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Dosimetric and medical aspects of the radiological accident in Goiânia in 1987

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FOREWORD

In September 1987 a ^{137}Cs medical teletherapy source was stolen, removed from its shield and ruptured, causing a radiological accident in Goiânia, Brazil. The causes and consequences of the accident were reported by the IAEA in "The Radiological Accident in Goiânia" (IAEA, Vienna, 1988).

Now, ten years after the accident, this TECDOC describes the experience of some of the scientists and physicians who were involved in the management, monitoring and treatment of the victims of the Goiânia accident. Many scientific papers have been published on the subject in different journals. This publication compiles up to date conclusions on the ten year follow-up of the health effects of the Goiânia accident and summarizes the experience that was acquired. It consists of material prepared primarily at the Institute of Radiation Protection and Dosimetry of the National Nuclear Energy Commission of Brazil, under the supervision of D.R. Melo and J.L. Lipsztein.

The IAEA wishes to thank all those involved in the compilation of this publication. The IAEA officers responsible for the review and preparation of this TECDOC were M. Gustafsson and I. Turai of the Division of Radiation and Waste Safety.

EDITORIAL NOTE

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CONTENTS

1. INTRODUCTION

1.1. BACKGROUND

In September 1987, in Goiânia, a city of one million inhabitants and capital of the Brazilian State of Goiás, a rotating assembly of the shielding head of a teletherapy unit was removed and the capsule containing 50.9 TBq (1375 Ci) of ^{137}Cs was dismantled. This serious radiological accident resulted in four fatalities, injuries to many people, and the widespread contamination of the central part of Goiânia.

The accident yielded lessons that cover the pre-accident period, the response and the post-accident phases. It is important to know about the operational difficulties that were faced in Goiânia including the differences between the technical evaluation and public opinion in order to inform individuals and organizations that may face similar emergency situations.

The accident also had several adverse effects that are not mentioned in publications concerned with emergency planning and preparedness. These include psychological aspects, such as fear and depression amongst the population, and discrimination against the victims and important products of the local economy. All these lessons must be analysed in terms of the implications for safety culture and the experience gained. There is still much to be learned from the radiological accident in Goiânia.

A complete internal dosimetry study was conducted, which included six years of in vitro and in vivo bioassay monitoring. This study included data on people who had ingested radionuclides as a result of the accident and were treated with Prussian Blue (PB), a drug given to enhance the elimination of caesium form the body, and on others who were not treated with the drug. A 7.5 years cytogenetic follow-up of unstable chromosomal aberrations was also conducted for the most exposed patients. In March 1988, a medical follow-up protocol was established between the National Nuclear Energy Commission of Brazil and the Leide das Neves Foundation, in Goiânia, in order to assist the victims of the accident. For ten years, the patients have been examined and treated by physicians from the Leide das Neves Foundation, in collaboration with the team responsible for the early medical response.

1.2. OBJECTIVE

This TECDOC describes the dosimetric and medical aspects of the Goiânia accident, including the experience of some of the scientists and physicians who were involved in the management, monitoring and treatment of the victims. Many scientific papers have been published on the subject in different journals. This publication compiles up to date conclusions on the 10 year follow-up of the Goiânia accident victims, and summarizes the experience that was acquired.

1.3. SCOPE

This publication is intended for institutions, radiation protection specialists, physicians specialized in the treatment of radiological or nuclear accident patients and emergency response groups. It provides useful information for the handling of accidents involving internally contamination with radiocaesium, for the implementation of monitoring and medical intervention procedures, and dose assessment.

1.4. STRUCTURE

Chapter 2 is a brief description of the accident. Detailed technical information is provided in eight sections, describing the methods and results of bioassay, dosimetry, and treatment, as well as the complications observed. Each section has conclusions and references. Chapter 11 summarizes the ten year experience of dosimetry and medical aspects of the Goiânia accident, including an update of the medical follow-up for the period of 1990–1997.

2. DESCRIPTION OF THE ACCIDENT

2.1. DETECTION OF THE ACCIDENT

On the afternoon of 29 September 1987 the National Nuclear Energy Commission (CNEN) of Brazil was notified by a physicist of Goiânia about a serious radiological accident.

Goiânia, the capital of Goiás State in the mid-west of Brazil, is 1348 km from Rio de Janeiro and 919 km from São Paulo, where the main Brazilian institutes of radiation protection are located. The production of grains and breeding of cattle are the main economic activities in the Brazilian mid-west. At the time of the accident, Goiânia had about 800 000 inhabitants.

Officials of the Department of Health of the State of Goiás and other local authorities, with the help of physicists, identified several sites and residences at the urban area with elevated dose rates of ionizing radiation. At some sites it was impossible to quantify the exposure level as the instrumentation (a scintillation detector used for prospection for uranium) used by the physicist presented full scale response. Some of the residents of the houses were hospitalized at the Hospital of Tropical Diseases. Although many of these patients had symptoms, as described in the medical literature, characterizing high exposure to ionizing radiation, they were admited to hospital with suspicion of "some" tropical disease. Afterwards, one of the physicians suspected that the symptoms presented by the patients might be related to ionizing radiation.

The contaminated residences were evacuated and isolated. The inhabitants were removed to the Olympic Stadium of Goiânia where some tents, usually used by the Army, were pitched in the soccer field.

The physicist was contacted by the health authorities in order to investigate "a metallic assembly" which had been brought inside a bag by a woman and a man saying that this "thing" had some "bad properties" as they thought it was responsible for the disease of many of their relatives and friends. The woman, wife of a junkyard owner, died at the end of October 1987, due to external exposition to ^{137}Cs, although she had also presented some internal contamination. The man, a worker at the same junkyard, still has injuries due to a dose received during the removal of the assembly. Based on the statement of these two persons, it was possible to make a relation between this assembly and the patients admitted at the hospital with a "strange disease", and also with equipment that had been removed from the interior of an abandoned building in downtown Goiânia. The Goiânia Institute of Radiotherapy (IGR) had moved from this building in 1985, taking a ^{60}Co teletherapy unit but leaving in place a technologically obsolete ^{137}Cs teletherapy unit, which until that date had been used to treat cancer patients [2.1].

Some young men without a permanent job and living on small services, learned that there was equipment at the abandoned building. At a non-identified date (possibly on September 13), these unauthorized people entered into the building and, after trying to dismantle the radiation head of the teletherapy unit, finally removed the rotating assembly where the caesium sealed source was located. One of the men, believing this assembly had a high value, took it to his residence. For several days, he tried to dismantle the rotating assembly. It is believed that on September 18 the source capsule was ruptured and this released the caesium. The ^{137}Cs source was in the form of caesium chloride salt and had, at the

time of the accident, an activity of 50.9 TBq (1375 Ci) [2.1]. As this salt is highly soluble, it was easily dispersible, leading to the contamination of many people and the environment. Measurements performed on October 2 indicated that the residual contamination in soil in the residence gave a dose rate of 1.1 $Gy \cdot h^{-1}$. This residence had high contamination and afterwards it was demolished, and the soil removed.

2.2. CONTAMINATION OF THE ENVIRONMENT WITH ^{137}Cs

The source assembly was sold to a junkyard. The junkyard owner believed it had some value as it glowed blue in the dark like a precious stone. Others believed it had mystic properties. This information was spread among his relatives and friends, who from that day on came to visit him in order to see for themselves. These visitors were contaminated with the ^{137}Cs, mainly on their hands and clothing. Consequently, they spread the caesium every place they went. Residences 100 km from Goiânia were found with caesium contamination. Some friends received small pieces of the "glowing stone", approximately the size of rice grains, as a gift. Some of them scrubbed the material on the skin in order to appreciate its brightness. The handling of the caesium caused, in most cases, internal contamination by ingestion. This was the case of a 6 year old girl who ate a sandwich while playing with a small piece of the caesium source. She received a high level contamination and died on 23 October 1987 with an estimated internal dose of about 4 Gy due to an estimated intake of 1×10^9 Bq [2.2].

Over 2 weeks or so, the ^{137}Cs source remained freely exposed, without shielding, exposing externally many persons. As it was fragmented the contamination was dispersed. In total four main foci of contamination were identified: three junkyards and the residence where the source was ruptured. The strong winds which blew at the end of September dispersed caesium along the yards, gardens and roofs of the houses. The caesium initially deposited on the surface soil reached the main river of the region, the Meia-Ponte River, owing to the heavy rain that had fallen in the city. Three weeks after the discovery of the accident, analyses of the surface waters, sediments and fish were initiated. Caesium was detected in sediments located 12 km from the place of the accident [2.3].

2.3. TECHNICAL MANAGEMENT OF THE ACCIDENT

At dawn, on 30 September 1987, the first three technicians of CNEN arrived in Goiânia. At the first hours of the same day, another team composed of physicists and a physician joined the first one. That morning, the main newspapers of the country ran stories on the radiological accident. Over the next 6 months (mo) a number of technicians and experts arrived in the city. Many international organizations contributed to the resulting work, in particular the International Atomic Energy Agency.

Through all the phases of the accident, including decontamination, 755 professionals took part. In order to compensate for lack of training, the workers were divided in teams and the task of co-ordination was given to a suitable persons. The workers were monitored by film badges and Quartz Fibre Electrometer (QFE) pens. Considering film badge results, about 70% of the doses were less than 1 mSv. The highest dose was 16 mSv [2.1].

Since Brazil did not have appropriate planning to dealt with radiological emergencies such as that in Goiânia, it was necessary to develop over the first days several technical and administrative procedures to lead the teams to carry on tasks with efficiency and to permit measurement results to be correctly interpreted and compared. In addition, it was necessary to

set action level for evacuation of residences, isolation of public areas, and decontamination of residences, public places, cars, utensils, materials and personal goods which showed contamination. Another consequence of the absence of previous planning was the small number of detectors available. It was necessary to borrow them from several institutions. The instrumentation obtained was from different manufacturers and some of them had different scales. Besides, it was found that instrumentation with digital scales, when operated in strong sunlight, presented wrong results. The environmental humidity also reduced the performance of some detectors [2.4]. This fact required special attention in order to avoid wrong interpretations of the measurements.

The teams faced several adversities in at the first days in Goiânia, such as the difficulties to send to the Institute of Radiation Protection and Dosimetry, in Rio de Janeiro, samples of faeces and urine to be analysed in order to evaluate the level of internal contamination. There was no appropriate standard packing for shipment by air and the airlines sometimes refused to transport the samples believing they were dangerous.

The following priorities were established by CNEN in order to organize the actions in Goiânia: (i) care of the victims and population, (ii) identification of the contamination foci, and (iii) elimination or decrease of the dispersal of ^{137}Cs to the environment. The major public hospital of the city, Goiânia General Hospital, was equipped to receive the patients admitted to the Hospital of Tropical Diseases. A staff of physicists, physicians and technicians was organized to operate the ward. A whole body counter was installed, in November 1987, at this hospital, to follow up decorporation of ^{137}Cs by the administration of PB. The victims that did not need hospitalization were sent to a lodging-house under medical and radiological protective supervision. The 14 patients that required specialized treatment were transferred to Marcílio Dias Naval Hospital in Rio de Janeiro, which was equiped to receive victims of nuclear accidents, as it integrates the emergency plan of the nuclear power plant of Angra dos Reis in Rio de Janeiro [2.5].

A great effort was made by CNEN's co-ordinators to inform the population about the accident, its consequences and the actions taken. All requirements of the media (press, radio and television) for interview, as well invitations to take part in debates at several community groups, were attended. Additionally, a pamphlet was produced on "What you should know about radioactivity and radiation" with the objective of explaining in simple language some concepts that led to misunderstandings, such as the difference between external exposure to radiation emitted by caesium and contamination by ^{137}Cs.

A telephone service operated 24 hours a day to receive information and complaints, and answer inquiries concerning the accident. This service was well used by the population, and became a way to clarify and disseminate information. However, it was very difficult at first to attend to all the inquiries requesting visiting "in loco" aiming to check for possible contamination. The deaths of birds in cages, of cats and pigeons in the street, and of fish in aquaria were wrongly attributed by the population to caesium contamination.

The Olympic Stadium (where the first evacuees were sent) became the site for referals place. A monitoring service of people and objects was carried out at this stadium. In total, about 110 000 persons reported to the Olympic Stadium to be monitored. Of these, 249 were contaminated either internally or externally [2.5]. Depending upon the level of contamination, they were attended to at the stadium or sent to the hospital. Blood samples were collected from some of these persons and from the patients admitted to the hospital, in order to estimate, by cytogenetic methods, the dose received [2.6].

Initially, the contaminated sites were identified based on information provided by the persons examined. Some places had a high level of contamination. In total, 85 residences were found to have a significant level of contamination [2.7], and of these 41 were evacuated. To confirm that the main sites had been identified, an aerial surveying was carried out by helicopter. About 67 km^2 of urban areas of Goiânia city was monitored [2.1]. This survey indicated only one new contamination focus near the previous sites that had already been identified. Afterwards, a car equipped with two Geiger–Müller detectors and one NaI(Tl) detector covered approximately 80% of the urban area of the city [2.8]. Small sites of contamination of public places were located where some persons involved with the accident had transited.

As the contaminated sites were identified and isolated, decontamination could be carried out. This was the most difficult step, due to the lack of proper packaging for waste disposal and the lack of an appropriate place for storage. It was necessary to build a repository for the waste. In order to facilitate transport of the waste, the location needed to be near Goiânia. Resistance of the population concerning the choice of a site for the repository delayed its construction. An agreement between the local authorities and CNEN allowed the construction of a temporary repository at the city of Abadia de Goiás, in a sparsely populated area, located 20 km from Goiânia. A new site was to be designated in the future for a permanent repository. While the repository was being built, industries located in Goiânia made metal boxes specially designed to store the radioactive waste. The boxes were 1.2 m^3 in volume with a maximum load of 5 tonnes.

The repository was ready in the middle of November 1987, when decontamination began. At the main foci of contamination houses were demolished, soil removed and the ground covered with concrete. The less contaminated houses had their walls, floors and roofs decontaminated. The personal items and utensils that presented some level of contamination were treated as waste because the population refused to receive decontaminated objects. Besides the houses, 45 public places, including streets, squares and shops were decontaminated. Low level waste was placed into either industrial drums with 200 L capacity or metal boxes. Roll-on-roll-off shipping containers with 32 m^3 were also used. Intermediate level waste was put in 200 L drums, and these were put in a special cylindrical concrete packaging with 200 mm reinforced concrete walls (concrete well). At the end of December 1987, the main foci were decontaminated. A total of 3 800 drums, 1400 boxes, 10 containers and 6 concrete wells were used [2.1]. The drums and boxes were wrapped in plastic to protect them from the heavy rainfall.

During the last years, the waste from the accident was repackaged. Two permanent repositories with an area of 1 600 000 m^2 were built near the temporary repository. The first one stores about 40% of the waste volume which has low level specific activity. Under the current legislation in Brazil, such waste could be disposed of at an urban waste repository. The second stores the higher level radioactive waste. The two repositories, in the form of two hills, were covered with grass. This site was transformed into an environmental preservation area and reforested with typical species of the region.

CNEN will take control of this place over the next 50 years, and a laboratory of radioecology and an information center on the accident and the repository have been built.

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3. IN VITRO AND IN VIVO BIOASSAY

3.1. INTRODUCTION

Individual monitoring for intakes of radionuclides may be achieved by body activity measurements, excreta monitoring and the combination of the techniques. The choice of measurement technique is determined by several factors: the radiation emitted by the radionuclide, the metabolic behaviour of the contaminant and its retention in the body taking account of both biological clearance and radioactive decay [3.1].

The in vitro bioassay method was used initially for screening people from the Goiânia population with caesium internal contamination. During the first two months after the accident the evaluation of caesium internal contamination was made through urine and feces analysis. The reason for this was mainly the distance between the accident site and any radiation protection centre with the capability of performing internal monitoring by in vivo measurements. The other reason was that most of contaminated people had also external contamination, that would cause an overestimation of the ^{137}Cs body burden if evaluated through in vivo measurements. The whole body counter was installed in Goiânia in November 1987. These measurements had fundamental importance to the study of caesium metabolism, to evaluate the effectiveness of the caesium decorporation therapies, mainly PB administration, as well as other medical treatments.

3.2. IN VITRO MEASUREMENTS

Total feces and urine excretion from hospitalised patients in Rio de Janeiro and Goiânia, were collected daily. Excretion samples from people confined in special housing centers, was collected only every 4th day, because people complained of the discomfort of the daily excreta collection. At the time the patients were released from hospital and special housing centres, most of them stopped collecting samples, and in vitro bioassay became irregular or stopped completely. The containers with samples were handled with care to avoid cross contamination, were packed in boxes and were shipped by air to Rio de Janeiro to be processed at the in vitro bioassay laboratory of the Institute for Radiation Protection and Dosimetry (IRD).

The in vitro bioassay laboratory facilities consists of a counting room (with the measurement systems), a chemistry laboratory and a furnace room, which was transformed into a storage room. It has two entrances: one from the inside and the other from the outside of the building. Immediately next to the outside entrance is a storage room. The boxes with samples were brought through the outside entrance and placed in the storage room, until analysis. The layout of the laboratory helped to make the appropriate radiation protection procedures, and it allowed being able to keep the building free from any contamination from the transport of the samples. The laboratory was previously prepared to attend an emergency situation. All the surfaces and equipment of the three rooms were covered with plastic sheets. The storage room was divided in two parts: one to store received samples and the other to store the waste samples. The laboratory was completely monitored daily to avoid the spread ^{137}Cs contamination.

3.2.1. Sample preparation

The urine samples were collected in plastic bottles. The total volume of the sample was measured. An aliquot of 0.25 L was transferred to a plastic bottle, free of contamination, labelled with the name of patient, day of sample collection, and total volume. The bottles were packed in sealed plastic bags and immediately transferred to the counting room. Some samples had high specific activity and needed dilution. An aliquot varying from 0.02 L to 0.10 L was transferred to a plastic bottle and 1 M nitric acid, was added until 0.25 L was reached [3.2].

The feces samples were also collected in appropriate plastic containers. The samples were completely transferred to a similar container of 0.5 L, free of contamination. The samples were weighed, and labelled with the name of patient, day of sample collection, and total mass. The fecal mass was stirred with nitric acid, 1 M, until homogenized. The volume of nitric acid was 0.25 L or 0.40 L depending on the fecal mass. The container was packed in sealed plastic bags before counting [3.2].

Among the contaminated population were two very young girls aged 1 and 2 years. Their excreta were collected in disposable diapers. The diapers, with urine and feces, were put into similar containers used for feces analysis, and also packed in sealed plastic bags before counting.

3.2.2. Measurement system

The excreta samples were measured for caesium content using a planar 0.076 × 0.076 m NaI(Tl) detector enclosed in lead shielding (0.60 m height–0.60 m width–0.10 m thick). The caesium activity of the samples was very high and 1 min of counting time was enough to have a significant statistical counting rate ($p < 0.05$). The minimum detectable activity was 5.3 Bq L^{-1}, for a 1 min counting time, $p < 0.05$ [3.3].

The Brazilian specialists had no previous idea of the ^{137}Cs activity level in the excreta samples. The counting geometries used for the calibration of the measurement system were the same as those used in the routine monitoring. As the bioassay laboratory was designed to monitor workers with low level exposure, the usual procedure was to concentrate the radionuclide in the urine by reducing the total volume to 0.25 L. For feces samples, the usual procedure was to stir the fecal mass adding nitric acid, 1 M, until homogenized, and the volume was taken to 0.25 L or 0.4 L. When the first samples arrived at the laboratory, the Brazilian specialists did not realize the magnitude of the contamination. As the medical staff needed to have the bioassay results in a short time to decide on a PB treatment and also to screen contaminated people, a large amount of samples had to be analyzed each day, even in the weekend. The Brazilian specialists had no time to modify the counting system to a more appropriate system to measure high levels of ^{137}Cs activity.

The calibration of the system was made using phantoms of urine, feces and diapers. For urine, an aliquot of 0.25 L of urine was taken from a non-exposed person, the aliquot was put into a plastic bottle with 0.003 L of concentrated nitric acid, to avoid the caesium adsorption on the walls of the bottle [3.4]. A known amount of ^{137}Cs was added to the solution and the bottles were sealed in plastic bags. For feces, two geometries of 0.25 L and 0.40 L were used. A total daily fecal excretion was taken from a non-exposed person. The fecal mass was transferred to a plastic container of 0.50 L, appropriate for g spectrometry. The fecal mass was

TABLE 3.1. COUNTING EFFICIENCY OF THE NAI(TL) DETECTOR FOR DIFFERENT GEOMETRIES

Samples	Geometry	Counting efficiency
Urine	0.25 L	4%
Feces	0.25 L	4%
Feces	0.40 L	3%
Diapers	–	2%

TABLE 3.2. MAGNITUDE OF THE ^{137}Cs ACTIVITY OF THE ANALYSED SAMPLES IN THE PERIOD FROM OCTOBER TO DECEMBER 1987

Order of magnitude of the ^{137}Cs sample activity (Bq)	No. of samples
10	186
10^2	269
10^3	1065
10^4	1408
10^5	438
10^6	34
10^7	2

stirred, nitric acid (1 M), was added until the mass was homogenized at 0.25 L. The same procedure was made for the 0.40 L geometry. For the diapers, the excretion of a non-exposed 1 year old baby was collected in a diaper. The diaper was put into a container and a solution with a known activity of ^{137}Cs was added. The phantoms were counted in the measuring systems. Table 3.1 shows the counting efficiency of the detector for the different geometries used for urine, feces and diapers.

Approximately 4000 samples from a total of 90 people were analyzed during the period from October to December 1987, ^{137}Cs activity of the analyzed samples, are shown in Table 3.2. Eighty-six percent of the samples had activities in the range of 10^3 to 10^5 Bq [3.3].

3.3. IN VIVO MEASUREMENTS

Due to the large number of people internally exposed to ^{137}Cs and the seriousness of the accident, it would have been desirable to set up a counting system in the city of Goiânia, so that many people could be measured as quickly as possible. The in vivo measurement system should be designed to measure high levels of ^{137}Cs activity in the body. Whole body counting (WBC) was attempted for the fourteen patients that were brought from Goiânia to the Navy Hospital in Rio de Janeiro city where an *in vivo* shadow-shield monitoring system was available. However, as foreseen, it was not possible to make any measurements. The activities were far too high for that system, as were they for all other existing facilities in the country, which had been designed to measure internal contamination levels just slightly higher than the ICRP reference limits [3.5]. It was necessary therefore to redesign, construct and test a special whole body counting system appropriate to measure high ^{137}Cs activities.

After the performance of this special whole body counting system was studied, a new design of WBC was developed with the capability of measure a wide range of activities from photon emitting radionuclides with energies above 200 keV, without significant dead time

problems and with a high counting efficiency. This new in vivo measurement system made possible occupational monitoring as well as the measurements of people contaminated in accidents, which involves the detection of high activities of radionuclides. This system allows the use of multiple measurement geometries, established rapidly without losing the detection efficiency.

3.3.1. Construction of the measurement system

The design and construction of a whole body counter system with specific characteristics, to be installed at the Goiânia General Hospital (GGH) in the city of Goiânia began on 29 October 1987, with the aim of using the in vivo bioassay technique to quantify the internal contamination The GGH was chosen so as to make easier the monitoring of hospitalized patients. These were clinically debilitated due to their acute radiation exposure and were kept isolated. Also monitored were those people who were isolated in the special housing center and those with low contamination levels who were out-patients. The accident affected a large number of people with ages varying from newborn to adult. The caesium body burden varied much from person to person. It was therefore, necessary that the measuring system had a counting efficiency which would allow measurements of different levels of caesium activity as well as different body sizes. This system was also used to screen internally contaminated people from the Goiânia population. As the number of people measured each day was high, the counting time was an important parameter to be considered in the measurement system.

