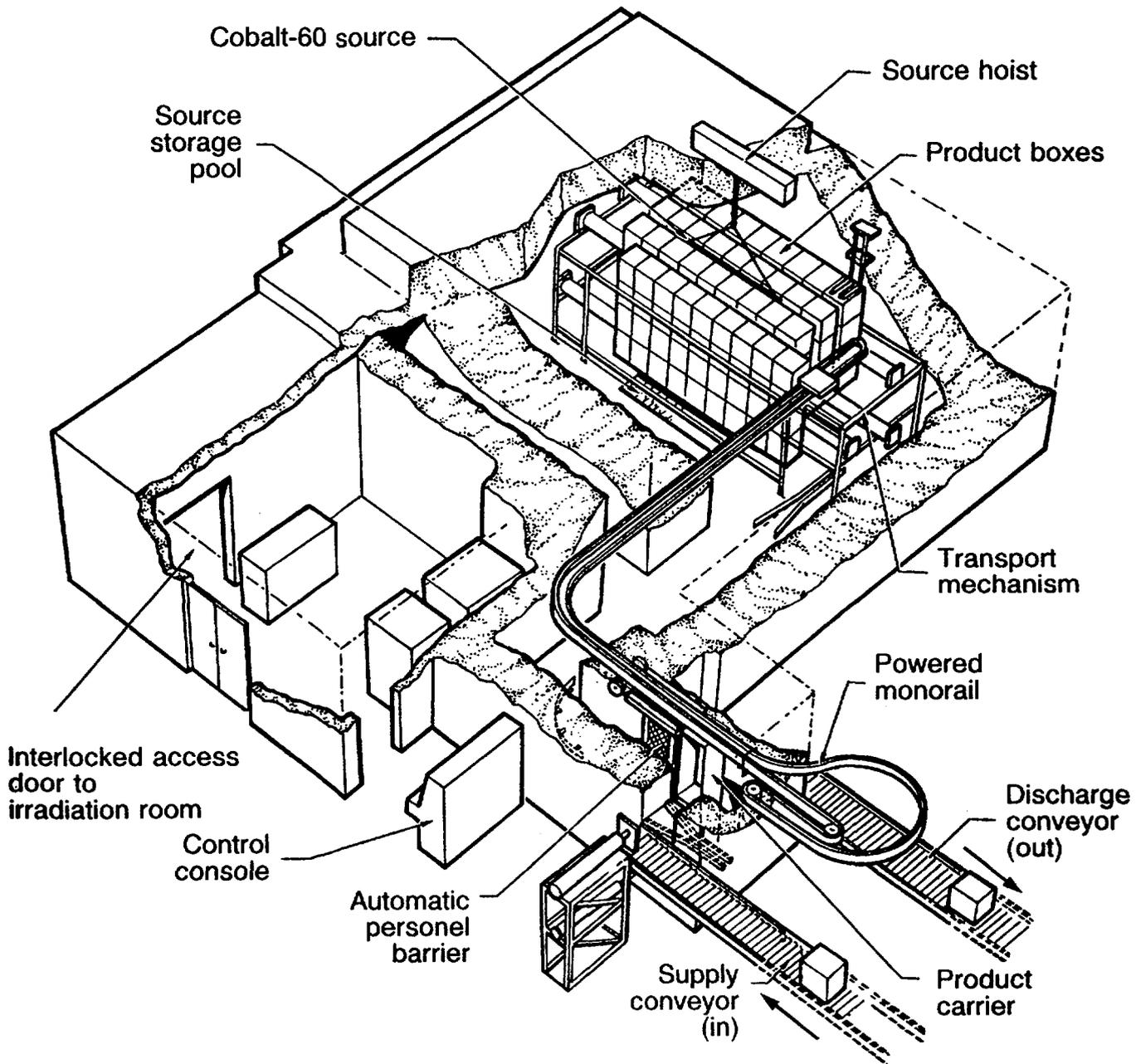
FIG. 3. *A cutaway three dimensional diagram of the JS6500 irradiator and the irradiation facility. (By courtesy of Nordion International Inc.)*