The system was installed in a 4.0 m width, 3.5 m length and 3.5 m high room, where seven layers of 2 mm thick lead sheets, 2.0 m long and 1.0 m wide were placed on the floor, in layers equidistant from the walls. The walls and the ceiling were not shielded. The measurement system consisted of a 20 cm diameter × 10 cm thick NaI(Tl) detector, shielded and collimated by 5 cm of lead, wrapped around the crystal, fastened in an iron framework (2.23 m high, 0.9 m wide, 0.85 m long). The subject was positioned lying on a fiber glass chair (like the ones used at swimming-pools) below the detector. This configuration was close to an arc geometry. The distance from the center of the chair to the geometric center of the detector was 2.03 m, as shown in Fig. 3.1. This distance, between the detector and the subject, allowed some advantages over the other WBC described in the literature [3.6]. The range of measured ^{137}Cs activities was 440 times lower than the annual limit of intake (ALI) [3.5] up to a value of ten times higher than the ALI for ^{137}Cs. The counting efficiency for a child was the same as that of an adult 2 m high. This system showed to be very efficient for *in vivo* measurements. The dead time was lower than 8% for the subject with highest internal contamination, and the minimum detectable activity (MDA) was equal to 9 kBq for a 2 min counting time ($p < 0.05$) [3.7].

3.3.2. System calibration

One of the difficulties of the system calibration, was to find a ^{137}Cs source with sufficient activity to simulate the real condition of measurement. The available source with high activity was around 1.5 kBq, which was very low to calibrate the system with the distance of 2.03 m from chair to detector. First was used a point source, from the IAEA, reference FH35D - number 50 1717, with an activity of 333 kBq. Later, a ^{137}Cs standard source, with activity of 118 ± 2 kBq, calibrated by the Metrology Department from the Institute for Radiation Protection and Dosimetry (IRD/CNEN), in Rio de Janeiro was used in an anthropomorphic phantom to simulate the ^{137}Cs distribution in the body. The source was

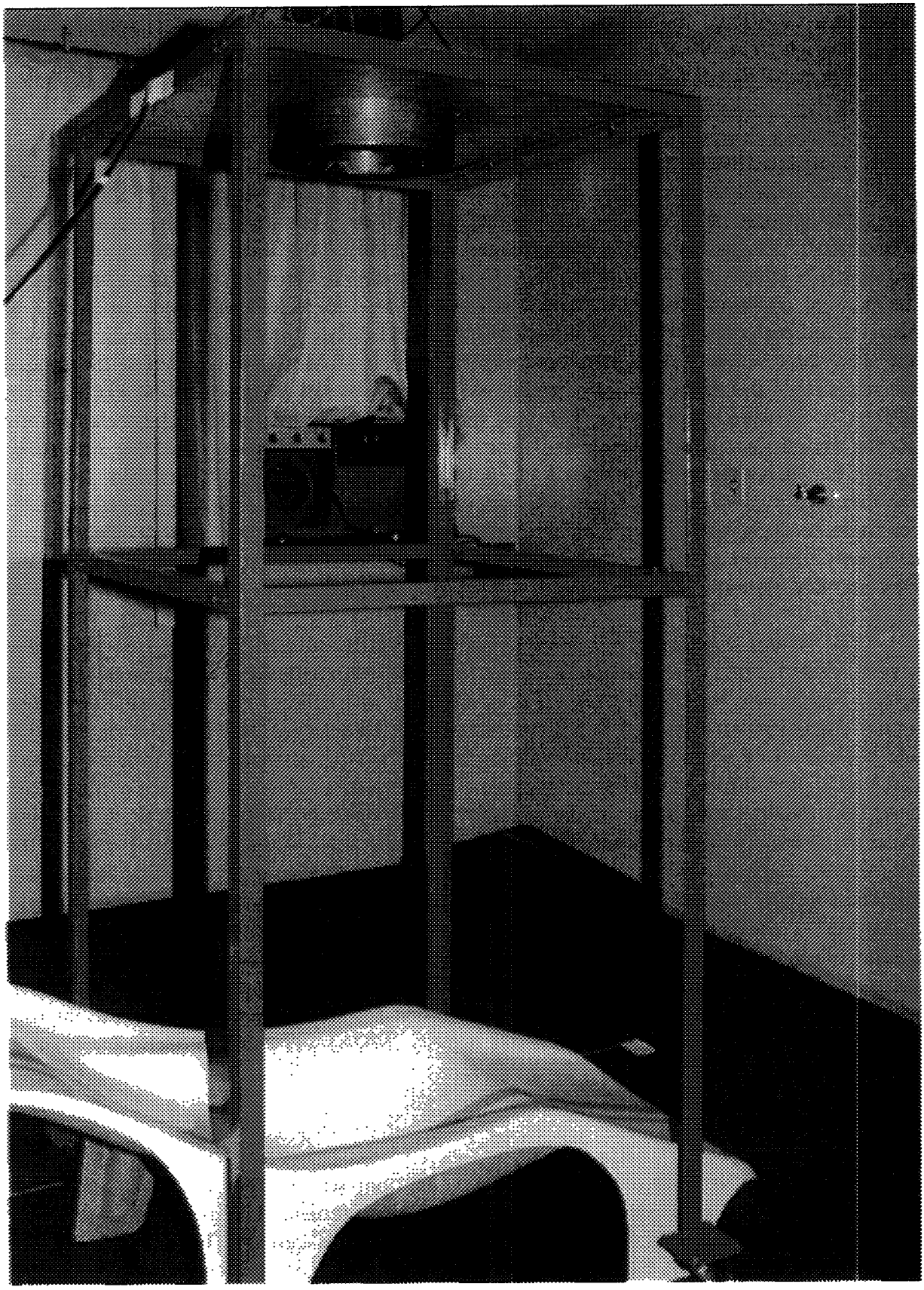

FIG. 3.1. Whole-body counter system installed at the Goiânia General Hospital (GGH).

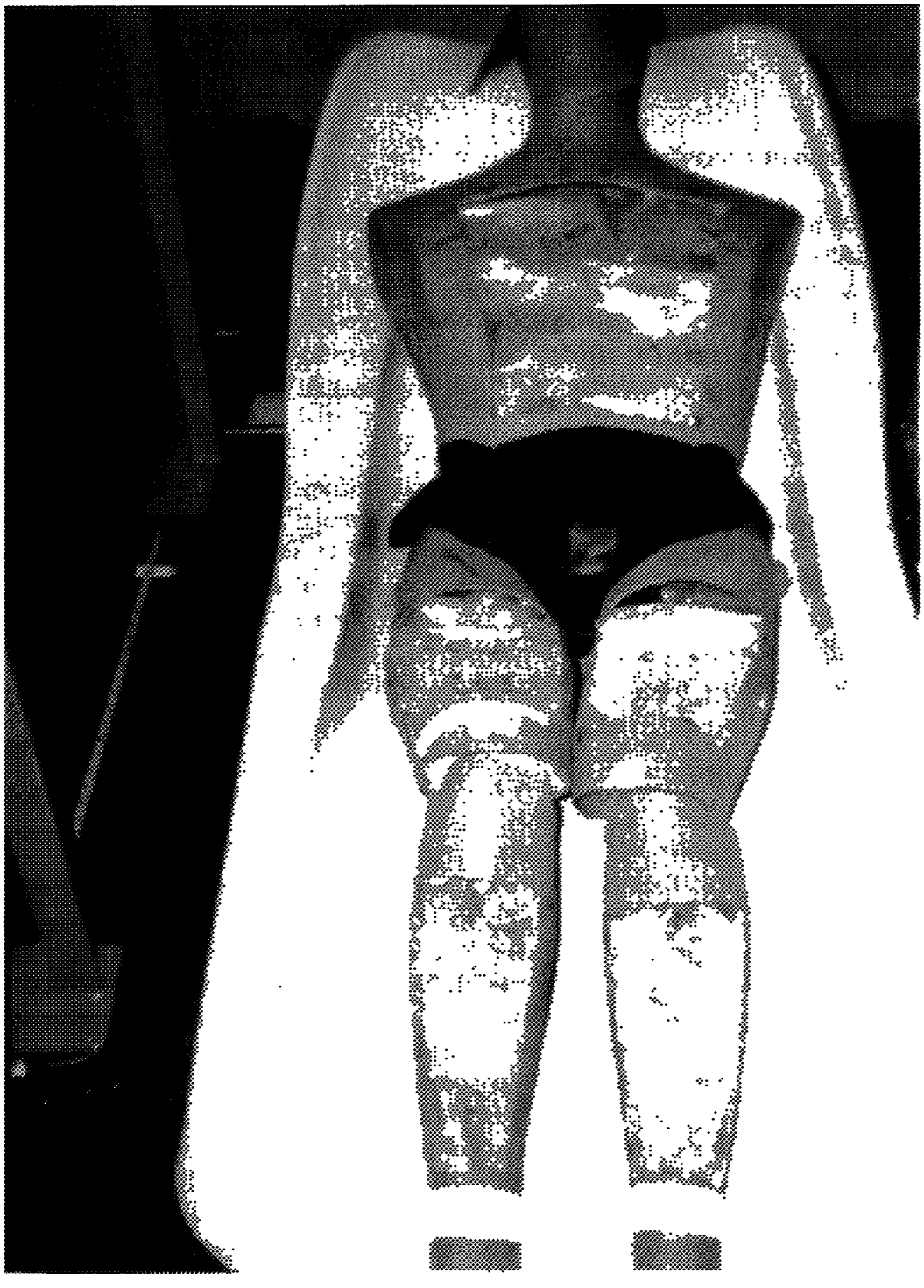

FIG. 3.2. Anthropomorphic phantom used to calibrate the measurement system.

diluted in a 0.1 N nitric acid solution and distributed uniformly within the phantom in 60 polyethylene bags. Each bag contained approximately 0.25 L of the solution. As shown in Fig. 3.2, the bags were placed into an adult-sized phantom, fiberglass mannequin, hollow, thin-walled (3 mm) [3.8]. In order to estimate the background, the same amount of polyethylene bags with 0.1 N nitric acid was put into the phantom. The counting procedures were the same as those applied to the phantom contaminated with ^{137}Cs. The validity of the arc geometry was tested and verified by placing the bags in a smaller, shorter-length phantom. The counting efficiency remained the same, within statistical limits, regardless of the size of

the phantom. Thus, using the arc geometry, the same calibration factor could be used for a contaminated infant or a 2 m adult, since the average distance from the center of the crystal of all points along either the adult or child body was the same [3.7].

3.3.3. Measurement procedures

The same procedures applied to routine *in vivo* measurements were also applied to the accident subjects, i.e., changing clothes, disposable overshoes, measurement of height and weight, and completion of personal data sheets. Subjects were not required to shower immediately before measurement since daily showering was performed as a rule. However, they were routinely monitored for external contamination using a ß counter before whole body counting. In addition, those subjects who had transferable external contamination were decontaminated before counting [3.6].

A high anxiety was observed in the subjects during the measurement procedures. Occasionally, the stress caused claustrophobic reactions which resulted in a delay to start the measurement or a premature end. Efforts were made to minimize these reactions and frequently, a quick talk with the subject was sufficient to reduce this anxiety. Special situations used to occur when children were monitored. In these cases, a staff member stayed in the counting room with the child, during the measurement. Afterwards, a second measurement was done without the child to check any "background".

3.3.4. System relocation

The whole body counter at GGH was in operation from 23 November 1987 until 15 January 1988, when it was then transferred to a house, at the same street where the ^{137}Cs source was opened, 57th Street. This place was chosen for a follow-up programme since all the patients had been released from the hospital and special housing centres and most lived in the neighbourhood. The house was purchased by CNEN and was transformed into a laboratory for whole body measurements, in vitro bioassay and environmental research. In order to keep monitoring the contaminated people, it was necessary to set up a new *in vivo* measurement system in a short time. As the background counting rate at the street was found to be about four times higher than at the GGH, it was necessary to identify the origin of the high background and to adopt a corrective action before further *in vivo* measurements could be made. Some shielding designs were tested, such as using a few millimetres of lead. The problem of excess background was finally solved by shielding the top part of the detector covering. The increased room background was due mainly to ^{137}Cs roof contamination, which was confirmed subsequently by an environmental research team [3.7].

The in vivo measurement system was installed in a 3.45 m wide, 4.30 m long, 2.83 m high room. Fifteen layers of 2.0 × 1.0 m, 2 mm lead sheets, were placed on the floor equidistant from the walls, below the detector. The rest of the floor and walls up to 1 m high were covered with one layer of 2 mm lead sheets. The NaI(Tl) detector, was the same as that used at the GGH. With this new design, the minimum detectable activity (MDA), for the same 2 min of counting, was lower than at the hospital, i.e., 7.3 kBq for ^{137}Cs, which corresponds to approximately 0.18% or 0.12% of the annual limit on intake (ALI) for radiation workers for ingestion or inhalation [3.4], respectively. After establishing the best shielding design, subjects measurements began on 5 February 1988 [3.7].

3.3.5. System optimization for newborn measurements

One of the ^{137}Cs internally contaminated people was a pregnant woman, in her fourth month of pregnancy at the time of the accident (September, 1987). Her child was born in February, 1988. According to Wilson and Spiers [3.9], the ^{137}Cs transfer factor from mother to fetus is equal to 1. This fact justified a careful investigation (the caesium body burden of the mother at her first WBC measurement was 200 kBq). The first infant measurement was made 3 days (d) after birth. To perform this measurement, with this WBC system, a staff member lay in the counting position with the infant held over her body, as shown in Fig. 3.3. The infant ^{137}Cs body burden of 4 kBq was estimated after subtracting the background spectrum of the room. In order to measure the infant alone it was necessary to optimize the *in vivo* measurement system based on the measurement time, the correspondent minimum detectable activity (MDA) and the counting efficiency of the system. It was verified that the measurement system that best fulfilled all the required parameters consisted of setting over the monitoring chair, right below the NaI(Tl) detector, a baby size PVC matrix, as showed in Fig. 3.4. With this measurement geometry the distance detector type "PVC" matrix was 1.98 m. For the calibration of this system, the same procedure as described before was used. A phantom was constructed to simulate the infant body. The minimum detectable activity for a counting time of 60 minutes was 993 Bq with a counting efficiency of 20 ± 3 cpm/kBq.

FIG. 3.3. First infant measurement with the help a staff member.

FIG. 3.4 Optimized geometry for infant measurement.

3.3.6. Operational adjustments

Over a time period of several months, the ^{137}Cs body burden of the subjects decreased, and for some of them the measured activity was close to the minimum detectable activity. Therefore, in May 1988, 8 months after the intake, it was required to change the height of the iron framework from 2.23 m to 1.36 m, maintaining all the other characteristics, as shown in Fig. 3.5. With this configuration the system was calibrated, using the same procedure

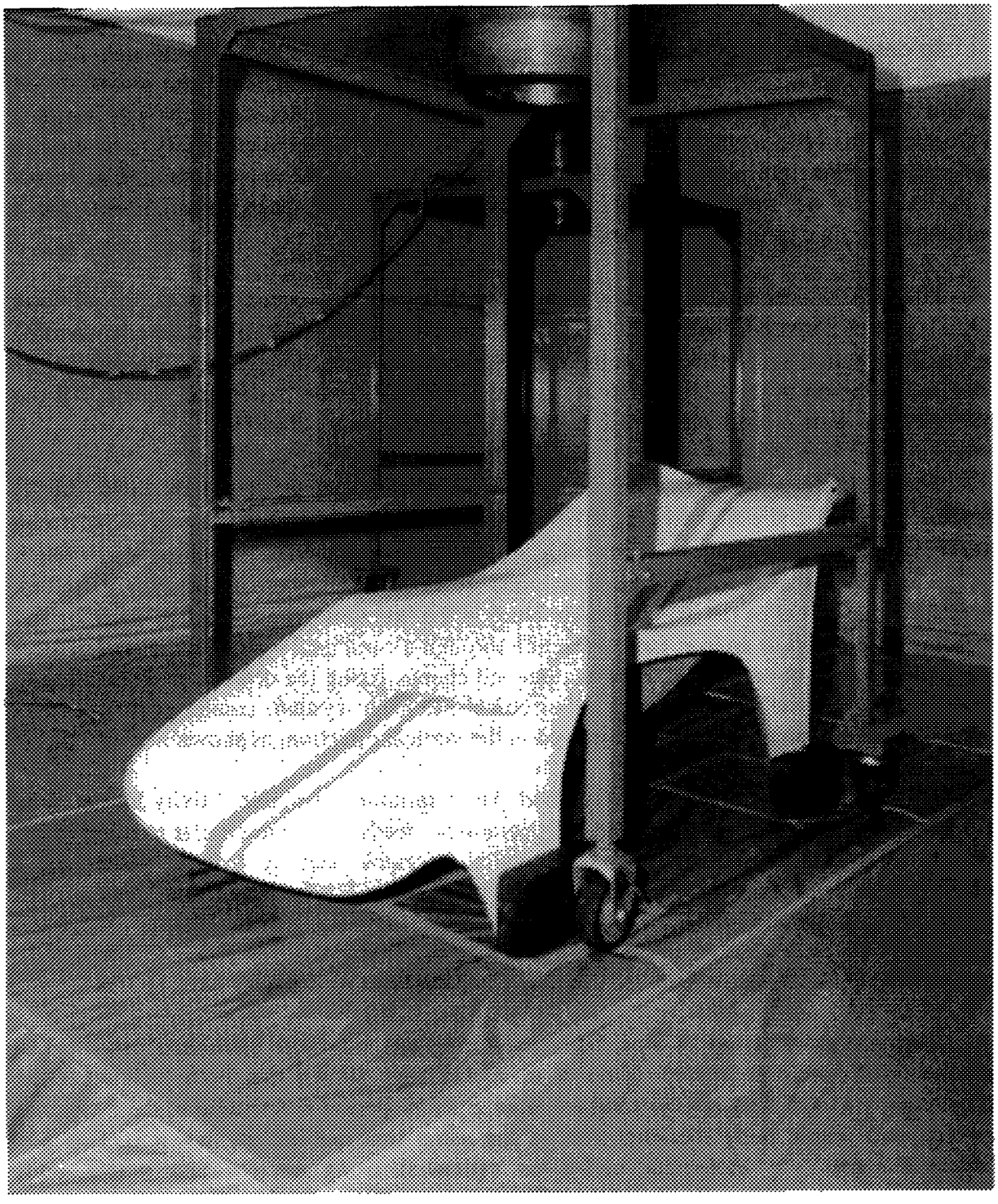

FIG. 3.5. New configuration of the whole body counter system, with the distance detector-chair reduced from 2.23 m to 1.36 m.

described before. The minimum detectable activity was 1.75 kBq for 2 min counting time. In the same way the optimized system for the infant WBC was calibrated. The minimum detectable activity for a counting time of 60 minutes was 260 Bq and the counting efficiency was of 64 ± 10 cpm/kBq. The distance detector type "PVC" matrix was reduced from 1.98 m to 1.31 m.

3.3.7. Implementation of a multiple geometry system for whole-body measurements

In order to maintain the follow up of the internally contaminated subjects and, also, to implement the occupational monitoring of workers from the radioactive waste repository, at the end of July 1991 a multiple geometry system for whole body measurements was installed in Goiânia. This system was the first constructed in the world, with the capability to be used in both accidental or routine situations. With this system it is possible to measure high activities in the body, as occurred in the Goiânia accident, and also to make measurements for a worker's individual monitoring programme.

For the installation of this new system some changes were needed, such as: the addition of ten layers of 2 mm lead sheets, 2.0 m × 1.0 m, placed over on those fifteen already installed on the floor equidistant from the walls, resulting in 5 cm of lead shielding. The rest of the floor and walls up to 2 m high were covered with two layers of 2 mm lead sheets. All the shielded areas were coated with plastic wall panels, for finishing purposes.

The multiple geometry system consists of a 20 cm diameter × 10 cm thick NaI(Tl) detector, shielded and collimated by 10 cm of lead wrapped around the crystal, fixed to an iron framework (2.30 m high × 1.68 m wide × 1.40 m long) supported by ball-bearings which slide over two rails fixed to the floor. These rails are 4 m long and were equidistant of 1.68 m, allowing a movement of the iron frame structure in the horizontal direction. The detector and shielding were fixed to an iron frame structure through a combined system composed of steel cable, fixed to the upper part of the structure, and clamps fixing the detector and shielding to the structures vertical axis. Through an electrical-mechanic system, connected to the steel cable, the detector-shielding could be moved in the vertical direction, as shown in Fig. 3.6.

The system performance was very good. The minimum detectable activity for counting geometries already used, corresponded the operational needs and were similar to other WBC systems [3.10]. Table 3.3 shows the minimum detectable activity (MDA) values for a counting time of 30 min for different counting geometries. For the infant, the detector was positioned as shown in Fig. 3.7.

3.4. COMPARISON BETWEEN IN VIVO AND IN VITRO BIOASSAY METHODS

During a short period of time, both monitoring methods were simultaneously applied and the results were compared. Melo et al. [3.11] have shown that both techniques are compatible, the total ^{137}Cs activity (Bq) excreted in a time period was similar to the difference between two whole body measurements at the same time period, as shown in Fig. 3.8. Table 3.4 shows the biological half-times estimated using excreta and whole body measurements data, during the period that patients were submitted to PB treatment.

TABLE 3.3. MINIMUM DETECTABLE ACTIVITY (MDA) FOR 30 min OF COUNTING TIME, FOR DIFFERENT GEOMETRIES

Counting geometry	$MDA_{30\ min}$ (Bq)
Baby [a]	31
Adult (70 cm)[b]	218
Adult (80 cm)[c]	302

[a] calibration with baby-sized phantom, with detector positioned 40 cm from the chair.
[b] calibration with adult-sized phantom, with detector positioned 70 cm from the chair.
[c] calibration with adult-sized phantom, with detector positioned 80 cm from the chair.

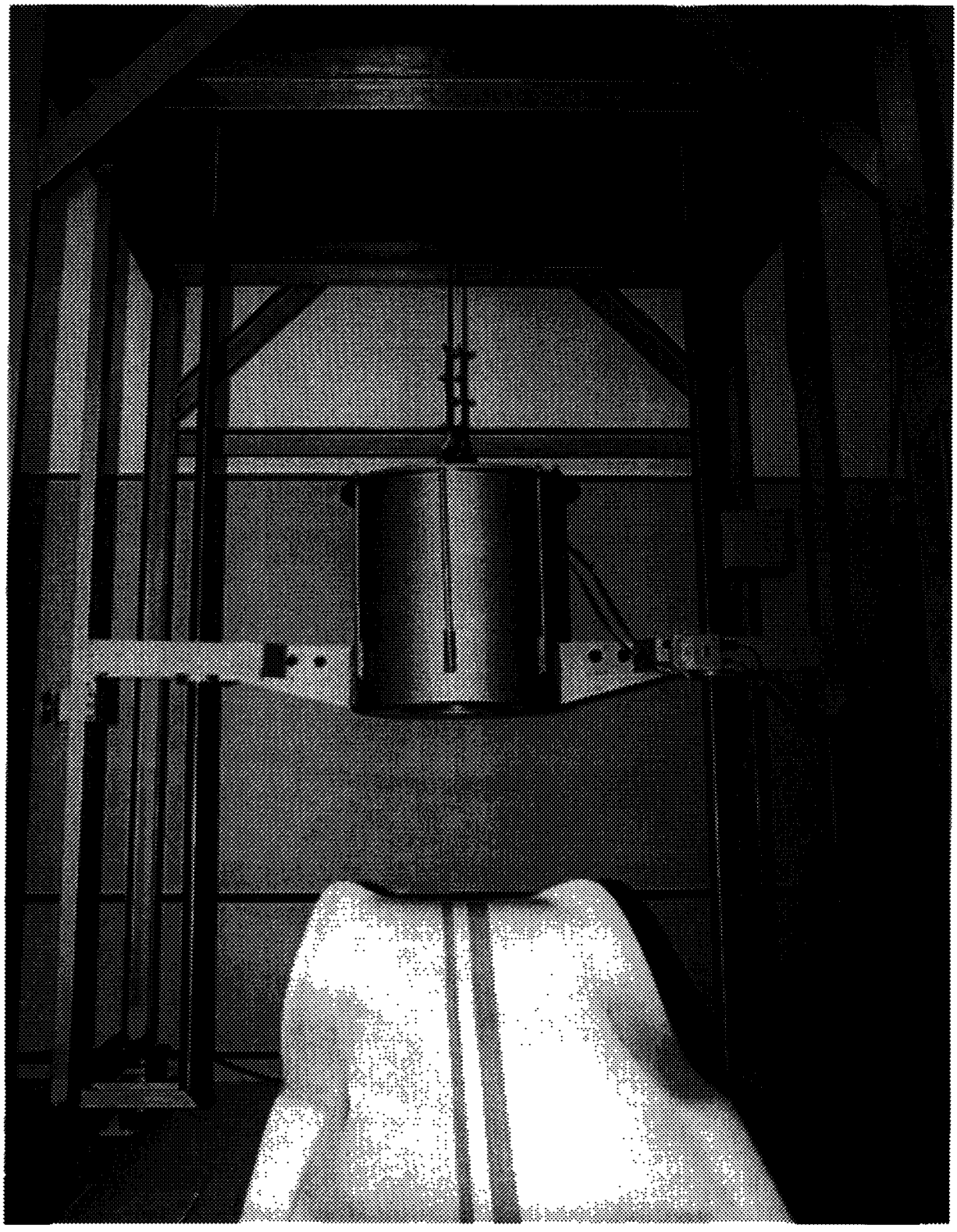

FIG. 3.6. Multiple geometry system implemented for whole body measurements.

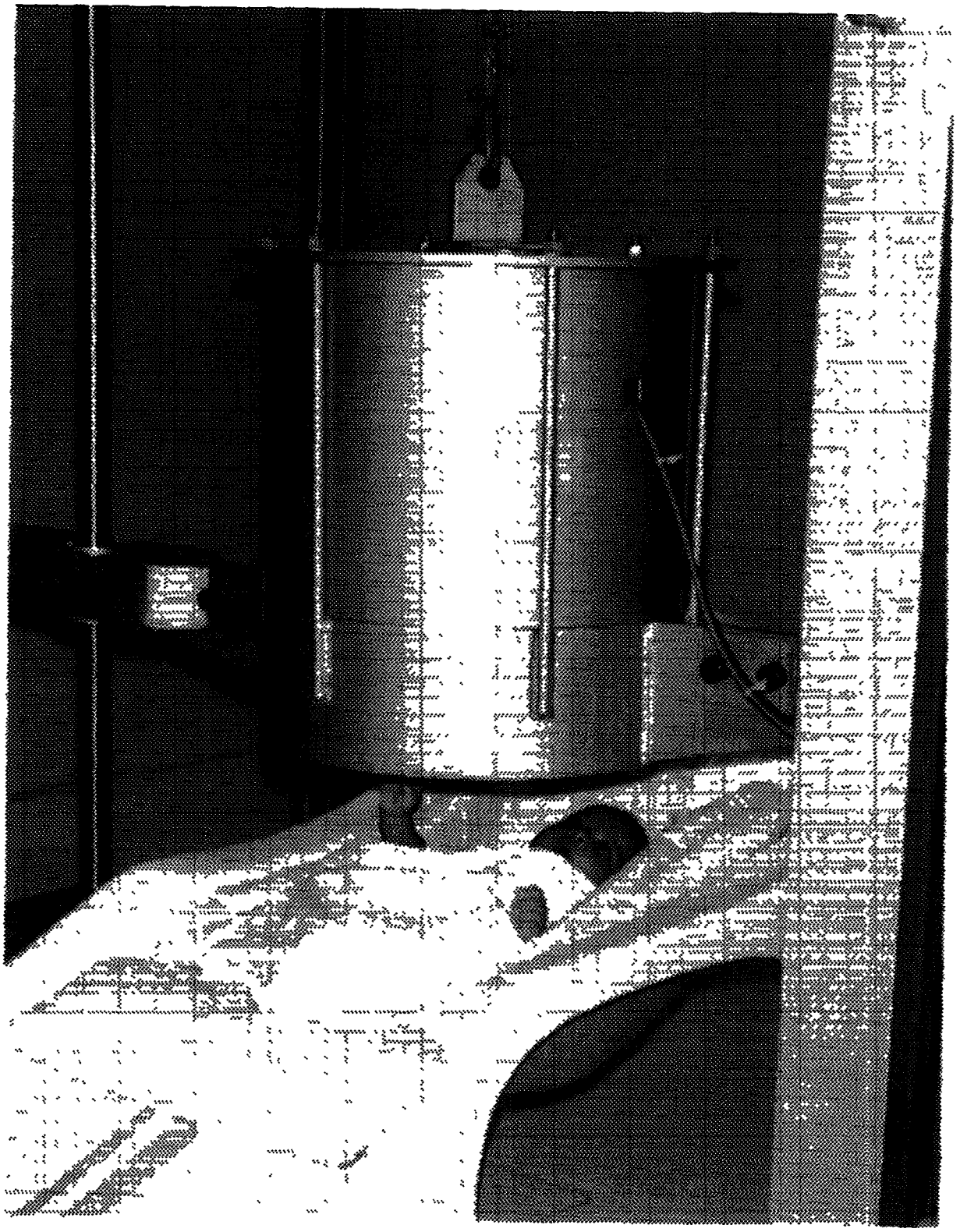

FIG. 3.7. Geometry for infant measurement using the multiple geometry system.

TABLE 3.4. ^{137}CS BIOLOGICAL HALF-TIMES ESTIMATED THROUGH IN VIVO AND IN VITRO MEASUREMENTS RESULTS

Subject	PB dosage (g d^{-1})	$T_{1/2}$ (d)[a] in vivo	Period of[b] time (d)	$T_{1/2}$ (d)[a] in vitro	Period of[b] time (d)
LCNF	10	26	47–86	24	26–84
RSA	10	18	60–76	17	63–73
IAF	10	27	52–83	25	53–82
PNF	3	23	48–112	25	53–103
TNF	0	21	47–83	22	12–89

[a] ^{137}Cs biological half-times in days.
[b] days after intake.

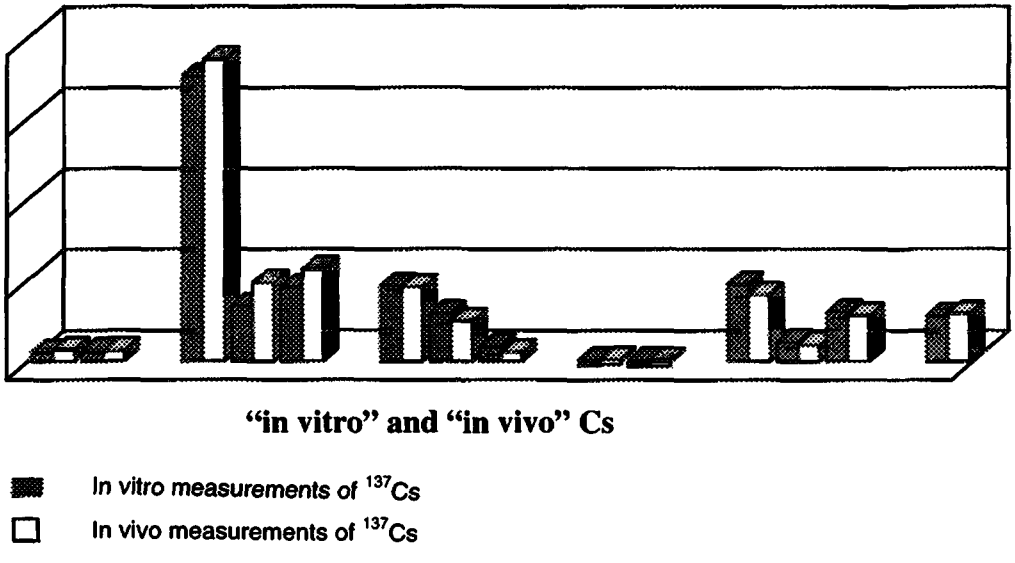

FIG. 3.8. Comparison of the reduction of ^{137}Cs body burden and total ^{137}Cs excreted at the same period of time.

3.5. SIMPLIFIED METHOD TO ESTIMATE ACTIVITY OF INCORPORATED ^{137}Cs [3.11]

To quickly estimate the activity of incorporated ^{137}Cs, a method was developed based on the relationship between the dose rate at the body surface measured by portable radiation detectors and the ^{137}Cs body burden measured by whole body counting techniques using data of 3 adolescents and 8 adults with high levels of ^{137}Cs contamination [3.11].

Persons with the highest ^{137}Cs internal contamination also had external contamination, mainly on their hands and feet. The contamination survey began with gamma dose rate measurements made by portable Geiger–Müller (GM) detectors to identify any highly contaminated areas. Maximum gamma dose rates of 5 $mSv \cdot h^{-1}$ were found on the hands of one patient. The main difficulty in monitoring for body surface contamination was the interference caused by the gamma radiation coming from the incorporated ^{137}Cs. External decontamination procedures were used to reduce the skin contamination levels. This monitoring continued during the complete period of hospitalization, even when whole body counting was operating and the external contamination was very reduced or measurable. Measurements in 26 points on the patient's body surface were made with a GM detector. After the end of the emergency phase, the dose rate and the whole body counting data of 3 adolescents and 8 adults, were analysed. The axillas and body burden data provided the best fit and a linear relationship of ^{137}Cs body burden and dose rate was found, for patients of the same age range. The possible reasons for axillas being a good reference point for measurement are: the axilla has a constant measurement geometry of measurement and, there is reduced interference from surface contamination, as this area is and, there is reduced interference from surface contamination, as this area is not usually contaminated externally. For adolescents (from 13 to 15 years old and average body weight of 41 kg) and for adults (from 20 to 60 years old and average body weight of 66 kg) the relationships found by Hunt and Oliveira [3.12] are:

^{137}Cs body burden:

- Adolescents: (correlation coefficient = 0.95)
  $(MBq) = 0.30 \times axillas.dose.rate \sim (\mu Sv \cdot h^{-1})$

- Adults: (correlation coefficient = 0.92)
  $(MBq) = 0.37 \times axillas.dose.rate \sim (\mu Sv \cdot h^{-1})$.

As the detection limit for ordinary GM detectors is around 1 $\mu Sv \cdot h^{-1}$, the detection limit for incorporated ^{137}Cs using this method lies at around 0.30 MBq for adolescents and 0.37 MBq for adults.

The strong correlation between ^{137}Cs body burden, obtained through whole body measurements, and dose rate in the axillas region, obtained through Geiger–Müller detector measurements, indicates that measurements using Geiger–Müller detector can be used as a rapid screening method for high level of internal contamination. This technique can be very helpful for decision making in the emergency situations, since it is very important to have an available technique to quickly estimate the internal contamination. A monitoring routine should be started as soon as possible, and also, ideally, the same equipment should be used throughout.

3.6. IN VIVO MEASUREMENTS FOR SPECIFIC REGIONS OF THE BODY [3.12]

The fact that radiation was not detected did not mean that the wounds were free of contamination. Some results could may have indicated absence of contamination due to the low sensitivity of the detectors used (portable Geiger–Müller and scintillation detectors) in the early measurement phase, or as a consequence of caesium migration from the surface to deeper sites in the skin.

To verify this hypothesis, measurements to permit the observation of the k_α and k_β X ray spectrum, characteristic from ^{137m}Ba from the decay of ^{137}Cs. The ratio k_α/k_β gives information, in terms of depth of the ^{137}Cs detected. Therefore, in order to make possible the determination of the remaining ^{137}Cs, local and generalized, in the body, a new detection system had to be designed and built.

The detection system developed [3.13] to perform *in vivo* measurements of specific regions of the body aiming to determine the Cs activity remaining in the scar tissues consisted of a high purity germanium detector (HPGe), type N, collimated with a 10 cm (wide) × 0.5 mm (thick) layer of copper; the detector was mounted on a steel rack 200 cm long, 80 cm wide and 190 cm high, designed and constructed specially for this specific monitoring. The structure contained a support also made of steel which could be positioned in different locations and allowed horizontal and vertical movement, as shown in Fig. 3.9. The calibration of the system was performed using a 39.33 kBq point source of ^{137}Cs, obtained from Isotope Products Laboratories. The source was positioned under the detector, at 1 cm below the center and counted for 5 minutes.

Ten subjects that still had some incorporated ^{137}Cs contamination, 3 years after intake were identified measured with the HPGe system. The evaluation of the measurements performed with the HPGe detector as based on the detection of the K_α and K_β X rays of ^{137m}Ba (32.07 and 36.68 keV, respectively). The ratio K_α and K_β was used to qualitatively compare the depth of the location of caesium contamination in different subjects. Depending on the scar caused by the radiation burns and on the activity remaining, this measurement took from 4 to 8 hours.

3.6.1. In vivo measurements in the scar tissues

Two people (DAF and IAF) still had significant levels of activity in the scarred skin tissues. DAF had a scar on the inside surface of his right leg, near the knee. A slight increased counting rate in the right knee when compared to the left knee. However, these results could not be used to determine the depth of the contamination in the wound sites, since the activities were close to the minimum detectable activity for the k_α and k_β X rays. IAF (who had had repair surgery) had a scar on his right thigh resulting from a severe burn.. A significant level of activity was found in this location when compared to the normal tissue. The long biological half-time in scar tissue implies a larger radiation dose delivered to the surrounding healthy tissues. It was not found any significant activity over the scar tissues of other 8 selected subjects.

3.6.2. In vivo measurements of ^{137}Cs distribution in the body in a long period after intake

Measurements to obtain information on the distribution of the caesium in the body after ingestion, were also performed, using the HPGe detection system described above. A woman (LOMS), who had a very high internal contamination (calculated intake of 300 MBq) showed a higher concentration over the liver than in other regions of the body. The X ray counting rates showed an apparently higher concentration of ^{137}Cs in the right kidney in relation to the left kidney. The authors concluded that this result is probably due to the influence of the high caesium activity in the liver, since the right liver and the right kidney are located in the same region of the body as seen by an external detector. These results are in agreement with those found by Rosoff et al. [3.14] that found an elevated/increased ^{137}Cs concentration in liver in a

FIG. 3.9. Detection system used to perform in vivo measurements in specific areas of the body.

study involving the distribution of caesium post mortem in several organs and tissues of human body. Melo et al. [3.15] also observed a high concentration of caesium in skeletal muscle tissue, liver, spleen and kidney of beagle dogs. Among those 10 selected subjects, four of them had a high counting rate over the region of liver. The authors concluded that the distribution of ^{137}Cs in the body may not always be considered homogeneous in a certain time after intake.

3.7. CONCLUSIONS

By using in vitro bioassay in a flexible and developing mode it was possible to estimate the amount of incorporated radionuclides during different phases after the accident thus enabling studies of the caesium metabolism, the effectiveness of decorporation therapies and medical treatments.

In vitro bioassay method for monitoring of internal contamination in emergency situation has been shown to be appropriate for screening individuals with internal contamination, useful for qualitative information on PB action through feces to urine ratio analysis and also useful for quantitative information on ^{137}Cs elimination from the body, since the biological half-times estimated using *in vitro* bioassay results were similar to those estimated through *in vivo* results. However, a large number of samples were needed for quantitative information due to high fluctuation of data and also sampling had to be done with care to avoid external contamination and mislabeling of samples.

In vivo bioassay method for monitoring of internal contamination in emergency situation, has shown that the improvised whole body counter proved to be appropriate for monitoring very high levels of internal contamination. Multiple geometry system has shown adequate for measuring high and low levels of ^{137}Cs internal contamination, either for children or for adults. Monitoring with Geiger–Müller detector may be used as a rapid screening method for detecting very high internal contamination level.

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4. CAESIUM BIOKINETIC MODEL

4.1. INTRODUCTION

Caesium belongs to the Group I alkali metal series, which includes, in order lithium, sodium, potassium, rubidium, caesium and francium. Relman [4.1] has shown evidence of the close similarity of the physiology of rubidium and caesium to that of potassium. However, significant quantitative differences have been noted between the physiological behavior of these ions. Potassium traverses cell membranes more rapidly than caesium, with greater differences occurring for passive transport than for active transport and for rapidly exchanging tissues than for slowly exchanging tissues (predominantly skeletal muscle). Beaugé and Sjodin [4.2] have observed that for the alkali metals, the rate of transfer across cell membranes will determine their equilibrium concentration in the intracellular fluids. These authors have also suggested that potassium in the extracellular fluid inhibits the entry of caesium ions into muscle cells presumably by competing for transport sites. Caesium ions are transported into muscle cells by a system of sites or carriers that requires a source of metabolic energy (i.e. Na^+-K^+-ATPase) for ion turnover to occur. However, caesium efflux from the intracellular compartment appears to occur by a process not mediated by metabolism. It probably depends on the permeability of the cell membrane, which is lower for caesium compared to potassium. Therefore caesium is more strongly retained in the cell.

Caesium that enters in the body by ingestion is rapidly absorbed via the gastrointestinal tract. Moore and Comar [4.3] have observed in an experiment with rats, that 98.2% of the total amount of ingested caesium is absorbed at the end of one hour. Similarly, because caesium compounds are soluble, significant absorption of inhaled caesium to body fluids is expected. Once in the blood, caesium is taken up by tissues not from the plasma directly but from the extracellular fluid surrounding the cells of the tissues. The equilibration with the extracellular space must be extremely rapid [4.4].

^{137}Cs retention in the body has been described by different retention models. In these models, ^{137}Cs retention is assumed to be influenced by many factors such as age, gender, body weight, concentration of aldosterone and others. Variabilities of caesium retention in the human body as a function of age have been reported by Bengtsson et al. [4.5] and McCraw [4.6]. Leggett [4.7] analysing data reported by Lloyd et al. [4.8] suggested a dependence of the caesium content on the total body potassium content. Rundo and Turner [4.9] have suggested that ^{137}Cs retention is controlled by the secretion rate of aldosterone. These authors have also suggested, without direct evidence, that the biological half-times show cyclic changes associated with menstruation, decreasing at ovulation, then increasing at the onset of menses. The retention of caesium in the body has been shown to be associated to the body mass by Eberhardt [4.10], Cryer and Baverstock [4.11], Baverstock [4.12] and Melo et al. [4.13].

Retention of caesium in the body $R(t)$ has been described by a sum of two exponential components, as shown in Eq. 4.1 [4.7, 14 and 15].

$$R(t) = a_1 e^{-\frac{0.693t}{T_1}} + a_2 e^{-\frac{0.693t}{T_2}} \qquad (4.1)$$

where: $a_2 = (1-a_1)$, a_1 and a_2 = fractions of the initial activity distributed between tissue compartments, and T_1 and T_2 = biological half-times of ^{137}Cs in the two tissue compartments.

4.2. CAESIUM BIOKINETIC MODEL [4.13]

As described in Chapter 2, the people involved in the Goiânia accident had their skin contaminated with caesium, and the main pathway of intake of the was ingestion, from eating with dirty hands and from contaminated utensils. According to the literature, CsCl is taken up rapidly and completely from the gastrointestinal tract to blood [4.3, 4.16].

People from Goiânia were monitored for caesium incorporation through excreta analysis and whole body measurements, as described in Chapter 3. The frequency of monitoring was dependent on the caesium body burden. The most contaminated individuals collected excreta samples every day, and when in vivo monitoring was started they were measured in the whole body counter once a week. Those that presented less contamination, had fewer excreta samples collected and the whole body monitoring only every two weeks.

Data from 17 children (10 girls and 7 boys 1–10 years old), 10 adolescents (4 female and 6 male) and 30 adults (15 female and 15 male) contaminated in the accident were used to formulate the caesium biokinetic model. Since the accident was notified to the competent authorities only two weeks after the source was breached and people got contaminated, the information on the short term component of the caesium retention was lost. Thus, a study on the metabolism of ^{137}Cs in beagle dogs was conducted to complement the Goiânia accident results.The experiment with beagle dogs is described in detail by Melo et al. [4.13]. Ten male dogs aged 3.0 months, 4.4 months, 7.1 months, 2.5 years and 13.5 years, received approximately 44 kBq of ^{137}Cs, in a single injection in 5 mL of sterile physiological saline, given via cephalic vein. The dogs were maintained in metabolic cages for 42 d, and water was available ad libitum. Whole body measurements were performed twice a week to determine the retention kinetics of ^{137}Cs. All excreta from the dogs were collected daily and measured for ^{137}Cs activity. At the end of the experiment, at 42 d after the injection, the dogs were sacrificed, and organs and tissues were analysed for ^{137}Cs content.

The data from the study on dogs [4.8] together with additional data from Lloyd et al. [4.8] were used to derive the short term component of the ^{137}Cs retention. Lloyd et al. [4.8] present the only data in the literature that refer to ^{137}Cs kinetics after a controlled single intake of ^{137}Cs by individuals of different ages. These complementary data were also used to reinforce the long term component of the retention function derived from the Goiânia results. It was shown that first-order kinetic equations are appropriate to mathematically describe whole body retention of ^{137}Cs, *R(t)*. In addition, data from individuals who had very high internal contamination indicates that a small fraction of ^{137}Cs is retained in the body with a very long half-time. Thus, ^{137}Cs retention *R(t)* is described by the sum of three exponential terms:

$$R(t) = a_1 e^{-\frac{0.693t}{T_1}} + a_2 e^{-\frac{0.693t}{T_2}} + a_3 e^{-\frac{0.693t}{T_2}} \qquad (4.2)$$

where a_1, a_2, and a_3 are the fractions of the initial activity in body compartments with respective biological half-times T_1, T_2, and T_3 , and $a_1 + a_2 + a_3 = 1$.

4.2.1. First term of the retention equation

The first term of the retention equation (Eq. 4.2) represents the clearance of ^{137}Cs from plasma, extracellular fluids and organs with a fast turnover rate to urine in the first hours after

intake. The parameters of this term were derived from the dog experiment [4.13] and data from Ref. [4.8].

The Spearman non-parametric statistical test [4.17–4.18] was applied using the dog data to evaluate the correlation between a_1 and T_1 and the biological parameters of age, body weight, skeletal muscle weight and potassium body burden. There was no significant correlation between the short term half-time (T_1) and any biological parameter tested. Skeletal muscle weight and body weight were the variables that presented significant partial correlations with the a_1 parameter ($p < 0.05$); a_1 showed negative correlations. As skeletal muscle weight is a difficult parameter to measure, and as the correlation coefficient for skeletal muscle and for the body weight were similar, a_1 was assumed well described as a function of body weight, in the regression model. For the dogs, the range of a_1 values was 0.18–0.33. For younger dogs weighing between 5 and 7.5 kg, a_1 ranged from 0.19–0.33, with an average value of 0.27, while for the older dogs, weighing between 8.4 and 12.8 kg, a_1 varied from 0.18–0.23, with an average value of 0.20.

The study by Lloyd et al. [4.8] showed that for children and adolescents, weighing between 18 and 50 kg, a_1 ranged from 0.20–0.28 with an average value of 0.23, while for adults, weighing 60 and 80 kg, a_1 ranged from 0.08–0.16, with an average value of 0.15. The range of a_1 values was thus relatively small and the younger individuals had a higher short-term retention fraction than the adults, similar to the results obtained from the dog experiment. Based on these results, it was suggested that a_1 values should range between 0.2 and 0.3 (central value = 0.25) for children and adolescent and between 0.1 and 0.2 (central value of 0.15) for adults, Table 4.1.

Similar to the dog results, individual data points, described by Lloyd et al. [4.8] also showed no significant statistical correlation ($p < 0.05$) between T_1 and the biological parameters of age, body weight and sex. The range of T_1 values was 0.9–5.4 d (average value equal to 3.0 d) while for dogs, the range of T_1 values was 1.4–3.0 d (average value equal to 2.4 d). Based on these results, the suggested value for T_1 in the model is 3.0 d, in a range between 1 and 5 d, for all age groups, Table 4.1.

TABLE 4.1. PARAMETERS OF THE ^{137}CS RETENTION FROM EQUATION (4.4) [4.13]

Age	Range of body weight (kg)	Parameters of the ^{137}Cs retention equations					
		a_1	T_1 (days)	a_2	T_2 (days)	a_3	T_3 (days)
0–16 years	3–6	0.25	3	0.75	13	–[a]	–
	7–10	0.25	3	0.75	19	–	–
	11–15	0.25	3	0.75	25	–	–
	16–30	0.25	3	0.75	37	–	–
	31–40	0.25	3	0.75	49	–	–
	41–50	0.25	3	0.75	57	0.001	500
	51–60	0.25	3	0.75	65	0.001	500
	61–70	0.25	3	0.75	72	0.001	500
Adult female		0.15	3	0.85	65	0.001	500
Adult male		0.15	3	0.85	90	0.001	500

[a] Data not available.

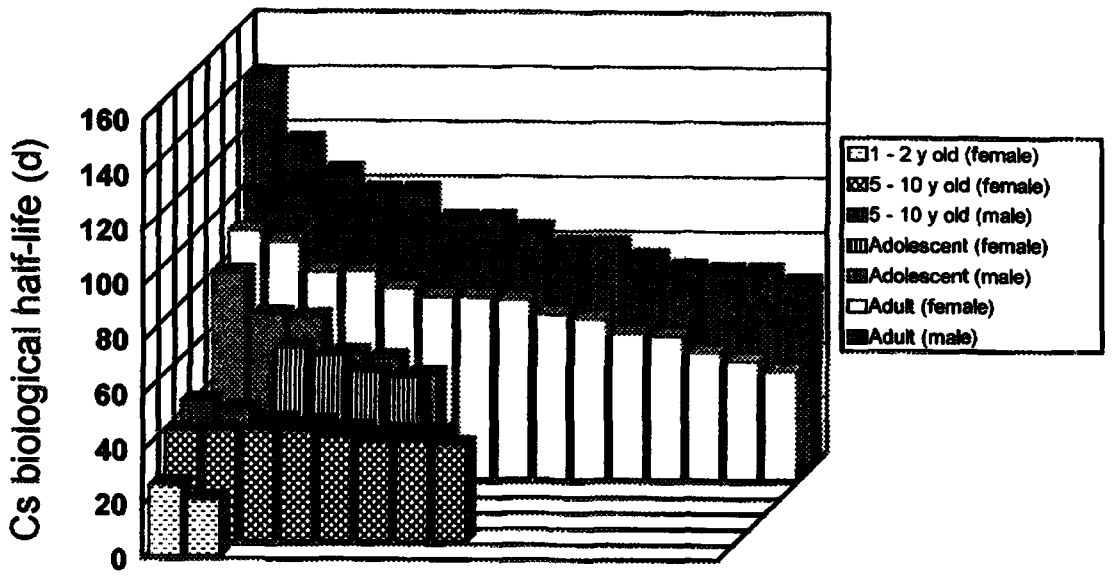

FIG. 4.1. Biological half-times of ^{137}Cs in seven different groups related to the 2nd phase of the retention equation: 1–2 years old, 5–10 years old, adolescent, adult female, adult male.

4.2.2. Second term of the retention equation

Melo et al. [4.13] found a significative positive correlation between a_2 and body weight ($p < 0.05$), as a result of the application of the Spearman non parametric statistical test [4.17–4.18] to the data from the dog experiment as well as to the data reported by Lloyd et al. [4.8].

Results from studies of people contaminated in the Goiânia accident and from the experiment with beagle dogs have both shown a significant difference in the biological half-times for different age groups, as shown in Fig. 4.1. In order to determine which biological parameter, age, body weight, height and sex, should be included in the regression model for T_2, stepwise partial correlation methods were used [4.17–4.18]. Table 4.2 shows the correlation coefficients for the different analyses performed. When all subjects were analysed together significant correlations of T_2 with age, body weight, height and sex, were observed but body weight was the only variable included in the regression model ($p < 0.05$), since the partial correlation with all other variables were not significant after inclusion of body weight into the model. The set of data from the children and the adolescents were analysed separately, and the half-times were shown to be correlated with all biological parameters, except sex. Body weight was the only variable included in the regression model ($p < 0.05$), since, after its inclusion, partial correlation with all other variables were not significant. Data from the biological half-times in adults were correlated to sex, body weight and height, but sex was the only variable included in the regression model ($p < 0.05$), since body weight and height did not present significant partial correlations after inclusion of sex into the model. When data for adult females and adult males were analysed separately, there was no significative correlation between biological half-times and biological parameter ($p < 0.05$).

As a conclusion to this analysis, the second-term biological half-time T_2 is well described as a function of body weight, during the growing phase, until adulthood is reached ($p < 0.05$). Data from adults showed a significant difference in biological half-times between the adult male and the female ($p < 0.05$). This significant difference which was not observed

for children and adolescents may be explained by the fact that men have more skeletal muscle tissue than women. Statistical analysis suggests that T_2 is a step function of body weight. Five different groups were identified, as shown in Fig. 4.1, children from 1 to 2 years old (weighing 10 and 14 kg), children from 5 to 10 years old (weighing 13 and 31 kg), adolescents (weighing 31 and 69 kg), adult females (weighing 39 and 85 kg) and adult males (weighing 50 and 80 kg).

The Spearman non-parametric statistical test [4.17–4.18] was applied to the beagle dog data, to determine the correlation between T_2 and the biological parameters of age, body weight, skeletal muscle tissue weight and total body potassium content. There were significant correlations between the second-term biological half-times and body weight (0.929), age (0.927), skeletal muscle weight (0.905) and potassium content (0.851). However, body weight was the only variable that presented a significant partial correlation with T_2. The strong correlation between T_2 and body weight is explained by the strong correlation between body weight and skeletal muscle weight, by the predominance of active transport in the cells of this tissue and by the fact that muscle tissue is a slowly exchanging tissue. According to the experiment made by Melo et al. [4.13] in dogs, skeletal muscle is the tissue with the highest caesium concentration.

Eberhardt [4.10] used the logarithmic relationship for allometric functions of body mass of mammals (Eq. 4.3), reported by Stahl [4.19] and Lindstedt and Calder [4.20] to describe the ^{137}Cs biological half-time as a function of body weight:

$$y = aW^b \tag{4.3}$$

where y is physiological and morphological variables, W is the body mass and a and b are numerical coefficients.

The second-term biological half-times (T_2) obtained from the Goiânia data and from the study in dogs were shown to follow a similar relationship. As the correlation between the biological half-time and body weight is stronger for children and adolescent than for adults ($p < 0.05$), the average values of body weights and biological half-times for children and adolescents, grouped in intervals of body weight, were used to derive Eq. (4.4). The intervals of body weight chosen were 10–15 kg, 16–30 kg, 31–40 kg, 41–50 kg, 51–60 kg, and 61–70 kg. The Goiânia data indicated that for the weight range of 16–30 kg, for children 5 to 10 years old, the caesium retention is independent of age, body weight, and height. Thus, a constant half-time for this wide weight range was suggested.

$$T_2 = 4.9W^{0.643}\left(r^2 = 0.99\right) \tag{4.4}$$

$$T_2 = 4.6W^{0.711}\left(r^2 = 0.92\right) \tag{4.5}$$

Using the values of T_2 obtained from the experiment with the dogs, Eq. (3.5) was derived where T_2 is the second-term biological half-time (d) and W is the body weight (kg).

The similarity between the Eqs (4.4) and (4.5) established the link between ^{137}Cs retention in animals and in humans. Based on Eq. (4.4), the values of the second-term biological half-times for children and adolescents were calculated and are shown in Table 4.1.

TABLE 4.2. CORRELATION COEFFICIENTS BETWEEN T_2 AND BIOLOGICAL PARAMETERS, OBTAINED THROUGH A MULTIPLE REGRESSION ANALYSIS TEST [4.16–4.17]

Biological parameters	Correlation coefficients between T_2 and biological parameters				
	All subjects (n=57)	Infant to 16 years old (n=27)	adults (both sexes) (n=30)	Women (n=15)	Men (n=15)
Age	0.484 (p <0.001)	0.849 (p <0.001)	–0.233 (p=0.107)	0.176 (p=0.265)	–0.213 (p=0.223)
Body weight	0.773 (p <0.001)	0.906 (p <0.001)	0.381 (p=0.019)	0.339 (p=0.108)	0.352 (p=0.099)
Height	0.758 (p <0.001)	0.851 (p <0.001)	0.598 (p <0.001)	0.266 (p=0.169)	0.351 (p=0.100)
Sex	0.369 (p=0.002)	0.286 (p=0.074)	0.603 (p <0.001)	–	–
Significance	p < 0.001	p <0.001	p <0.002	p >0.566	p >0.201

These results show a good agreement with data from the literature. Schwarz and Dunning [4.21] observed a strong correlation between biological half-time (T_2) and body weight for children and adolescents. Rundo [4.22] observed an increase in the biological half-time with age during the growing phase until adulthood is reached and also that in adults the concentration of ^{137}Cs in males is roughly 1.5 times that in females.This difference between the sexes is much less marked in children. Tracy et al. [4.23] have shown that for children from Belarus, aged 8 to 12 years old, the biological half-times for ^{137}Cs did not depend on weight, age and sex.

The biological half-time for adults contaminated in the Goiânia is significantly correlated with gender ($p < 0.05$). Thus, in a model that estimates T_2 as a function of weight, the only possible model for adults is a step function in which the female is at a lower level than male. Applying Eq. (4.4) to average values of body weight from the Goiânia males and females, T_2 is found equal to 63 ± 4 d for women and 89 ± 5 d for males. For the adult male, the average value of the biological half-time was 89 ± 21 d (ranging from 66–141 d). These values are in agreement with ICRP [4.14–15] which suggest a range of 50–150 d. Rundo [4.22], Lloyd et al. [4.8], and Baverstock [4.12] have published values between 50–150 d. Henrichs et al. [4.24] observed an average value equal to 120 d (ranging from 70–210 d) for five males who consumed a meal of venison contaminated with ^{137}Cs. Schwarz and Dunning [4.21] found an average value equal to 96 d for adult males (ranging from 47–152 d), but did not find a significant statistical correlation ($p < 0.05$) between biological half-times and body weight.

For the adult females, the average value of the biological half-times for ^{137}Cs was 63 ± 15 d (ranging from 39–90 d). Henricks et al. [4.24] found an average value equal to 60 d (ranging from 48–86 d). Schwarz and Dunning [4.21] reported an average value equal to 65 d (ranging from 30–141 d), but did not find a significant statistical correlation ($p < 0.05$) between biological half-time and body weight. Clemente et al. [4.25] and Miltenberger et al. [4.26] have found a shorter biological half-time (T_2) for the adult females compared to adult males. Hormones may have contributed to the smaller caesium retention in females. An other explanation for the higher caesium retention in adult males compared to females is the larger male skeletal muscle tissue, which is the tissue responsible for the caesium retention.

During the Goiânia accident a pregnant woman was contaminated. The infant was born with a measurable ^{137}Cs body burden. The half-time for the infant from age 2 to 6 months, with weight variation from 7 to 10 kg was estimated in the range of 15 to 20 d [4.27], which is in agreement with the suggested model.

4.2.3. Third term of the retention equation

Four years after the Goiânia accident, four of the individuals involved still had measurable ^{137}Cs activities in their bodies. This group is formed by one adolescent 13.5 years old, one woman 29 years old and two men 28 and 43 years old, the ages related to the time of the accident. These results indicate that there is a third term in the retention equation for ^{137}Cs, with a very long half-time. The values estimated for this long biological half-time were 408 d for the adolescent, 467 d for the woman, 568 d for one of the men, and close to 500 d for the other man. The retention fraction (a_3) for this third term is not greater than 0.1% of the initial caesium activity in the body. For the adolescent it was possible to identify two other half-times 43 d and 78 d. The change in half-times from 43 to 78 d, may be attributed to the growth of the adolescent, whose weight increased from 38 to 45 kg.

The third component of the retention equation with a longer biological half-time, was reported in the literature for the first time by Melo et al. [4.13] assuming a biological half-time value (T_3) equal to 500 d and a retention fraction (a_3) equal to 0.1% of the initial body burden, Table 4.1. The long residence of ^{137}Cs is suggested by the authors to be due to the skeletal muscle tissue retention. Stather [4.4] has reported that in some tissues, for example the muscle, there is a slow exchanging intracellular component which equilibrates slowly with the medium in the extracellular space. Stather also demonstrated that a number of tissues accumulate ^{137}Cs to a greater extent than ^{39}K, and that the subcellular distribution model for potassium and ^{137}Cs in the kidneys, the liver, and the muscle are remarkably comparable. These results indicate that the greater proportion of intracellular ^{137}Cs is in the soluble fraction. Once inside the cell, it behaves very similarly to ^{39}K, so that it is only a differential effect of the cell wall that causes the observed difference in the behaviour. The authors [4.13] concluded that the soluble fraction in the intracellular space is probably responsible for the second component of the retention equation, and the subcellular fraction is probably responsible for the third component.

4.3. CONCLUSION

A set of data from 57 healthy persons contaminated in the Goiânia accident with ages varying from 1 to 73 years old and from an infant born with internal ^{137}Cs contamination were used to study the caesium retention in the body and its relation to the variables age, gender, body weight and height. A mathematical model for ^{137}Cs retention, consisting of a sum of three exponential terms was suggested, based on the data from the individuals contaminated in Goiânia, complemented by results from an experiment with beagle dogs and by data reported by Lloyd et al. [4.8]. The first component of the equation mainly represents the elimination in urine of the ^{137}Cs accumulated by the kidney within a few hours of its entry into blood. The second component of retention mainly reflects the progressive loss in the urine and feces of caesium retained in tissues. The third component reflects the retention in the subcellular fraction in the skeletal muscle tissue. The caesium biokinetic model is depicted in Fig. 4.2, and the parameters of the retention equation for each weight group are shown in Table 4.1.

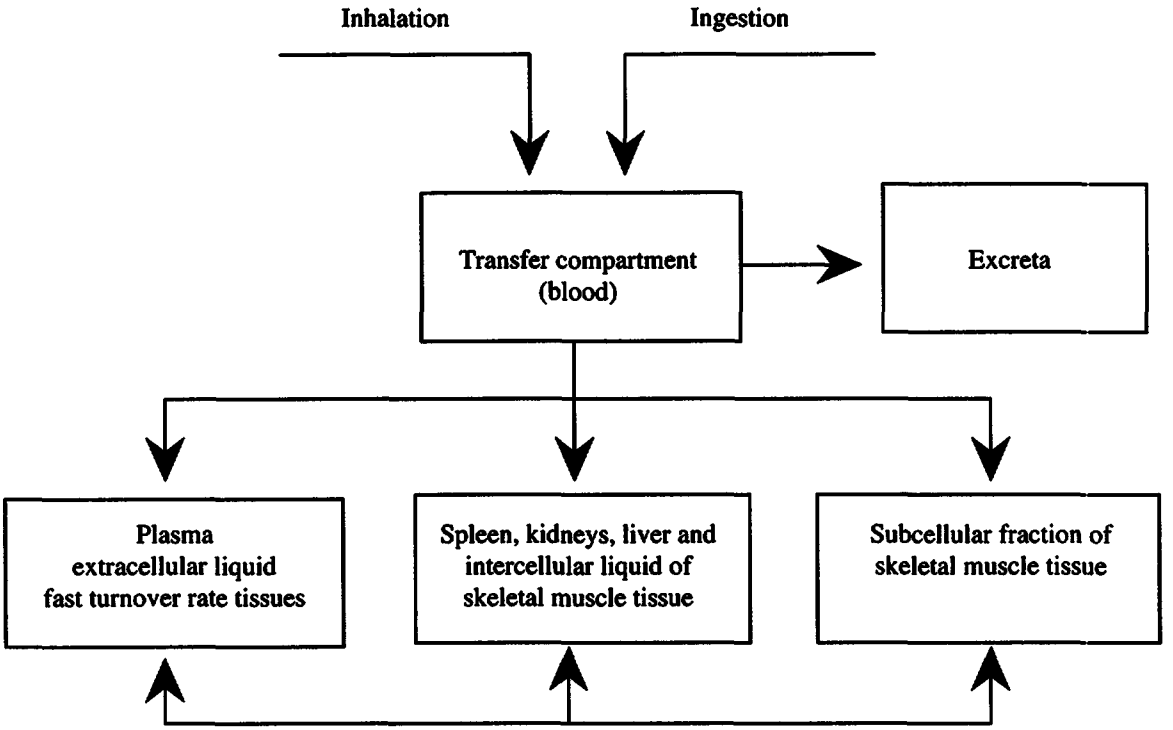

FIG. 4.2. Biokinetic model for ^{137}Cs metabolism.

The age dependent model adopted in ICRP [4.15] suggests the use of six different age groups 3 months, 1 year, 5 years, 10 years, 15 years old and adult. Table 4.3 reproduces the retention parameters of the ICRP model [4.15]. There are important differences between the two models, although both of them follow the same kind of retention equation, a sum of exponential terms, representing different retention half-times in the body. The ICRP [4.15] describes the retention of ^{137}Cs using two exponential terms while the model derived by Melo et al. [4.13] has a third exponential term, with a very long half-time, on the order of 500 d, representing 0.1% of the caesium internal uptake. Although this term does not add significantly to the dose received by the individuals, it is very important in terms of retrospective dosimetry, when individuals are monitored a long time after the date of the intake, and the intake has to be calculated from (or on the basis of) this monitoring result.

When compared to this model [4.13], the ICRP [4.15] predicts a 1.4 times lower committed effective dose for 5 years old and a higher dose for infants and adolescents [4.13]. Although the model described in this Chapter thus did not produce major differences in dose stimates, the improved model for caesium retention is very important in interpretation of data from children, specially at early times after exposure. For babies and infants, for example, the ICRP predicts that the caesium retention half-times are unique, 16 and 13 d respectively, while the model described by Melo et al. [4.13] predicts that 25% of the caesium is eliminated with a half-time of 3 d. For the 5 years old, the ICRP [4.15] predicts that 45% of the incorporated caesium is eliminated with 9 d half-time, while this model predicts that 25% is excreted with 3 d half-time.

TABLE 4.3. PARAMETERS OF THE ^{137}Cs RETENTION EQUATION FROM THE MODEL ADOPTED BY THE ICRP [4.15]

Age	Range of body weight (kg)[a]	Parameters of the ^{137}Cs retention equations			
		a_1	T_1 (days)	a_2	T_2 (days)
3 months	6[b]	–	–	1	16
1 year	9.8	–	–	1	13
5 years	19	0.45	9.1	0.55	30
10 years	32	0.30	5.8	0.70	50
15 years	55	0.13	2.2	0.87	93
Adult	70	0.10[c]	2[c]	0.90[c]	110[c]

[a]Data from [4.15].
[b]Data from [4.28].
[c]Appropriate for males, conservative if applied for calculating dose coefficients for females.

In relation to the second-term of the retention equation, which represents the turnover rate of caesium in tissues and organs with high caesium concentrations, the model described by Melo et al. [4.13] is based on half-times that are functions of the body weight and differentiates the adults by sex. This discrimination produces major differences in the interpretation of monitoring data for the adult female. For the adolescent, the weight differentiation is very important, since major differences in weight are expected in the 12 to 16 years old age range.

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5. EFFICACY OF PRUSSIAN BLUE THERAPY FOR DECORPORATION OF CAESIUM

5.1. INTRODUCTION

Prussian Blue (PB) is used to enhance the caesium elimination from the body. It is relatively nontoxic, well tolerated, and refractory to absorption from the gastrointestinal (GI) tract [5.1–5.2]. The effect of PB (ferric ferrocyanide) is quite specific for caesium; other monovalent alkali metals are probably bound with decreasing strength in the series Cs>Rb>K>Na because of their decreasing atomic radii [5.1–5.3]. Nielsen et al. [5.4] investigating the intestinal absorption of the ^{14}C in the cyanide group and ^{59}Fe from soluble PB ($K^{59}Fe[Fe(^{14}CN)_6]$) in three male volunteers, have concluded that the bioavailabilities of Fe(III), Fe(II) and cyanide from oral administration of KFeHCF are very low and that toxic side effects after appropriate oral doses (up to 3 g d^{-1} in adults) of this compound are not to be expected. It was concluded that PB can be considered an effective and safe antidote in cases of severe radiocaesium contamination.

Richmond and Bunde [5.1] administered ferric ferrocyanide (PB) to rats, which received approximately 31 kBq (0.84 μCi) of ^{137}Cs intravenously. PB was added to drinking water for 60 d at concentrations of 0, 0.025, 0.25 and 2.5 g l^{-1} and the rats were allowed to drink water ad libitum. Richmond and Bunde [5.1] did not find statistically significant differences on the total body burden for the control group and for the group that drank up to 0.025 g l^{-1} of ferric ferrocyanide in water. For the group which ingested PB at concentrations of 0.25 and 2.5 g l^{-1}, however, Richmond and Bunde [5.1] detected a significant reduction in whole body ^{137}Cs retention. This decrease resulted from reduced fractional deposition in and increased biological turnover from the major retention components. It was concluded that caesium secreted into the gastrointestinal tract is bound by PB and prevented from reentering the body for recirculation. Interruption of the reabsorbtion results in an accelerated total caesium excretion and in a drastic reduction (factor of 20) in the urinary- to-fecal excretion ratio. Prussian Blue appears to be the most effective antidote for radiocaesium contamination tested in animals.

Richmond [5.2] has investigated the effect of ferric ferrocyanide treatment in a healthy 37 years old adult male to whom ^{137}Cs had been administered orally. The treatment consisted of 2 g d^{-1} divided into ten 200 mg doses taken between 8:00 a.m. and 5:00 p.m. each day, for two consecutive five day periods, 12 d after ^{137}Cs ingestion. It was estimated that the biological half-time changed from about 140 d before treatment to about 50 d during treatment. This result agrees well with data reported by Madshus et al. [5.5] in which two subjects who ingested tracer doses of ^{137}Cs, were given 3 g d^{-1} of ferric cyanoferrate (II) divided into three or six portions and taken at regular intervals over a period of several weeks. The treatment with PB started 180 d after ^{137}Cs ingestion. Biological half-times changed from about 110 to 115 d to about 40 d.

Prussian Blue, when administered orally, acts in the lumen of the intestine decreasing the entero-hepatic circulation and increasing the caesium amount excreted by feces. Its effectiveness depends on the amount and rate of caesium excretion into the lumen of the GI tract and the availability of the PB to bind with caesium [5.6]. The IAEA [5.7] recommends the use of PB in cases of ^{137}Cs contamination, predicting a reduction of the ^{137}Cs biological half-time in the body to one-third of the usual value.

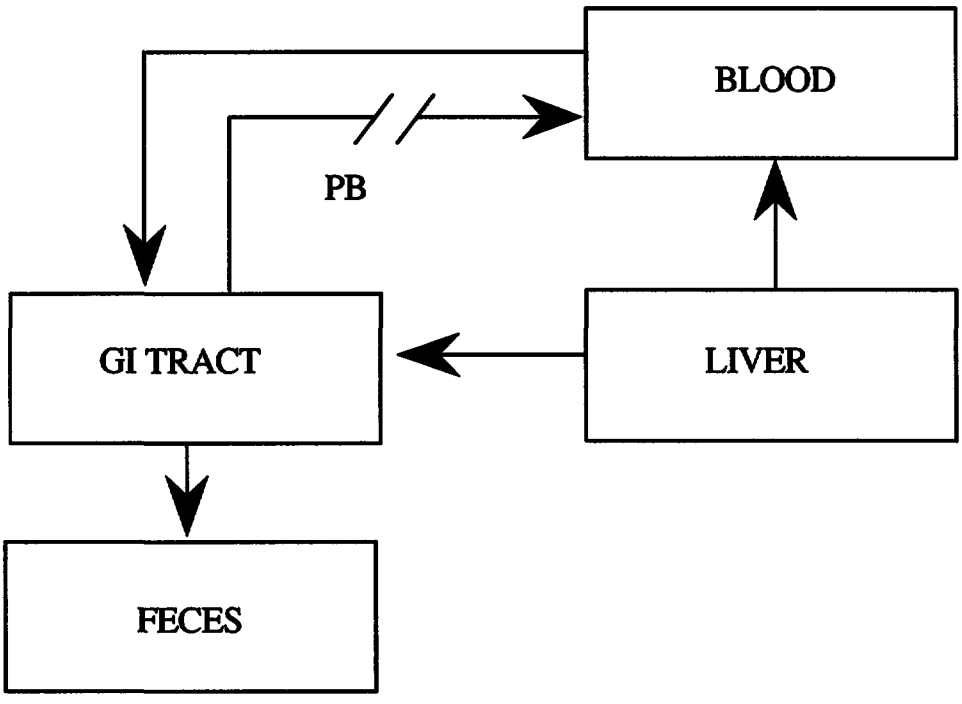

FIG. 5.1. Schematic representation of the Prussian Blue action in the body.

Prussian Blue administered to the individuals contaminated in the Goiânia accident, is commercially available as Radiogardase-Cs (68% $Fe_4[Fe(CN)_6]_3$). The manufactoring Laboratory recommends 3 g d^{-1} in 6 dosages of 0.5 g administered every two hours.

5.2. DATA FROM PEOPLE INTERNALLY CONTAMINATED IN THE GOIÂNIA ACCIDENT

Forty six individuals, internally contaminated in the Goiânia accident, were treated with Radiogardase in dosages varying from 3 to 10 g d^{-1} for adults and adolescents, and from 1 to 3 g d^{-1} for children. The drug was given orally 2, 3 or 6 times a day, depending on the total dosage, with a minimum of two hours between consecutive administrations. In four cases, 20 g was administered during 24 hours, but prior dosage was immediately reestablished, because individuals acquired gastric distress. Intestinal constipation is a side effect of PB that was observed in the majority of the people from Goiânia [5.8].

According to the NUREG/CR-4884 document, published by the US Nuclear Regulatory Commission [5.9], 0.8 of the total excreted caesium is eliminated through urine, and 0.2 through feces. As PB increases the amount of caesium excreted in the feces, feces to urine ratios were used as a qualitative indicator of the effect of PB in enhancing the caesium elimination from the body. Prussian Blue, as expected, significantly increased the concentration of ^{137}Cs in fecal excretion, which became the prevalent pathway of caesium elimination.

As described in Chapter 4, the caesium retention in the body may be mathematically described by a sum of three exponential terms, with parameters shown in Table 4.1. The probable date of ^{137}Cs intake was estimated for each person based on personal accounts of their contact with the ^{137}Cs source. Two of them (RSA and WMP), who had broken the source, probably became contaminated on September 13th. IAF, DAF, EDF, GGS probably

incorporated ^{137}Cs on September 21st and all the other individuals on September 24th, 1987. Prussian Blue treatment started at the earliest 10 d after intake [5.10], and thus did not have significant influence on the fast clearance of caesium from plasma to urine, which has a biological half-time equal to 3 d for all age groups [5.11]. The biological half-times of ^{137}Cs in the body under PB treatment were compared, for individual cases, to the half-times after treatment had ceased. This data is shown in Tables 5.1 to 5.3, where sex, age, weight and PB dosages for each individual are also specified. The average reduction of biological half-times was 69% for adults, 46% for adolescents and 43% for children. For the adults, the average ^{137}Cs biological half-times were the same for all three PB dosages, 25 ± 9 d, 25 ± 15 d and 26 ± 6 d respectively, when 3, 6 and 10 g were administered. As seen in Tables 5.1 to 5.3 the biological half-times of ^{137}Cs, under PB treatment, decreased to average values of 25 ± 11, 30 ± 12 and 24 ± 3 d for adults, adolescents and children, respectively. These results show that when the drug is administered more than 10 d after intake, the half-times of ^{137}Cs is reduced

TABLE 5.1. BIOLOGICAL HALF-TIME OF ^{137}Cs IN ADULTS INTERNALLY CONTAMINATED IN THE GOIÂNIA ACCIDENT [5.10–5.11]

Subject	Age (years)	Weight (kg)	Sex	$T_{1/2}$ (days) for adults under PB treatment			$T_{1/2}$ (days) after PB treatment
				3 g d^{-1}	6 g d^{-1}	10 g d^{-1}	
LOMS	29	66	F		20	33	58
LRNF	36	58	F	22			53
CFRS	19	50	M	42			66
WAS	21	70	M		18		98
RAS	23	66	M		17	17	99
GGS	28	69	M	21	17		75
EAS	31	69	M		17	25	85
KSS	32	61	M		21		80
OAF	33	80	M	26	63		106
DAF	35	70	M			27	89
IAF	41	63	M		18	29	70
EDF	43	73	M	17	39		80
ERF	46	64	M	21	15		75
Mean ± SD				25±9	25±15	26±6	

TABLE 5.2. BIOLOGICAL HALF-TIME OF ^{137}Cs IN ADOLESCENTS INTERNALLY CONTAMINATED IN THE GOIÂNIA ACCIDENT

Subject	Age (years)	Weight (kg)	Sex	$T_{1/2}$ (days) for adolescents	
				Under 10 g d^{-1} (PB)	After PB treatment
OAFJ	12	31	M	25	49
EBS	13	55	M	17	78
CRO	13	52	M	45	65
SPQ	13	58	M	41	75
LCNF	14	38	M	24	43
Mean±SD				30±12	

TABLE 5.3. BIOLOGICAL HALF-TIME OF ^{137}Cs IN CHILDREN INTERNALLY CONTAMINATED IN THE GOIÂNIA ACCIDENT

Subject	Age (years)	Weight (kg)	Sex	$T_{1/2}$ (days) for children	
				Under 3g d^{-1} (PB)	After PB treatment
CMS	4	14	F	21	39
PNF	5	20	F	22	42
CNF	7	22	F	21	42
PFMS	6	26	M	25	46
MNF	7	23	M	27	47
FJMS	7	23	M	23	33
CRINF	9	27	M	27	44
Mean±SD				24±3	

to a value around 26 ± 10 d, irrespective of the dosage of PB that was administered (3, 6 and 10 g) and of the age of the individual. As a consequence, the reduction in biological half-time is higher for adults than for children.

A multiple regression analysis test for dependent variables [5.12–5.13] was applied to the data on Tables 5.1 to 5.3 and it was concluded that there was no correlation between the biological half-times under PB treatment and any other parameters: Prussian Blue dosage, sex, age, body weight and height ($p < 0.05$).

Feces to urine ratio was not shown to be a good indicator in evaluating the efficacy of the different PB dosages in caesium decorporation. The increase in the feces to urine ratios when PB dosages was increased does not indicate an enhancement of the efficacy of the caesium decorporation treatment. The increased caesium concentration in feces causes a decrease in the concentration in the blood and the urine, but it does not change the total caesium activity which is excreted. For ten individuals treated with different dosages of PB, there was a significant correlation between the feces to urine ratios and the PB treatment that was given ($r^2 = 0.75$; $p < 0.05$). However, there was no significant statistical difference ($p < 0.05$) for the ^{137}Cs half- times under 3, 6 and 10 g d^{-1} PB treatment. The data used on the regression analysis is presented in Table 5.4 and the linear relationship is illustrated in Fig. 5.2.

TABLE 5.4. FECES TO URINE RATIO FOR PEOPLE SUBJECT TO PB TREATMENT

Subject	Prussian Blue dosage (g d^{-1})			
	0	3	6	10
EDF	0.19	1.13	1.45	
OAF	0.24	1.15	1.75	
GGS	0.02	1.58	1.95	
WMP	0.50		1.44	
RAS	0.28		2.05	5.76
EAS	0.17	1.61	2.52	2.84
LOMS			2.82	5.50
DAF			2.50	4.62
KSS		2.16	1.62	
ERF		1.44	1.25	

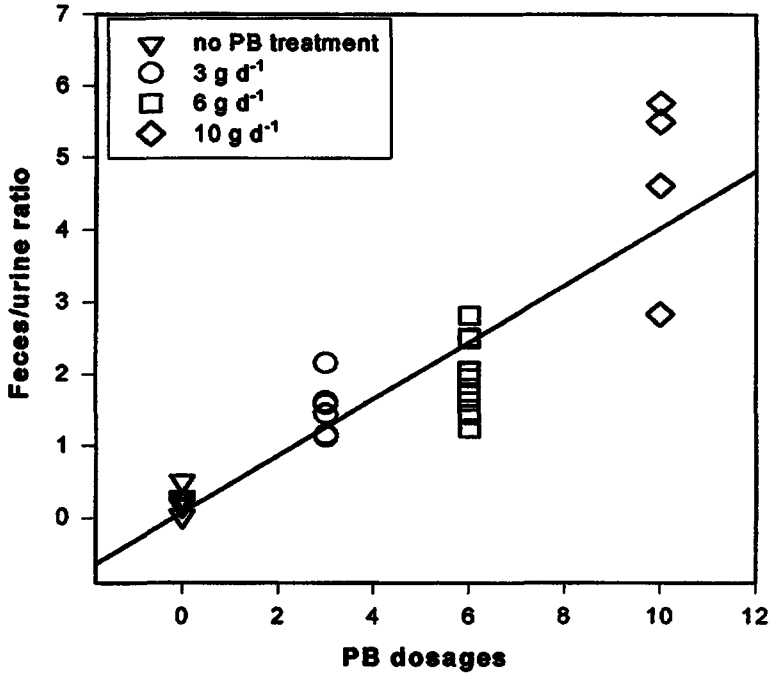

FIG. 5.2. Feces to urine ratio under Prussian Blue treatment for people internally contaminated in the Goiânia accident.

5.3. EXPERIMENT WITH DOGS

In order to complement the human data from the Goiânia accident, a 6 wk study was conducted using immature (4.7 months old), young adult (2.4 years old) and aged (13.5 years old) male beagle dogs. This study was conducted at the Inhalation Toxicology Research Institute and was reported by Melo et al. [5.14]. Six pairs of male beagle dogs were used in this study, three pairs were treated with PB and three pairs as controls. Each dog received approximately 44 kBq of ^{137}Cs in 5 mL of sterile physiological saline given in a single injection, via cephalic vein. The dogs were measured in a whole body counter immediately after ^{137}Cs administration to estimate their initial body burden. Whole-body measurements were then performed twice a week to determine the retention kinetics of ^{137}Cs. All excreta from the dogs were collected daily and measured for ^{137}Cs activity by gamma counting. The PB was added to the drinking water at a concentration of 2.5 g L^{-1}. The PB obtained from Aldrich Chemical Co., was deemed appropriate for this experiment, since it remained suspended in water purified by filtration. Water with PB was available to all treated dogs ad libitum. Untreated dogs were given purified water without PB. The consumption of water was measured daily and corrected for an evaporation rate of about 3.5% d^{-1} to determine the daily oral intake of PB. The average daily dosages of PB ingested by the animals are presented in Table 5.5. The dogs were maintained in individual metabolic cages for the duration of the study, which allowed quantitative separation of urine and feces. Immature and young adult beagles individually consumed similar quantities of PB daily, whereas aged dogs consumed about one-half as much (Table 5.5). However, these differences in PB consumption were not as great when compared on a PB dosage kg^{-1} of body weight. Independently of PB treatment, the whole body ^{137}Cs retention in each dog was shown to be well described by a two terms exponential equation, the parameters of which for each animal are given in Table 5.6. Prussian Blue treatment increased the whole body clearance of ^{137}Cs in all three age groups.

TABLE 5.5. WATER AND PRUSSIAN BLUE CONSUMPTION BY BEAGLE DOGS INJECTED WITH ^{137}Cs [5.14]

Age at exposure	Body weight (kg)		Water consumption (L d^{-1})[b]	PB intake (g d^{-1})[b]	PB intake (g kg^{-1} d^{-1})[b]
	Initial	Final			
4.7 months	7.4	9.2	0.83 ± 0.03	–	–
4.7 months	7.2	8.7	0.61 ± 0.03	–	–
4.8 months	7.4	8.4	0.62 ± 0.03	1.5 ± 0.08	0.18 ± 0.06
4.6 months	9.2	10.0	0.56 ± 0.02	1.4 ± 0.05	0.15 ± 0.04
4.7 ± 0.1 months[a]					0.16 ± 0.05[a]
2.45 years	12.3	14.2	0.61 ± 0.02	–	–
2.42 years	12.2	13.0	0.68 ± 0.03	–	–
2.44 years	10.8	11.8	0.60 ± 0.03	1.6 ± 0.08	0.12 ± 0.04
2.42 years	11.9	13.2	0.65 ± 0.04	1.6 ± 0.10	0.12 ± 0.04
2.4 ± 0.02 years[a]					0.12 ± 0.04[a]
13.8[d]	8.4	9.0	1.69 ± 0.06	–	–
13.4[e]	9.1	8.8	0.27 ± 0.02	–	–
13.1	7.3	7.0	0.37 ± 0.02	0.92 ± 0.05	0.12 ± 0.04
13.8	6.9	6.7	0.24 ± 0.02	0.60 ± 0.05	0.09 ± 0.06
13.5 ± 0.3 years[a]					0.11 ± 0.06[a]

[a]Mean ± S.D. for each group.
[b]Mean ± S.D.
[c]Not treated with PB.
[d]Dog suspected of having had hyperadrenocorticism, thus the relatively high volume of water consumption.
[e]Dog died unexpectedly of kidney failure on day 24.

TABLE 5.6. WHOLE-BODY CLEARANCE OF ^{137}Cs IN BEAGLES WITH AND WITHOUT TREATMENT WITH PRUSSIAN BLUE, IN 6 WEEKS OF EXPERIMENT [5.14]

Age group	Treated with PB	Clearance parameters[a]			
		A_1 (%)	T_1 (d)	A_2 (%)	T_2 (d)
4.7 months	No	29 ± 1[b]	2.8 ± 0.1	71 ± 1	19 ± 1.4
4.7 months	No	19 ± 2	2.8 ± 0.1	81 ± 2	21 ± 0.4
4.7 months	Yes	49 ± 2	2.4 ± 0.2	51 ± 2	11 ± 0.2
4.7 months	Yes	47 ± 4	3.1 ± 0.4	53 ± 4	11 ± 0.4
2.4 years	No	18 ± 1	1.7 ± 0.2	82 ± 1	30 ± 0.4
2.4 years	No	23 ± 1	1.8 ± 0.2	77 ± 1	25 ± 0.3
2.4 years	Yes	28 ± 1	1.5 ± 0.2	72 ± 1	15 ± 0.2
2.4 years	Yes	39 ± 1	1.4 ± 0.1	61 ± 1	16 ± 0.3
13.5 years[c]	No	23 ± 1	3.0 ± 0.4	77 ± 1	35 ± 1.2
13.5 years[d]	No	17 ± 3	3.0 ± 0.7	83 ± 3	44 ± 5.0
13.5 years	Yes	38 ± 3	2.4 ± 0.1	62 ± 3	14 ± 0.4
13.5 years	Yes	24 ± 2	1.5 ± 0.4	76 ± 2	12 ± 0.2

[a]Clearance described by $Y(t) = A_1 e^{-0.693/T1} + A_2 e^{-0.693/2}$, where $Y(t)$ is the whole body clearance ^{137}Cs, ($A_1 + A_2 = 100$) expressed as a percentage of the initial whole body burden, t is the time after exposure, T_1 and T_2 biological half-times of ^{137}Cs in compartments 1 and 2.
[b] Clearance parameter ± S.D.
[c] Dog suspected of having had hyperadrenocorticism.
[d] Dog died unexpectedly of kidney failure on day 24.

Prussian Blue treatment increased the fecal excretion of ^{137}Cs. In average, the percentage from the total excreted ^{137}Cs eliminated in the feces was 69 ± 4% for the six treated dogs vs. 43 ± 5% for the untreated dogs [5.14].

Prussian Blue increased the fraction that is cleared rapidly and decreased the half-times of the long term component, as compared with controls. For the young adult and for the aged dogs the parameters of the ^{137}Cs retention equation were similar, even though the PB dosage were different. Table 5.6 shows that PB apparently did not decrease the short-term clearance half-times, which were similar in all age groups. The average short-term clearance half-time was 2.0 ± 0.7 d for all dogs, treated and untreated.

As shown in Table 5.7, the effectiveness of PB was greater in the immature dogs than in the older ones, since the percentage of the initial body burden remaining 41 d after caesium intake is smaller. This age-related effect is mainly correlated with the greater increase of the short- term retention fractions (a_1) (Table 5.6), for the immature dogs than for the older ones.

TABLE 5.7. PERCENTAGE OF INITIAL BODY BURDEN (IBB) IN BEAGLES AT DEATH WITH OR WITHOUT TREATMENT WITH PRUSSIAN BLUE [5.14]

Age group	% IBB remaining at death in untreated dogs	% IBB remaining at death in PB treated dogs
4.7 months	16 (41)[a]	4 (41)
4.7 months	20 (41)	4 (41)
2.5 years	32 (41)	12 (39)
2.5 years	25 (41)	12 (39)
13.5 years	35[b] (41)	8 (41)
13.5 years	59[c] (24)	7 (41)

[a] ( ) = days after injection of ^{137}Cs to death or sacrifice.
[b] dog suspected of having had hyperadrenocorticism.
[c] dog died unexpectedly of kidney failure on day 24.

In an earlier experiment, Stather [5.15] used rats of 4, 9 and 19 weeks of age. These rats were given PB in the drinking water, in concentration of 10 g l^{-1}, starting two days prior to intraperitoneal injection of ^{137}Cs. The author found that the increase in the rate of loss in young rats was greater than in the older rats. The author concluded that the rate of loss of ^{137}Cs from the body under influence of PB depends upon the turnover rate of caesium in muscle tissue, which appears to decline with increasing ages. In a later study Stather [5.6] in an experiment with 21 week old rats injected with ^{137}Cs, the rats were assigned to three groups: control, PB treatment started two days prior to ^{137}Cs injection and PB treatment started three and half days after ^{137}Cs injection, has concluded that the elimination of ^{137}Cs is increased by administration of PB, the effect being more marked when the drug was administered two days before the ^{137}Cs injection. This conclusion, however, is challenged by other results from the reported experiment on dogs. PB decreased the biological half-times related to the second-term (T_2) for all age groups. Table 5.8 shows that the average reduction on the biological half-times of the treated dogs in comparison to untreated ones was 63% for the aged dogs, 45% for the young adults and 45% for the immature ones. The biological half-times during PB treatment were similar in all age groups, with average values of 11 d for the immature, 15 d for the young adult and 13 d for the aged dogs. Since the aged dogs had lower PB intakes due to their lower water consumptions, one may assume that these half-times are also independent of the PB dosage. This result shows that the effectiveness of PB apparently

TABLE 5.8. RATIO OF BIOLOGICAL HALF-TIMES UNDER PRUSSIAN BLUE TREATMENT TO NO PRUSSIAN BLUE TREATMENT FOR PEOPLE INTERNALLY CONTAMINATED IN THE GOIÂNIA ACCIDENT AND FOR BEAGLE DOGS

Data from people		Data from dogs	
Age group	T_2(PB)/T_2(no PB)	Age group	T_2(PB)/T_2(no PB)
Children	0.57	4.7 mo	0.55
Adolescent	0.54	2.4 y	0.55
Adult	0.31	13 y	0.37

does not depend on the turnover rate in the skeletal muscle tissue of the younger animals, which facilitates the passages of the nuclide from the muscle cells to the extracellular fluid and thus its secretion into the gut lumen [5.15].

One aged dog suspected of having hyperadrenocorticism, consumed unusually large amounts of water each day, about 8 times that of the other untreated dog of the same age (Table 5.5). From the total caesium excreted, 58% was via urine and 42% via feces [5.14]. As shown in Table 5.6, this high water consumption apparently did not alter the whole body clearance of ^{137}Cs, assuming that caesium retention is similar for young adult and aged dogs. This fact is consistent with data obtained from the Goiânia accident victims as discussed below.

To further validate the conclusions of the dogs experiment, the Spearman non-parametric statistical test [5.12–13] was applied and it was concluded that for the treated dogs, there were no correlations between retention parameters (biological half-times and retention fractions of both terms) and PB dosage, dog's age, initial body weight and potassium content ($p < 0.05$). These results are similar to the ones obtained using the Goiânia data.

5.4. FURTHER RELATED HUMAN DATA

Some contaminated individuals underwent increased water consumption, in an effort to increase the ^{137}Cs elimination through urine. However, no increase was found [5.8], probably because large water consumption results only in urine dilution, while caesium in blood and extracellular fluids is strongly homeostatically regulated [5.14]. As caesium and potassium are chemically similar and, in some aspects, are metabolized in the same way, physicians had administered diuretic to some patients, to enhance the potassium excretion. Eighteen patients from Goiânia received furosemide (40 mg d^{-1}) or hydrochlorothiazide (50 to 100 mg d^{-1}) and remained under rigorous clinical and laboratorial monitoring in order to prevent possible side effects. The concentrations of ^{137}Cs were measured daily in urine and feces and the results obtained demonstrated the inefficiency of these drugs in eliminating the nuclide. Their administration was suspended, except for those cases requiring them for other reasons. For the same purpose, a forced fluid regimen, which consisted of 3000 mL of water or potassium-rich elements such as orange juice, was attempted. The twelve patients who were subjected to this diet (they were evaluated previously and presented normal cardiovascular and renal functions), received PB concomitantly [5.8], and ^{137}Cs elimination did not differ from those who received PB but were not in a forced fluid regimen.

These results match very well with those reported by Rosoff et al. [5.16] and by Harrison and McNeill [5.17]. Rosoff et al. [5.16] have studied the behavior of ^{137}Cs in the body of eleven patients, with neoplastic and pulmonary diseases, after the administration of

some diuretics. Infusions of 500 mL of physiologic saline given on the thirteenth and fourteenth days after the administration of ^{137}Cs were ineffective in increasing the urinary or fecal caesium excretion. Similarly, the administration of 50 mg of hydrochlorothiazide given orally on three consecutive days was of no avail in enhancing the ^{137}Cs excretion. The administration of 40 mg of prednisone per day given for 14 d was also ineffective in raising the urinary ^{137}Cs excretion. A potassium ion-exchange resin, kayexalate, given orally was ineffective in increasing the urinary or fecal ^{137}Cs excretion. Harrison and McNeill [5.17] have monitored four normal subjects to whom a single dose of ^{137}Cs was given. Two of them were treated with 2 g d^{-1} of chlorothiazide. Although chlorothiazide increased potassium excretion to 1.5 times the control values, it had no significant effect on caesium excretion or in reducing the body burden of caesium. These results demonstrated that caesium and potassium are not utilized interchangeably. Caesium is retained preferentially over potassium and changes in potassium turnover have no effect on caesium turnover.

5.5. CONCLUSIONS OBTAINED FROM BOTH SOURCES OF DATA

The compilation of data gathered from the people submitted to PB treatment for caesium decorporation in Goiânia [5.10], and the data obtained from the experiment with dogs [5.14] was used to derive important and helpful conclusions for the decorporation treatment to be applied to individuals internally contaminated with ^{137}Cs:

- PB was shown to be an effective and safe drug for caesium decorporation treatment.

- The efficiency of PB treatment is dependent on the time of administration of the drug. Prussian Blue treatment is more effective when the drug is administered immediately after caesium intake. The dog's data has shown that the most relevant parameter for PB treatment is the increase of the fraction of ^{137}Cs eliminated with short biological half-time, an increase which is higher for youngsters than for adults. As seen in Table 5.7, the percentage of the initial body burden present at sacrifice for immature dogs was very small.

- If PB administration is delayed, it cannot influence the fast clearance of caesium from the body, only reducing the long term retention.

- The second-term (long-term) biological half-times, for all age groups, are reduced to similar values of around 13 ± 2 d for dogs and 25 ± 10 d for people from Goiânia. As older people and dogs have higher retention of caesium in the body, the reduction of biological half-times (T_2) was higher for the aged than for the young (Table 5.8).

- The average reduction of biological half-times (T_2) was 69% for adults, 46% for adolescents and 43% for children from Goiânia. For dogs, the average reduction was 63% for aged, 45 for young adults and 45% for immature ones (Table 5.8).

- The action of PB treatment overwhelms the influence of the biological parameters on the biological half-time of the second term of ^{137}Cs retention in the body.

- The feces to urine ratio was not shown to be a good indicator in evaluating the efficacy of different PB dosages in caesium decorporation.

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6. CAESIUM METABOLISM IN PREGNANT WOMEN

6.1. INTRODUCTION

Two women internally contaminated with ^{137}Cs in the Goiânia accident made possible studies of caesium metabolism during pregnancy. The first one, assigned as RBG, had an estimated ^{137}Cs intake of 0.2 MBq in the fourth month of pregnancy and the second one, assigned as LOMS, became pregnant three years and eight months after a ^{137}Cs intake of 300 MBq. The first case, has been described in details by Bertelli et al. [6.1].

According to Melo et al. [6.2], and as described in Chapter 4 (Table 4.1), the caesium retention in women from Goiânia is depicted as a sum of three exponential terms:

$$R(t) = 0.1 \times e^{-\left(\frac{0.693}{2}\right)t} + 0.9 \times e^{-\left(\frac{0.693}{110}\right)t} \qquad (6.1)$$

where: the first term represents the clearance of ^{137}Cs from plasma, extracellular fluid and organs with fast turnover rate to urine in the first hours after intake (biological half-time of 3 d). The second term of retention equation reflects the progressive loss in the urine and feces of caesium retained in organs and tissues (biological half-time of 65 d), mainly skeletal muscle tissues, which represents the largest portion of body weight. The third term reflects the retention in the subcellular fraction of the skeletal muscle tissue (biological half-time of 500 d). For women internally contaminated in the Goiânia accident, the average value for the biological half-time was determined as equal to 65 d (ranging from 39 to 90 d).

According to the literature, pregnancy accelerates the ^{137}Cs excretion from the woman's body. The biological half-time, related to the second retention component, is reduced to 50 to 65% of that from the non-pregnant women. Possible mechanisms for the decreased retention of caesium in pregnancy might be: elevated oestrogen, progesterone and aldosterone levels, rapidly growing tissue mass, increased metabolic rate or changes in renal function [6.3–6.5]. Zundel et al. [6.4] suggest the change in renal function seems to be the most likely explanation, since during pregnancy the glomerular filtration rate rises by as much as 50% resulting in an increased load of caesium being transferred to the tubules and, unless an equal increase in tubular reabsorption follows an increase in the excretion of caesium.

Zundel et al. [6.4] investigated some of these possibilities through the oral administration of two hormones (oestrogen and progesterone) to non pregnant women, but it appeared to have little or no effect on the caesium metabolism, although, it is unknown whether the half-times might have been altered if other hormones had been used. The authors evaluated twenty four pregnant women contaminated with ^{137}Cs, at environmental levels originated from fall-out. The average half-time was 47 d, 58% of the average half-time observed in fifteen non-pregnant controls.

Among these twenty four pregnant women 6 were evaluated both before and after delivery. For these, the 47 d average half-time during pregnancy was 66% of their average half-time while non-pregnant.

Rundo and Richmond [6.6] related the reduction in the rate of urinary excretion of the hormone aldosterone and a simultaneous decrease in excretion of ^{137}Cs. During pregnancy,

women have a markedly elevated aldosterone production in order to keep the hydroelectrolitic equilibrium [6.7]. Rundo and Turner [6.5] have observed changes in the ^{137}Cs biological half-time in women who were pregnant or who had recently given birth. They observed that the biological half-time of caesium just before parturition averaged 59% of the value (87 ± 33 d) after the birth of the baby and concluded that there is a step change on biological half- time at partus. But, what is not clear from their studies, is when the change takes place, how it progresses during the course of the pregnancy, and what the controlling mechanism is. The authors postulate that the change actually starts before conception. The biological half-time of ^{137}Cs shows cyclic changes associated with menstruation, decreasing at ovulation and then increasing on the onset of menses. If conception occurred instead, the half-time continued to decrease. However, they do not have direct evidence for this hypothesis. Another possible reason for the enhancing of caesium elimination from the body might be the 50% increase in the blood flux that occurs during pregnancy [6.7].

6.2. FIRST CASE — INTERNAL CONTAMINATION WITH ^{137}Cs IN THE FOURTH MONTH OF PREGNANCY

^{137}Cs body burdens of the mother and the infant were evaluated through whole body measurements, as described in Chapter 3. The results of ^{137}Cs measurements in the mother, infant and placenta, at the time of birth, are summarized in Table 6.1. The similarity between the values of ^{137}Cs concentrations for the mother, the placenta and the infant indicates an easy and homogenous transport of caesium from mother to fetus and also a lack of any placental barrier for ^{137}Cs. The ^{137}Cs transfer factor from mother to fetus was equal to 1. This result matches well with data by Wilson and Spiers [6.8]: who found the same caesium concentration in mother and infant. According to Stieve [6.9] and Lloyd et al. [6.10], the mechanism of transport of caesium through the cell membranes is similar to that of potassium which can be replaced by caesium to a certain extent. The transport seems to be independent of the stage of gestation as the same concentrations were found in fetuses of different ages.

Figure 6.1 shows the caesium retention curves of the mother and infant. Just one whole body measurement was performed during pregnancy, in the sixth month. The second measurement was done one week after birth. A ^{137}Cs biological half-time of 46 d was estimated for the mother, through regression analysis using a single exponential model for the set of data obtained after birth. It is interesting to note that the single data point from the measurement performed during pregnancy fits well in the regression curve of the data taken after delivery. It indicates that the biological half-time probably was the same during pregnancy and after birth, 46 d, contradicting the literature. This value is in the same range of biological half-times found by Melo et al. [6.2] for non-pregnant women from Goiânia (from 39 to 90 d) but it is below the average value of 65 d. The reduced value of biological half-time (46 d) may be explained by the additional excretion through breast milk.

TABLE 6.1. DATA FROM PREGNANT WOMAN THAT BECAME INTERNALLY CONTAMINATED IN THE FOURTH MONTH OF PREGNANCY

	Activity (Bq)	Concentration (Bq/kg)
Mother	61, 087	912
Infant	3, 885	971
Placenta	377	919

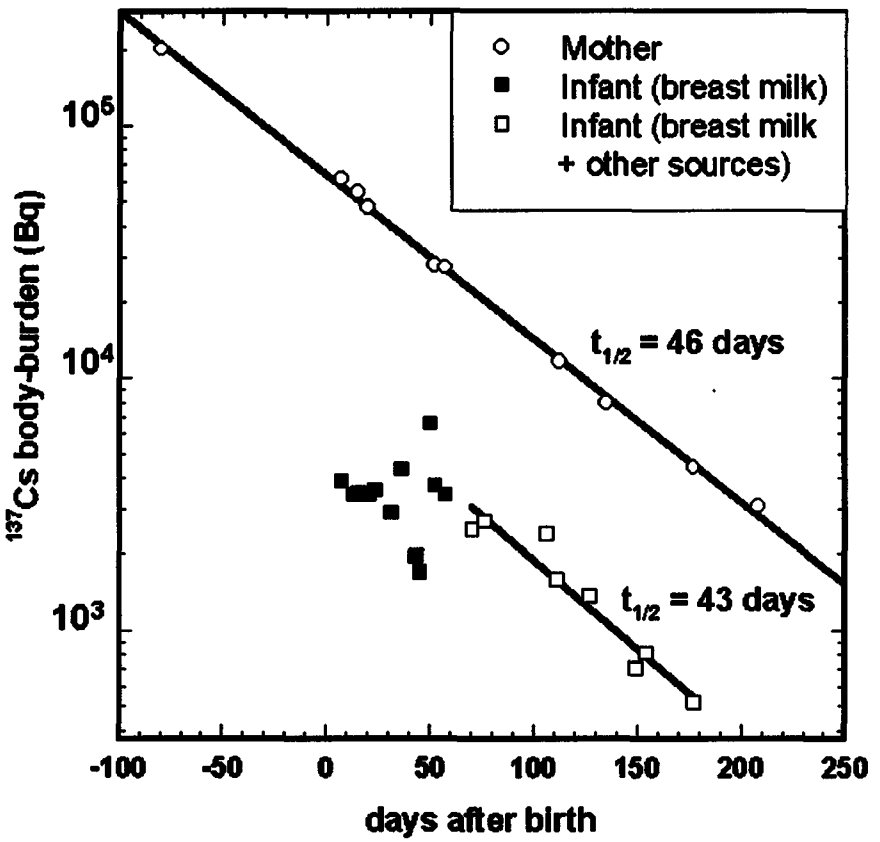

FIG. 6.1. ^{137}Cs retention curves of woman that became contaminated in the fourth month of pregnancy and her baby.

As seen in the retention curve of the infant, showed in Fig. 6.1, during the first sixty days after birth, the caesium body burden of the infant did not change. In this period of time breast feeding was the only source of nourishment. This result reflects an equilibrium between intake from mother's milk and loss by excretion. Sixty days after birth, an exponential rate of loss begins to take place. During this period of time, the alimentary diet of the baby was a mixture of breast milk and other sources of nutriment. The biological half-time estimated for this period, until 7 months of age, was 43 d, similar to the mother.

Bertelli et al. [6.1] have found that the retention of ^{137}Cs in the nursing infant is governed by the mother, who can be represented as a preceding biokinetic compartment. The infant/mother activity ratio curve is similar to the curve formed by the increase of infant's mass with time showing a strong correlation of activity with body mass.

TABLE 6.2. DATA FROM WOMAN THAT BECAME PREGNANT THREE YEARS AND EIGHT M ONTHS AFTER INTAKE

	Activity (Bq)	Concentration (Bq/kg)
Mother (initial body burden)	300,000	
Mother (at time of birth)	9.77	132
Infant	0.037	10
Placenta	<MDTA[a]	–

[a]MDTA-= 0.16 Bq (for 6 hours of counting time).

In order to estimate the ^{137}Cs biological half-time for infant, without contribution of breath feeding as a continuous source of intake, Bertelli et al. [6.1] based on the whole body counting data, and using the data of Bengtsson et al. [6.3] who reported 20% specific activity in milk relative to the mother and assuming milk consumption rate of 0.8 Ld^{-1}, estimated a ^{137}Cs biological half-time of 20 d for the infant (from 2 to 6 monthsof age) and a fractional transfer of 16% of that excreted by the mother into milk.

6.3. SECOND CASE — PREGNANCY THREE YEARS AND EIGHT MONTHS AFTER THE ^{137}Cs INTAKE

This woman had a high level of ^{137}Cs internal contamination, 300 MBq during the Goiânia accident, and became pregnant 3 years and 8 months after intake. Table 6.2 shows the data from the mother, the infant and placenta, at the time of birth. The caesium concentration in the mother's body was 13 times higher than in the infant's body. There was no measurable caesium activity in the placenta. The transfer factor of ^{137}Cs from mother to fetus was equal to 0.08. One possible reason for this small transfer factor is that the pregnancy occurred in the period when caesium is eliminated very slowly from the body. At this time caesium is supposed to be concentrated mainly in skeletal muscle tissue, more specifically in the subcellular fraction of this tissue. According to Rezende [6.7], during the pregnancy the blood flux becomes about 50% higher in most of the organs and tissues except brain, liver and skeletal muscle tissue. Our results indicate that the physiological changes caused by pregnancy did not increase the caesium removal from the cells.

Figure 6.2 shows the ^{137}Cs retention in the body of this woman for the whole period that she was monitored in the whole body counter. The first portion of the curve represents the period she was subject to PB treatment, in dosages that varied from 6 to 10 grams per day. The biological half-time was 37 d. The second portion, during which the biological half-time was 58 d, represents the period after PB treatment. This value of biological half-time is within the range of half-times from the Goiânia's women that never were submitted to PB treatment (average: 65 d, range 39 to 90 d). The third portion refers to the long term retention represented by the third component in the retention equation (Eq. 4.2), as described in Chapter 4, with a biological half-time of 475 d, estimated from the whole body measurements performed during the last month of pregnancy.

When the retention equation derived from data before pregnancy is used to estimate the ^{137}Cs body burden during pregnancy, the estimated value is very similar to the observed value. This confirms that the physiological changes caused by the pregnancy do not modify the ^{137}Cs retention.

Figure 6.3 shows that during the first sixteen days after giving birth, the ^{137}Cs biological half-time decreased to 27 d. This decrease might be associated to the loss of water from the

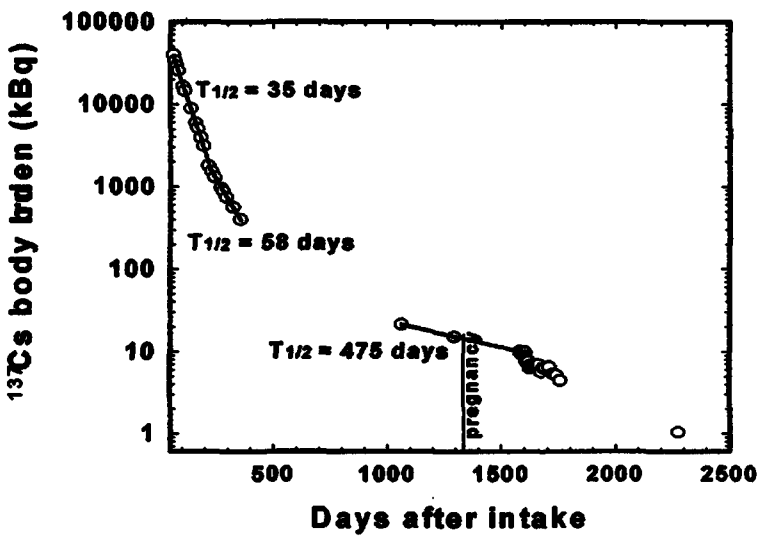

FIG. 6.2. ^{137}Cs retention curve of woman that became pregnant three years and eight months after intake.

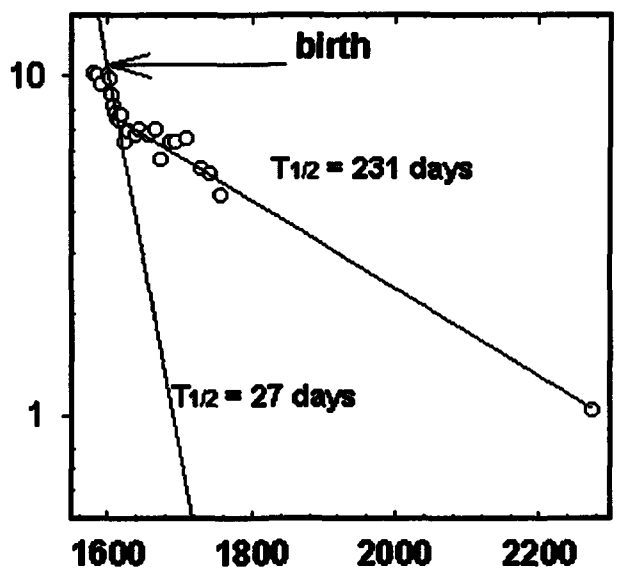

FIG. 6.3. ^{137}Cs retention curve of woman (second case) in the period after giving birth.

body, since the woman lost 8 kg of her body weight during these 16 d. During this period of time a strong correlation between ^{137}Cs body burden and body weight ($r^2 = 0.99$), was found. This woman had a high water retention during pregnancy. The mechanisms that acts in the elimination of this extra water from her body, probably is the increasing of membrane permeability, which allowed the ^{137}Cs to be removed together with the water. After this period, the biological half- time increased to 231 d. These data reinforce the conclusion that skeletal muscle tissue is responsible for the longer component of the retention equation.

6.4. CONCLUSION

The important conclusion of the comparison is that ^{137}Cs concentration fetus (C_F)/^{137}Cs concentration mother (C_M) ratio is equal to 1 for the pre-conception intake and equal to 0.08 for the intake that takes place some years prior to conception. In the second case, the pregnancy occurs during the period of longer ^{137}Cs retention, when caesium is retained in a compartment (skeletal muscle tissue), which is not influenced by the hormonal and physiological changes caused by pregnancy.

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7. INTERNAL DOSE ASSESSMENT

7.1. INTRODUCTION

In the Goiânia accident, 16 days elapsed between the stealing of the source and the discovery of the accident. During this time some individuals contaminated their skin with fragments of the broken source and ate with contaminated hands and from contaminated kitchen utensils. Internal contamination was due to ingestion and penetration through wounds.

During the first one and a half months, fecal and urinary excreta from contaminated individuals were collected and analysed for ^{137}Cs concentration, on a regular basis. In November 1987, a whole body counter was installed in Goiânia and *in vivo* monitoring was used to study the retention of caesium in the bodies of the contaminated individuals.

Prussian Blue (PB) was administered to some individuals to enhance the elimination of ^{137}Cs from the body. Up to December 1987, PB was adminstered under medical supervision since individuals were confined to hospitals or special housing centres, during this period. Patients were sent home with instructions to continue the PB treatment. Some of them, however, had difficulty in following medical orders, without the specialized supervision.

There was no standard pattern for treatment of individuals with PB, and many times the same individual received varying dosages of PB. There were no statistically significant differences in ^{137}Cs half-times due to the different dosages of PB. As individuals were sent home, half-times of ^{137}Cs for many patients increased, probably because they did not follow the prescription with the necessary care. As PB treatment ended, the half-times in general increased.

Melo et al. [7.1] have shown that for the same age/weight range the average biological half-times after PB treatment did not differ significantly from the average half-times of the people who never got PB.

A set of half-times, corresponding to the different treatment periods, were obtained for the individuals that used PB. The half-times were calculated using both the excreta and the in vivo data, utilizing the best available results. As shown by Melo et al. [7.2] the results obtained from in vivo and in vitro monitoring methods when simultaneously applied, were compatible.

7.2. DOSE CALCULATION

The committed whole body absorbed doses were calculated using the ^{137}Cs model described in Chapter 4 and by Melo et al. [7.1]. The parameters of the equation were taken from Table 3.1 except for the second term half-time which was substituted by each individual's value. For the individuals that were treated with PB, different half-times were used, for each treatment period. The third term of the retention equation (Eq. 3.2) was not taken into account.

The methodology described by Melo et al. [5.2], which follows the ICRP technique [7.3] was used to calculate the absorbed dose. The total number of transformations for the individuals that were not treated with PB were calculated through Eq. (7.1):

$$U = I_0\left[a_1\int_0^{\infty} e^{\frac{-0.693}{T_1}t}\,dt + a_2\int_0^{\infty} e^{\frac{-0.693}{T_2}t}\,dt\right] \tag{7.1}$$

where a_1 is the fraction of the initial activity associated with the fast clearance of ^{137}Cs, with values 0.25 for children up to 16 years old and 0.15 for adults; T_1 is the short term half-time, with value equal to 3 d; a_2 is the retention fraction related to the second term of the retention equation, with values 0.75 for children up to 16 years old and 0.85 for adults; T_2 is the second term biologicaalf-time; I_0 is the estimated intake.

For the individuals that were treated with PB, the total number of transformations were calculated using Eq. (7.2):

$$U = I_0 a_1\int_0^{\infty} e^{\frac{-0.693}{T_1}t}\,dt + I_0 a_2\left(\int_0^{t_1} e^{\frac{-0.693}{T_2}t}\,dt + \int_{t_1}^{t_2} e^{\frac{-0.693}{T_2}t_1} e^{\frac{-0.693}{T_{21}}t}\,dt + \int_{t_2}^{t_3} e^{\frac{-0.693}{T_2}t_1} e^{\frac{-0.693}{T_{21}}(t_2-t_1)} e^{\frac{-0.693}{T_{22}}t}\,dt + \int_{t_3}^{\infty} e^{\frac{-0.693}{T_2}t_1} e^{\frac{-0.693}{T_{21}}(t_2-t_1)} e^{\frac{-0.693}{T_{22}}(t_3-t_2)} e^{\frac{-0.693}{T_2}t}\,dt\right) \tag{7.2}$$

where I_0, a_1, a_2, T_1 and T_2 are the same as specified for equation 7.1 and, T_{21} is the half-time during PB treatment at the hospital, T_{22} is the half-time during PB treatment at home, when different from T_{21}.

In occasional cases, the half-times were further differenciated for certain periods of time and another term was introduced into Eq. (7.2).

The intakes for each individual were estimated using the results from the whole body monitoring and the Melo-Lipsztein improved model for caesium, described in the Chapter 4 and by Melo et al. [7.1], with the parameter T_2 substituted by the real T_2 obtained. When appropriate T_{21} or/and T_{22} as described in Eq. (7.2), were used for the individual that were treated with PB.

The specific absorbed energy from each transformation was calculated using the age-specific photon absorbed fractions derived by Cristy and Eckerman [6.4] and a program developed in our laboratory [7.2] and [7.5].

Table 7.1 summarizes the estimated committed absorbed doses in the whole body from incorporated ^{137}Cs for the individuals that were not treated with PB. Values of the committed absorbed doses for the people to whom PB was administered are presented in Table 7.2. where also estimates of the committed absorbed dose for each individual if PB was not given are also shown. These values were calculated assuming that the biological half- time of ^{137}Cs without treatment is the same as the biological half-time of ^{137}Cs upon cessation of treatment.

TABLE 7.1. COMMITTED INTERNAL WHOLE BODY DOSES FOR THE INDIVIDUALS THAT WERE NOT TREATED WITH PRUSSIAN BLUE

Subject	Sex	Age (years)	Weight (kg)	Committed dose (Gy)
TNF	F	1	10	1.1×10^{-1}
CMS	F	2	14	4.0×10^{-1}
CM	M	5	13	3.7×10^{-3}
LCF	F	5	17	9.0×10^{-3}
AFTDM	F	5	23	1.8×10^{-1}
PEM	F	6	17	4.8×10^{-3}
RKS	M	6	21	5.8×10^{-3}
CASJ	M	7	20	5.7×10^{-2}
AGM	F	7	29	1.2×10^{-2}
SINF	F	8	24	5.3×10^{-3}
GCB	F	12	31	3.0×10^{-2}
MAP	F	13	38	1.7×10^{-3}
SAF	F	13	51	1.3×10^{-3}
AF	F	15	49	8.0×10^{-4}
ICF	M	16	55	9.0×10^{-3}
PHF	M	21	68	5.0×10^{-4}
JMS	M	22	56	2.6×10^{-2}
DRO	M	23	69	3.0×10^{-4}
JA	M	24	61	5.3×10^{-3}
MPG	F	25	58	6.3×10^{-2}
STDP	F	28	61	2.6×10^{-2}
MJAF	F	30	39	6.7×10^{-4}
MCS	F	32	47	6.9×10^{-3}
DF	F	42	69	1.2×10^{-3}
CPS	F	44	85	9.9×10^{-3}
OD	M	55	71	4.3×10^{-2}
GTS	F	56	71	8.9×10^{-3}
JSS	F	59	57	2.1×10^{-3}
JAB	M	73	70	4.3×10^{-3}

7.3. CONCLUSIONS

The observed efficacy of PB in dose reduction (DRF_{PB}) varied from 1.1 (practically no effect) to 6.2 (very significant efficiency). The median of DRF_{PB} is 2.1, i.e. in average for 21 persons treated (cf. Table 7.2), PB has decreased the dose to the whole body from the incorporated ^{137}Cs by half.

TABLE 7.2. COMMITTED WHOLE BODY DOSES FOR THE INDIVIDUALS WHO WERE TREATED WITH PRUSSIAN BLUE

Subject	Sex	Age (years)	Weight (kg)	Committed dose (Gy)	Committed dose without PB (Gy)	**Ratio**[a]
CRMS	F	5	17	1.8×10^{-1}	3.6×10^{-1}	**2.0**
PNF	F	6	20	1.2×10^{-1}	2.2×10^{-1}	**1.8**
PFMS	M	7	26	1.2×10^{-1}	2.1×10^{-1}	**1.8**
MNF	M	8	23	4.6×10^{-2}	9.0×10^{-2}	**2.0**
FJMS	M	8	25	1.4×10^{-1}	2.4×10^{-1}	**1.7**
CRINF	M	10	27	1.4×10^{-1}	2.5×10^{-1}	**1.7**
OAFJ	M	13	31	1.8×10^{-1}	3.5×10^{-1}	**2.0**
LNF	M	13	38	7.0×10^{-1}	1.2×10^{-0}	**1.8**
EBS	M	13	55	2.0×10^{-1}	6.7×10^{-1}	**3.3**
CRO	M	13	55	2.2×10^{-2}	3.9×10^{-2}	**1.7**
SPQ	M	14	58	3.5×10^{-2}	6.8×10^{-2}	**1.9**
CFRS	M	19	50	1.4×10^{-1}	2.9×10^{-1}	**2.0**
RSA	M	23	66	9.1×10^{-1}	5.0×10^{-0}	**5.5**
GGS	M	28	69	9.7×10^{-1}	3.8×10^{-0}	**4.0**
LOMS	F	29	66	8.5×10^{-1}	3.1×10^{-0}	**3.6**
KSS	M	32	61	3.7×10^{-1}	1.4×10^{-0}	**3.7**
OAF	M	33	80	4.9×10^{-2}	1.4×10^{-1}	**2.7**
LRNF	F	36	58	1.6×10^{-2}	3.9×10^{-2}	**2.4**
IAF	M	41	63	3.0×10^{-1}	1.9×10^{-0}	**6.2**
EDF	M	43	73	2.0×10^{-1}	8.1×10^{-1}	**4.0**
ERF	M	46	64	4.6×10^{-3}	2.2×10^{-2}	**4.8**

[a]Ratio of committed dose without PB treatment to committed dose with PB treatment.

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8. DOSE ASSESSMENTS AND CYTOGENETIC FOLLOW-UP

8.1. INTRODUCTION

Chromosome aberration analysis, in particular dicentrics, in peripheral blood lymphocytes is the most sensitive biological indicator for radiation exposure. The dose is estimated by comparison of the observed yields of unstable chromosome aberrations (i.e. dicentrics and centric rings) with standard dose response curves generated following in vitro irradiation of human lymphocytes [8.1].

The type of exposure of the people involved in the Goiânia accident was complicated to evaluate, since two weeks had elapsed between the breaching of the source and the discovery of the accident. Most of the affected individuals received the exposure during a prolonged period, either fractionated and/or protracted at varying dose rates. Thus, the exposure was chronic rather than acute, and their total doses were, in many cases, also due to exposure from caesium external and internal contamination. In order to assess the absorbed radiation doses of individuals involved in the accident, peripheral blood lymphocytes from 129 persons were scored for unstable chromosomal aberrations, through the technique of cytogenetic dosimetry [8.2, 8.3].

No dose response curve for low dose rate ^{137}Cs was available to us during the course of the critical, emergency period of the accident. The doses were assessed through a dose-response curve generated for ^{60}Co g ays at a dose rate of 0.12 Gy min^{-1}. The main limitation for the use of this curve is the fact that it was built for an interval of doses between 0.5–4 Gy. Some individuals had received higher doses.

After the critical period of the accident, a new in vitro calibration curve was generated for ^{60}Co. The doses were than reassessed, using the frequencies of unstable aberrations initially observed in the subjects.

The persistence of unstable chromosomal aberrations in human peripheral lymphocytes is the subject of much controversy. Some authors claim that the disappearance of aberrations is exponential and that the average half-time for the disappearance of dicentrics is 3 years [8.4–8.10]. The exact relation between dicentric yield and time is not known, so difficulties in dose estimation arise for past exposures, due to a temporal decline of lymphocytes bearing unstable chromosomal aberrations [8.1].

The persistence of unstable chromosomal aberrations in peripheral lymphocytes has been used to estimate the lifespan of human lymphocytes *in vivo*. A lymphocyte containing a dicentric or centric ring has a probability of around 50% of surviving a mitosis [8.11]. Thus the decay in the frequency of dicentrics and centric rings, measured over time, can give an estimate of the intermitotic time of the lymphocytes (the mean time spent in G_0). The dicentric yield decreases if the blood is sampled months or years after irradiation. However, the exact relation between dicentric yield and time is not known, and only relatively few studies have so far been reported [8.4–8.9, 8.12–8.26].

An extensive cytogenetic follow-up of a group of patients after partial-body radiotherapy, during more than 30 years, led to the estimate that the lymphocyte mean life time is 1600 d, with a corresponding half-life of 3 years [8.17]. In this study, the lymphocyte half-life was estimated for the period between 1400 and 3400 d after exposure, despite the fact

that a rapid fall in the frequency of chromosomal aberrations was observed by the authors during the initial period of the follow-up.

Brewen et al. [8.4] and Preston et al. [8.6] reported a follow-up of an individual accidentally exposed to ^{60}Co g rays, who received a relatively homogeneous whole body exposure of 1.4 Gy. The frequency of dicentrics remained unchanged over 5 weeks and then fell so that by about 70 d it was 50% of the initial value, remaining relatively constant up to 3 years.

In another study, performed by Léonard et al. [8.8] during 21 years in an individual irradiated in 1965 with an average whole body dose of 5 Gy of g rays and neutrons, the mean lymphocyte life time was also estimated to be 1600 d. Nevertheless, the first blood sample was collected 9 months after the exposure. More recently, Lucas et al. [8.9] estimated the half-life of lymphocytes to be 3.8 years in a woman who, in 1985, had incorporated tritiated water, receiving a whole body dose of 0.4 Gy. In another recent study by Michie et al. [8.24], the mean T lymphocyte half-life calculated from their data was 730 d.

During the initial, critical period of the Goiânia accident, a cytogenetic follow-up of some of the patients (15 in total) was started to observe the disappearance rate of unstable chromosome aberrations. Blood samples from those 15 patients were collected repeatedly and scored for chromosome aberrations during a period of six years. It has been well documented that some lymphocytes that contain aberrations continue to exist in the peripheral circulation for many years after an irradiation [8.27]. However, a delay in blood sampling after an accidental irradiation will reduce the aberration yield. There are few data in the literature to enable a reliable correction factor to be applied [8.1]. The main objectives of our follow-up were to study the lifespan of human lymphocytes and estimate suitable correction factors to be applied to an observed frequency of chromosomal aberrations, if a delay in blood sampling has occurred.

Previous results of this follow-up have been published before [8.3 and 8.28]. More recently, the results were published of the six year study [8.29] and of the 7.5 year study [8.30]. As a continuation of the six year follow-up, lymphocyte samples from 10 individuals were collected 7.5 years after exposure. The aim was to observe which percentage of the initial frequencies of unstable chromosomal aberrations would still remain.

8.2. METHODOLOGY

8.2.1. Chromosome analysis

The experimental methodology used for the chromosome analysis during the follow-up studies was exactly the same used for the first dose estimates of the 129 individuals involved in the accident [8.2]. From each individual, a 10 mL peripheral blood sample was collected in a heparinized vacutainer. The erythrocytes were sedimented by centrifugation, and 2 mL of the buffy coat rich in leukocytes was collected and added to 10 mL of Ham's F-10 medium supplemented with fetal calf serum (25%) and 0.2 mL of phytohemagglutinin (Murex). The cultures were incubated for 48 h, and 0.04 mg of colchicine (Sigma) was added 2 h before harvest. After hypotonic treatment with KCl (0.075 M) for 15 min, the lymphocytes were fixed in methanol-acetic acid (3:1) and dropped onto clean, cold, wet slides. The slides were stained with aqueous Giemsa stain solution. Bromodeoxyuridine was included in some of the

cultures and the slides were subjected to the fluorescence plus Giemsa (FPG) technique. This showed that about 10 per cent of metaphases were second or later *in vitro* divisions. However, due to the extreme amount of samples to be processed during the Goiânia accident, the FPG technique was not employed and the small proportion of second and later metaphases was not excluded from our analyses.

The number of metaphases scored per sample depended on the observed frequency of unstable chromosomal aberrations. At the beginning of the follow-up, when the aberration frequencies were high, 100–200 metaphases were scored. Later on, the number was increased to about 400–500 metaphases per sample, as the observed frequencies decreased.

8.2.2. Calibration curve and reestimates of dose

A new in vitro dose response curve was generated with the same source of ^{60}Co g rays, at a dose rate of 0.1 Gy min^{-1}, for a range of doses between 0.5–7 Gy. All doses were repeated for a second donor.

The 129 subjects involved in the Goiânia accident had their doses reassessed through this calibration curve, using their initial frequencies of unstable aberrations. Some of these subjects were selected for the cytogenetic follow-up studies.

8.3. RESULTS

8.3.1. Reestimates of dose

The distribution of doses reestimated for the 129 subjects are presented in Table 8.1. Dose estimates for 24 subjects exceeded 0.5 Gy. Among those, 16 individuals exceeded 1.0 Gy and five exceeded 3.0 Gy. None of the estimates exceeded 6.0 Gy.

TABLE 8.1. DOSE DISTRIBUTION BY NUMBER OF SUBJECTS ESTIMATED BY CYTOGENETIC DOSIMETRY FOR THE GOIÂNIA ACCIDENT

Reestimated dose through cytogenetics (Gy)	Number of individuals
<0.1–0.49	105
0.50–0.99	8
1.00–1.99	8
2.00–2.99	3
3.00–3.99	2
4.00–4.99	2
5.00–5.99	1
Total	129

Table 8.2 shows the details of the individual dose estimates for those 24 subjects who received more than 0.5 Gy. This table also includes the dosimetry of all subjects involved in the follow-up.

TABLE 8.2. DOSE REESTIMATES BY CYTOGENETICS FOR THE SUBJECTS WHO RECEIVED THE HIGHEST DOSES IN THE GOIÂNIA ACCIDENT (INCLUDES ALL SUBJECTS INVOLVED IN THE FOLLOW-UP)

Subject	Initial frequency of dicentrics + rings	Estimated dose (Gy)
DAF#	1.253	5.3
RSA#	1.030	4.6
LDNF†	0.962	4.4
MGF†	0.824	3.9
AAS†	0.760	3.7
IBS†	0.570	2.9
EDF#	0.540	2.8
MGA#	0.533	2.8
IAF	0.270	1.9
GGS#	0.262	1.9
EBS#	0.260	1.9
WMP#	0.228	1.8
ERF#	0.160	1.5
OAFJ	0.100	1.1
PRM	0.075	1.0
LCNF#*	0.070	1.1
DFF	0.065	0.9
LOMS#*	0.053	0.9
RBG#	0.060	0.8
OAF#	0.050	0.8
KSS	0.060	0.8
PNF	0.029	0.6
SPQ	0.025	0.5
MPG	0.023	0.5
EAS#	0.020	0.4
CPS#	0.011	0.3
LRNF#	0.008	0.2
EBRJ	0.007	0.2
CFRS	0.002	0.1
MRM	0.002	0.1

#Subjects included in the follow-up; †deceased; *patients with very high level of internal contamination.

8.3.2. Cytogenetic follow-up

8.3.2.1. Six year study

Blood samples from 15 patients exposed during the Goiânia accident were reexamined at different sampling times after the exposure (from 30 to 2180 d, i.e. 6 years). These subjects were selected preferentially from among the highly or moderately exposed ones.

Of those 15 patients, nine had received 1 Gy or more (DAF, RSA, EDF, MGA, GGS, EBS, WMP, ERF and LCNF) and six between 0.2–1 Gy (LOMS, RBG, OAF, EAS, CPS and LRNF). Data are shown in Table 8.2, which shows the dosimetry for all patients who received more than 0.5 Gy and also the dosimetry for all patients involved in the follow-up. They were

of different ages, showed different levels of leukopenia during the critical phase of the accident and recombinant human granulocyte macrophage colony stimulating factor (rHuGM-CSF) was administered to some of them.

Almost all subjects had some level of internal contamination by ^{137}Cs. The level of internal contamination could alter the decay in the frequency of chromosomal aberrations, as it is known that incorporated ^{137}Cs distributes uniformly throughout the body, mainly in muscle [8.31]. One can expect it to lead to a continuous and fairly even irradiation of the body, and thus to the lymphocytes in both vascular and extravascular pools. With internal contamination by caesium more aberrations would be being generated as the earlier-generated ones are being lost. Of the fifteen selected patients, 13 had low to moderate degrees of internal contamination; thus their estimated absorbed doses were due mainly to exposure. Only two patients with high ^{137}Cs body burdens were included in the follow-up (LCNF and LOMS).

The results of the cytogenetic follow-up of these 15 subjects investigated are shown in the graphs of disappearance of aberrations (dicentrics plus centric rings) in Figs 8.1 and 8.2. The data were separated into two groups: patients with doses above 1 Gy (Group 1) and from 0.2–1 Gy (Group 2). Partial results of this follow-up have been published before [8.3, 8.28].

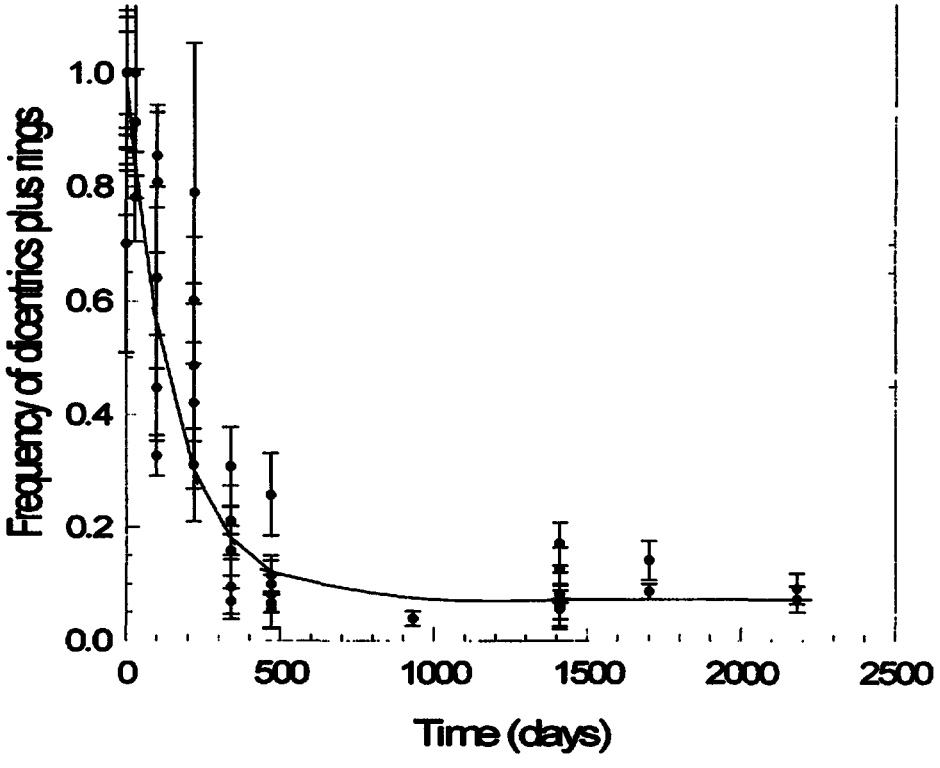

FIG. 8.1. Six year cytogenetic follow-up of 9 patients exposed to doses higher than 1 Gy (group 1).

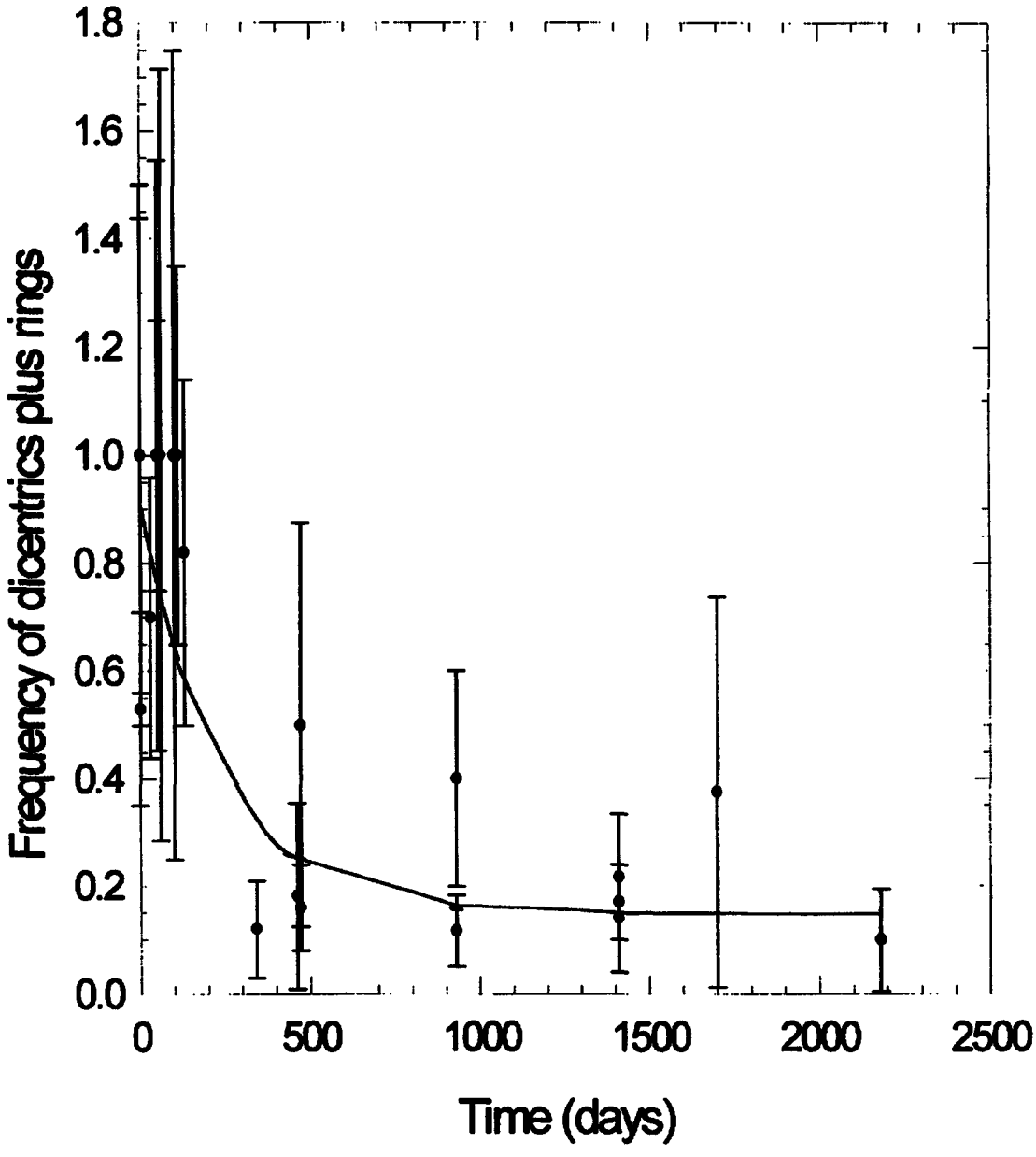

FIG. 8.2. Six year cytogenetic follow-up of 6 patients exposed to doses between 0.2–1 Gy (group 2).

In each plot, the data were fitted to a double exponential function, using the equation:

$$Y(t) = a \times e^{-bt} + c \times e^{-dt} \tag{8.1}$$

where: Y(t) is the frequency of aberrations in a given time t after the accident (in days), a and c are the initial aberration frequencies for the fast and slow components and b and d are their respective rate constants for disappearance.

The data of elimination of dicentrics plus rings show that there was a rapid fall in the frequency of aberrations during the first 1.3 years (470 d) after exposure, followed by a much slower, almost nonexistent elimination of aberrations (*d* coefficients are in the order of 10^{-12}). The half-time of disappearance of aberrations, during the period up to 1.3 years, was estimated as being 110 d for the group with doses above 1 Gy (Group 1) and 160 d for the patients with doses below that (Group 2).

The coefficients *a* and *b* of the exponential function of the short term of each of the nine subjects of group 1 appear in Table 8.3. The objective of this individual fitting was to obtain the individual rates of disappearance of unstable aberrations and, from them, the individual half- times ($T_{1/2} = 0.693/b$). The mean life time of lymphocytes with unstable aberrations can be estimated using $1/b$.

TABLE 8.3. BIOLOGICAL PARAMETERS AND INDIVIDUAL HALF-TIME ($T_{1/2}$) OF DISAPPEARANCE OF DICENTRICS PLUS CENTRIC RINGS

Subject	Sex	Age (years)	Level of leukopenia	GM-CSF factor	Fitted period (days)	Coefficients of exponential regression		$T_{1/2}$ (days)
						a	b	
DAF	M	35	severe	-	0-470	1.09771	0.00537	130
RSA	M	21	severe	-	0-470	1.05517	0.00665	100
EDF	M	42	moderate	+	0-470	0.53936	0.00752	90
MGA	F	57	severe	+	0-340	0.57386	0.00396	180
GGS	M	21	moderate	+	0-470	0.26844	0.00416	170
EBS	M	13	moderate	-	0-470	0.27109	0.00306	230
WMP	M	19	severe	+	0-340	0.23409	0.00439	160
ERF	M	47	moderate	-	0-470	0.16007	0.00710	100
LCNF	M	14	moderate	-	30-470	0.10000	0.00534	130

Besides the individual half-lives, Table 8.3 includes information about some biological parameters, such as sex, age, level of leukopenia shown during the critical period of the accident, initial frequency of chromosomal aberrations (represented by coefficient *a*) and the administration of rHuGm-CSF (recombinant human granulocyte macrophage colony stimulating factor) during the course of the first month after exposure. This drug was given as a continuous intravenous infusion in a daily rate of 500 mg m^{-2}, according to Brandão-Mello et al. [8.32].

In the present work, leukopenia was considered moderate for lymphocyte counts below normal but above 2000 mm^3 and severe below 2000. Leukopenia occurred during the first weeks after exposure, up to 1 month after the moment the accident was discovered. Some patients had been irradiated during the previous 15 d, before the accident was discovered. At the end of the first month after the accident was discovered (45 d after the accident actually started) almost all patients had already recovered from bone marrow aplasia or hypoplasia and showed normal blood cell counts. Subjects DAF and RSA had very severe leukopenia (less than 100 leukocytes mm^3). Nevertheless, their blood cell counts were near to normal when the second blood sample was drawn (6000 leukocytes mm^3), at the end of first month after the accident was discovered.

In order to evaluate the influence of biological parameters in the half-life of lymphocytes bearing unstable aberrations, a multiple regression for independent variables was performed. None of the biological parameters listed in Table 8.3 showed a correlation with the half-times of elimination of unstable aberrations.

Two subjects (LCNF and LOMS) had a high body burden of internal contamination by ^{137}Cs. For them, the initial frequency of aberrations first increased, in reasonable agreement with the estimated doses due to the internal contamination, as calculated by colleagues [8.33]. Later on the frequencies began to fall, following the decorporation of ^{137}Cs.

8.3.2.2. Mean functions of disappearance of unstable aberrations

One of the purposes of the present work was to deduce a correction factor to be applied in accident cases when there is a delay between exposure and blood sampling. With this purpose, two situations were considered, as follows.

In the first situation a correction function is suggested for when the delay is not very long (up to 1.3 years). As the data for the highly exposed group indicate that there is no correlation between the half-time of disappearance of aberrations and the initial frequency of aberrations, we can assume that an individual half-time of elimination of unstable aberrations is equal to the mean value of 110 d. Therefore, we suggest this mean value of 110 d for the half-time, to be applied to a simple exponential function, whenever it is desirable to correct an observed frequency of aberrations, as long as the elapsed time is known and there is an approximate idea of the dose received, which must be higher than about 1 Gy. If the dose received is supposed to be less than 1 Gy, we suggest the value of 160 d.

In the second situation a correction function is suggested for when the delay is very long, more than 1.3 years, up to six years. During this period, the frequencies of unstable aberrations reach an approximately constant value, corresponding to the long term value observed in all the patients exposed to high or moderate doses (>0.2 Gy). In order to observe if there is a correlation between the final and initial frequencies of aberrations, for all subjects investigated (moderate and high doses), a linear correlation was fitted. The term "final frequency" represents the mean frequency observed after 1.3 years (470 d), this point included. Subject WMP was excluded, according to this criterion (there are no points after 340 d). The coefficient of correlation (r) between the initial and final frequencies is 0.87 ($p < 0.05$). We suggest this linear function ($Y = ax$, where $a = 10$) as the correction factor for an observed frequency of unstable aberrations, for ranges of dose above to 0.2 Gy, whenever the elapsed time is longer than 1.3 years (470 d), and up to about six years, the period of time that this follow-up lasted. This means that one can simply multiply by 10 an observed frequency of unstable aberrations to obtain the approximate original one.

8.3.2.3. Seven-and-a-half year study

Blood samples from 10 subjects exposed to ^{137}Cs during the Goiânia accident were collected for chromosomal aberration analysis. Of those, five patients belonged to our cytogenetic follow-up group, i.e. they had been reexamined periodically for the frequency of unstable chromosomal aberrations (subjects EDF, GGS, LCNF, LOMS and RBG). The other five subjects were not included in the follow-up before (DFF, KSS, EBRJ, CFRS and MRM). For them, the only frequencies of aberrations available were the initial ones, obtained at the time of the exposure. The 10 subjects had received high, moderate or low doses during the Goiânia accident, according to our estimates of dose based on the initial frequency of unstable aberrations (Table 8.4).

TABLE 8.4. RATIOS BETWEEN THE FINAL AND THE INTIAL FREQUENCIES OBSERVED IN GOIÂNIA PATIENTS (7.5 YEARS FOLLOW-UP)

Subject	Estimated dose (Gy) (through cytogenetics)	Percentage of the initial frequencies (1987) of dicentrics + rings remaining in 1995
EDF	2.8	2 ± 1
GGS	1.9	3 ± 2
LCNF	1.1	2 ± 2
DFF	0.9	3 ± 3
LOMS	0.9	7 ± 7
RBG	0.8	10 ± 5
KSS	0.8	7 ± 5
EBRJ	0.2	57 ± 43
CFRS	0.1	100 ± 100
MRM	0.1	100 ± 100

The results indicate a substantial difference according to the doses the individuals had received. The disappearance of unstable aberrations seems to be dose dependent. For the group of patients with high or moderate doses, the frequencies of aberrations fell faster as a function of time. They fell to about 5% of the initial frequencies. For the individuals who had received low doses of radiation (< 0.2 Gy), the frequencies fell much more slowly, i.e. the frequencies remained very similar to the initial ones.

8.4. DISCUSSION

In the present study, for the highly exposed individuals (doses above 1 Gy), the mean half-life of lymphocytes containing unstable chromosomal aberrations was estimated as being 110 d, during the period up to 1.3 years after exposure. This value is in apparent disagreement with the usually accepted value of three years reported in the literature. The main reason for this discrepancy can be accounted by the fact that such values of three years had usually been estimated for intervals of time that did not include the initial period of the follow-up. For instance, in the study performed by Buckton et al. [8.7], in patients undergoing radiotherapy for ankylosing spondylitis, the mean frequency of dicentrics, after 4 years, had already been reduced to 10% of the original frequency. Nevertheless, in that same study, the estimated half-life of lymphocytes was 3 years, being calculated for the period between 1400 and 3400 d. Similarly, in another study, performed by Léonard et al. [8.8], the estimated mean life time of lymphocytes was 1600 d, with the first blood sample being collected only 9 months after the exposure.

The cases described by Dolphin et al. [8.5] and Lucas et al. [8.9] spanned a period from a fortnight to several years and they also showed a 3 years half-life. Nevertheless, Bauchinger et al. [8.22], like us, observed a biphasic decay in chromosome aberration from patients undergoing radiotherapy for treatment of seminoma. Immediately after radiation therapy a half-time of 0.4 years (150 d) and at 1720 d post treatment 3.6 years was estimated.

Brewen et al. [8.4] and Preston et al. [8.6] reported a follow-up of an individual accidentally exposed to ^{60}Co g rays, who received a relatively homogeneous whole body exposure of 1.4 Gy. The frequency of dicentrics fell after exposure so that by about 70 d it was 50% of the initial value, remaining relatively constant up to 3 years. This represents a difference from other published studies [8.15, 8.17 and 8.34] where the yield fell gradually from about 140 d to 3 years after exposure, and then leveled off at a frequency of about 10% of the initial frequency. In those studies the initial frequency of dicentrics decreased considerably immediately after exposure: by 40 d in the study of Norman et al. [8.15], by 60 d in the report of Sasaki and Norman [8.34] and by approximately 140 d in that of Buckton et al. [8.17]. In the study performed by Littlefield et al. [8.23] in three patients exposed during the accident in San Salvador, they observed that the initial frequency of unstable aberrations of the most exposed patient (8.3 Gy) was reduced to about half, 40 d after exposure.

Although for the highly exposed individuals we did not found any statistical correlation between the half-time of elimination of chromosomal aberrations and the absorbed dose, for the less exposed subjects the disappearance of chromosomal aberrations seems to have occurred more slowly.

The kinetics of elimination of aberrations seems to follow a two-term exponential function, with a short and a long term. The short term represents the initial rapid fall in the frequency of aberrations.

The prompt decrease in lymphocyte count is a consequence of damage of the hematopoietic centers. These include the spleen, the thymus, lymph nodes, and the bone marrow. The restoration of the leukocyte count after moderate irradiation is achieved partly by discharge of cells from storage spaces and partly by release from bone marrow of cells at an earlier stage of development than that at which they are normally released.

The quick fall can be explained by several hypotheses. Perhaps all of them coexist. The first one considers the possibility of discharge of less damaged lymphocytes from extravascular storage centers. A second one considers that the rapid fall can be explained by a dilution of cells containing aberrations by the production by bone marrow of new, normal cells, free of aberrations, during recovery from leukopenia. A third one considers the rapid fall as indicative of the presence of a subpopulation of T lymphocytes with a short lifespan; the long term would thus represent a subpopulation of T lymphocytes with a long lifespan.

The majority of patients had recovered from leukopenia in a short time (one month to a few months) after exposure, while the decrease in the frequencies of aberrations occurred slower and in a pattern not proportional to the level of leukopenia. The best examples are subjects DAF and RSA. They had a very severe leukopenia (100 leukocytes mm^3 and lymphocyte counts near to zero) during the first 45 d after exposure. However, at the end of 45 d, when the second blood sample was collected, they already presented leukocyte counts near to normal (6000 mm^3, with 2000 lymphocytes mm^3). Surprisingly, there was no drastic fall in their frequencies of aberrations proportional to this cell renewal; the frequency was just slightly lower than the initial value. Thus, the recovery in leukocyte counts of those patients, whose values increased from 100 to 6000 mm^3 (a factor of approximately 60 times), did not cause a proportional reduction in the frequency of aberrations. Littlefield et al. [8.23] also observed this same phenomenon in two patients from the San Salvador accident.

The results shown in the present work partly explain the discrepancies, among authors, about the half-time for the disappearance of unstable aberrations. It definitively seems to depend on the dose received by the subject at study.

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9. CLINICAL ASPECTS AND TREATMENT OF LOCALIZED RADIATION-INDUCED LESIONS

9.1. INTRODUCTION

Observations and experimental studies carried out over the past years have given us a better understanding of the response of the skin and adjacent tissues to radiation, not only as regards clinical phenomena which appear at different phases of this pathology, but especially as regards the effects resulting from different dose ranges [9.1–9.6]. The response of the skin tissue to ionizing radiation depends on the physical parameters of the radiation (dose, dose rate, energy and size of field irradiated) and especially on the radio-sensitivity of the different cell lines of affected tissues. In addition to the cells of the basal layer of the epidermis, other cells are also sensitive to radiation, such as the cells lining the pillous follicles, the endothelial cells and fibroblasts [9.1]. Damage to tissues can be expressed through intermitotic cellular death (interphase death) and interruption of cellular reproduction, or mitotic death. In intermitotic death, the damage will manifest itself relatively soon, while in mitotic death this is largely dependent on the turnover of each cell line.

The localized radiation-induced injury is an original, complex and infrequent pathology, and is associated with accidental or therapeutic exposures. Clinical symptoms may appear relatively late after exposure, or successively from the moment of irradiation, following a very typical clinical course. The earlier, the onset of symptoms, the more severe exposure. Briefly, we can list the range of symptoms — erythema, swelling, blisters, ulceration, necrosis and sclerosis, usually accompanied by functional disturbances — heat sensation, paresthesia, thermal and tactile sensitivity changes — and much pain.

9.2. CLINICAL ASPECTS OF LOCALIZED RADIATION-INDUCED INJURIES IN GENERAL

The most typical skin reaction is erythema, observed after acute doses over Gy. It is frequent after 5 Gy and constant after 8 Gy. The precocity of its occurrence is clinically important, since it indicates the intensity of exposure [9.7]. Erythema may appear during three periods of the lesion evolution: (a) primary — immediately after exposure, or within a few hours, in which case it is of short duration and atypical. This phenomenon is caused by an increase in the volume of blood to the affected region; (b) secondary erythema — appears two to three weeks later, generally preceeding dry or moist desquamation. It is a characteristic erythema and apparently caused by functional changes at the microcirculation level with vasodilatation associated with destruction of epithelial cells; (c) the so-called delayed erythema may occur from 2 to 4 months after irradiation, and is always associated with destruction of endothelial cells [9.1, 9.2, 9.7].

Swelling oedema is frequent and can appear relatively soon, affecting not only the irradiated area but also the neighboring tissues. It can result from doses above 10 Gy and shows a direct relationship with the intensity of dose, i.e. the higher the dose the more rapidly it appears. It lasts throughout the period of moist desquamation, diminishing during recovery and reappearing with the third wave of erythema. Swelling is caused by an increase in vascular permeability and loss of liquids to the extracellular compartment. Deep swelling, especially when affecting muscles, can be easily observed by computerized X ray tomography and magnetic resonance imaging.

Vesicles and bullae result from the total death of epidermal cells. They were one of the best documented clinical symptoms, as they began to appear during the second or third week after exposure when the patient is generally under medical care (Figs 9.1 and 9.2). Their onset was directly related to the intensity of exposure. The presence of hyaline fluid gives the blisters a translucent appearance. The threshold dose is between 12 Gy and 25 Gy after γ-exposure and somewhat higher after δ-irradiation.They characterize the evolutionary phase of radiation injury known as exsudative or wet epithelitis [9.8].

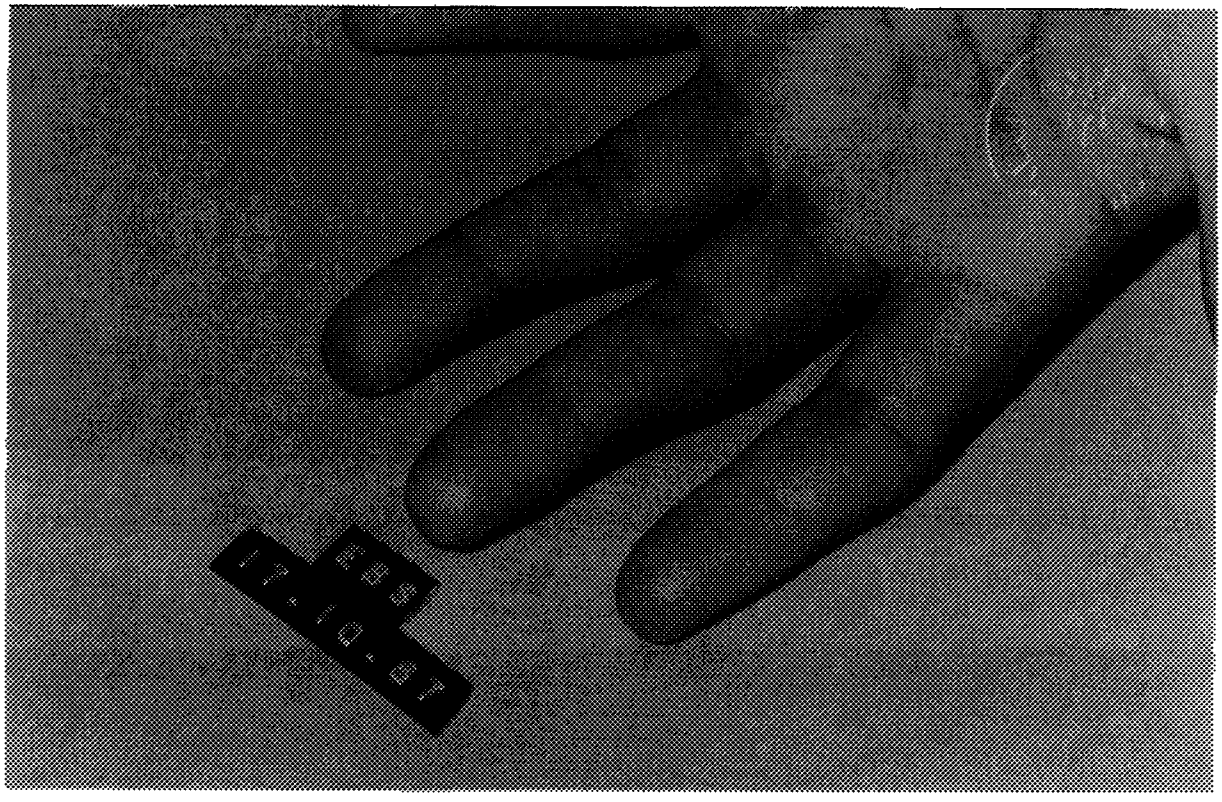

FIG. 9.1. 3 weeks after exposure. The classic aspect of a blister with its yellowish content. Residual secondary erythema can also be observed.

Ulceration occurred between four and six weeks after irradiation with doses higher than 30–50 Gy . Not very deep ulcers were eventually be covered with a fine, delicate layer of fibrin (Fig. 9.3). Necrosis appears several weeks later, either with blackening of the central zone of the lesion (Fig. 9.4), or with the appearance of a dense and firm fibrinous tissue (Fig. 9.5). The ulcer and its natural evolution, necrosis, results from total destruction of epidermis, dermis and ischemic process owing to occlusion of the dermal capillaries, which is a consequence of the destruction of endothelial cells.

Radiation-induced dermal fibrosis was relatively common following localized exposure to radiation. After tissue damage, adjacent cells, normally quiescent, are temporarily activated to repair the lesion. In radiation-induced injuries the repair mechanism may be continuously activated, leading to fibroblast proliferation and accumulation of collagen. Theoretically, this can affect any organ, but it is of particular interest to us when it affects muscles, tendons and aponeuroses. Usually, it appears several months or even a few years after irradiation, and is one of the most difficult complications of radiation lesions to handle. It is a challenge from the therapeutic point of view - clinical or surgical - especially when it affects the hands, fingers and flexion zones, which generally become ankylotic and deformed (Fig. 9.6).

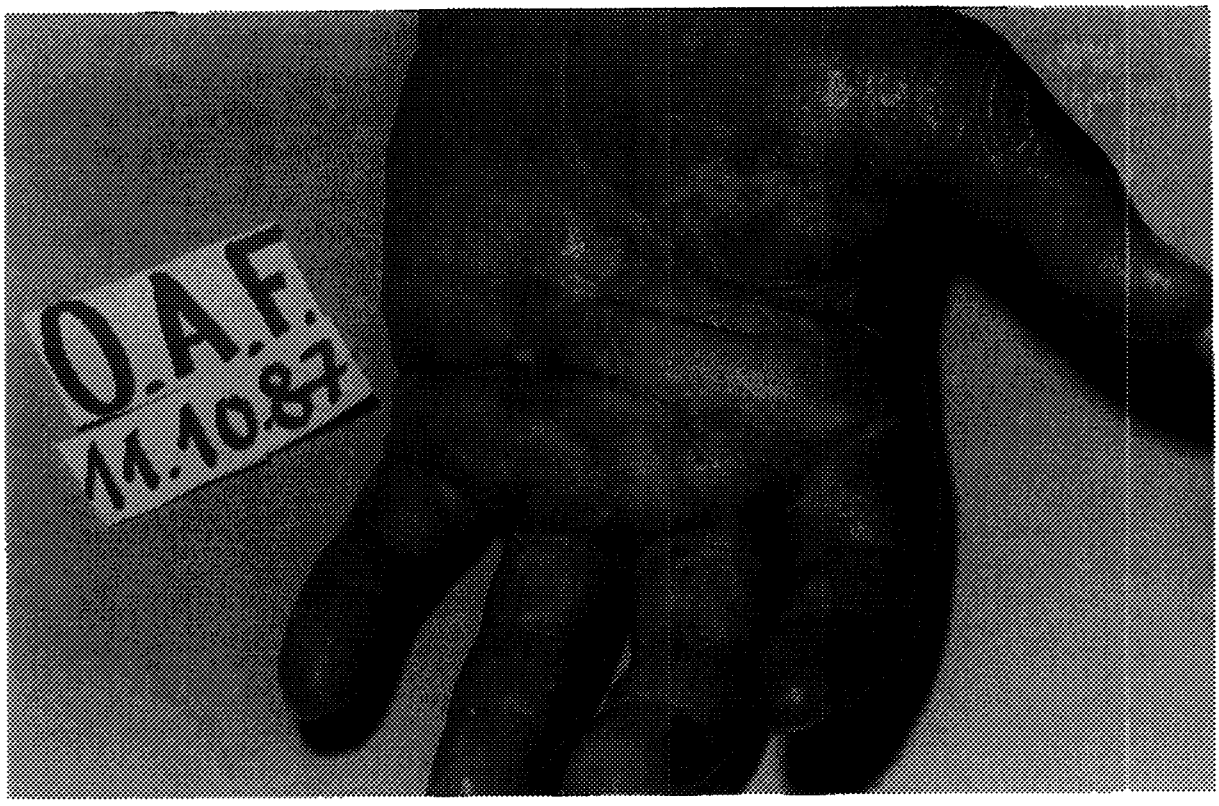

FIG. 9.2. 17 days after exposure. Large and tense blisters. Significant swelling limits fingers movement.

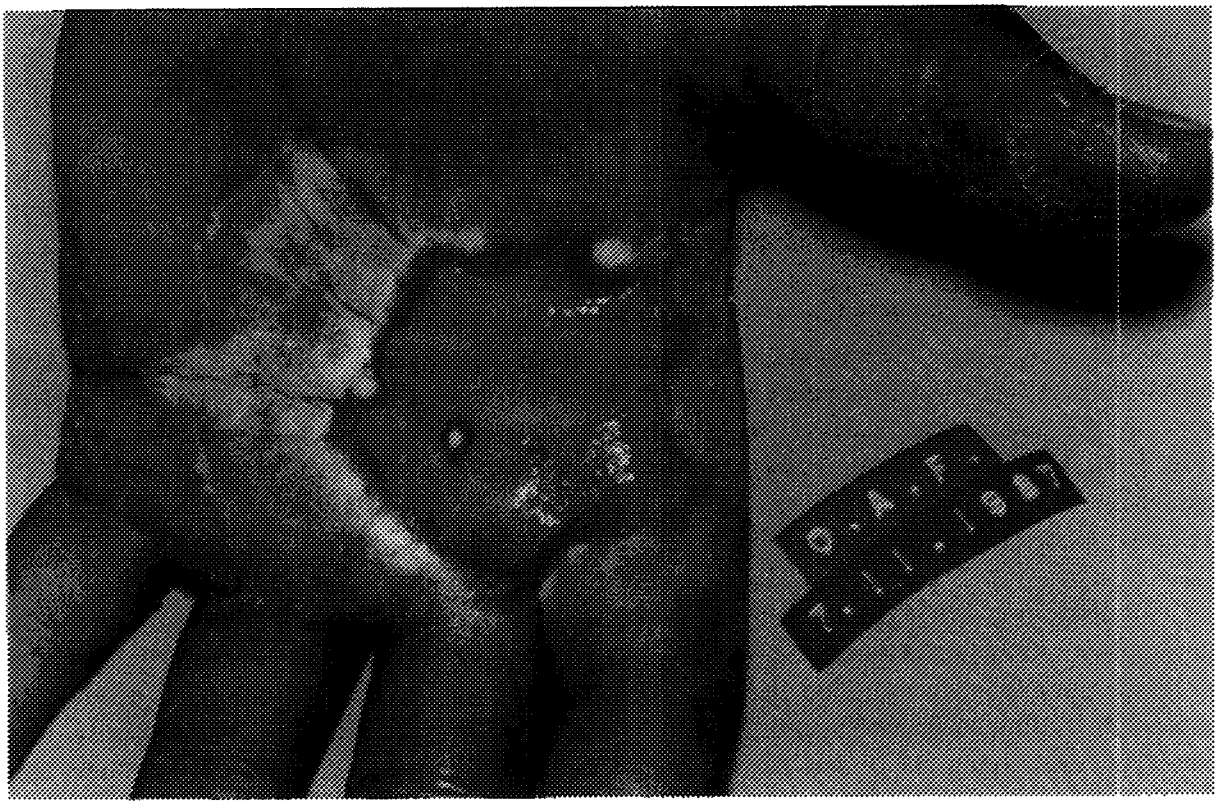

FIG. 9.3. 3–30 days after exposure. The skin was excised. A raw reddish surface is covered with a delicate layer of fibrinous exsudate. Note the centripetal character of the healing process and the attempt of re-epithelialization.

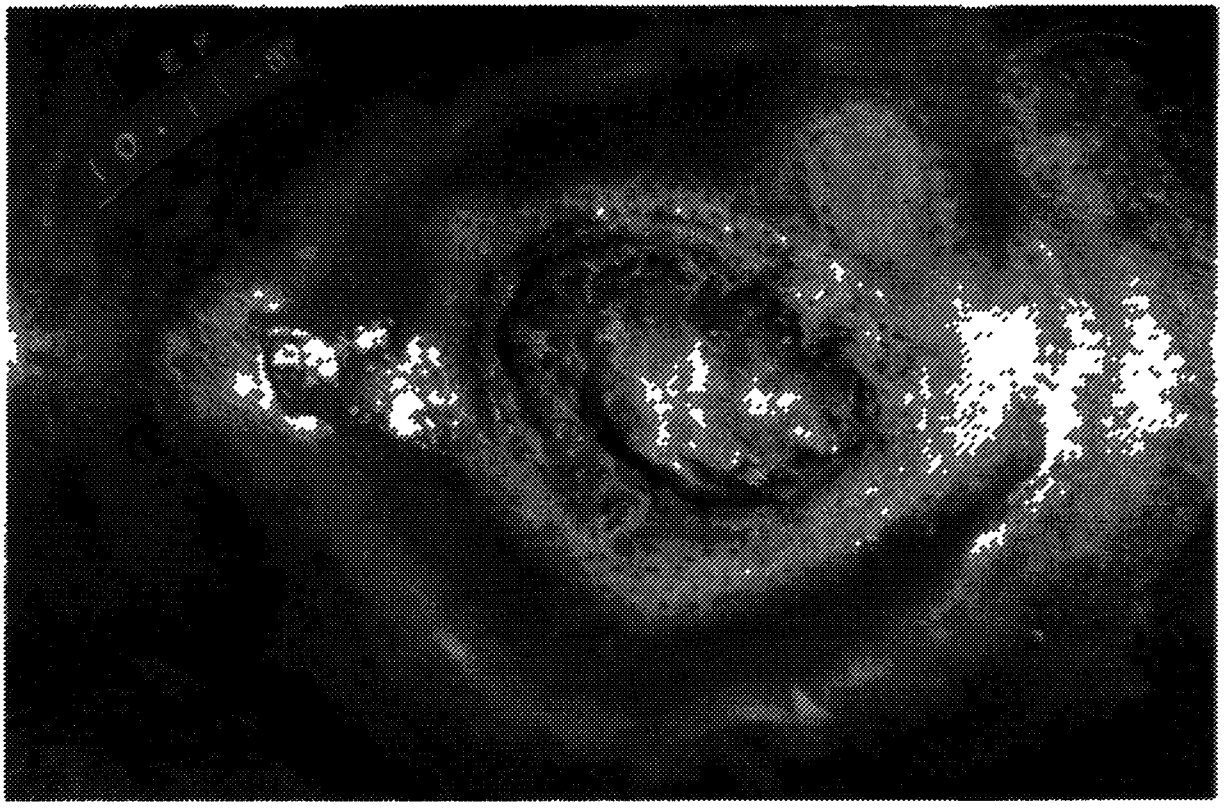

FIG.9.4. Detailed view of the bed of an deep ulcer after partial resection. The blackening of surrounding tissue, fat necrosis and skin suffering are clear indications of poor evolution of this injury.

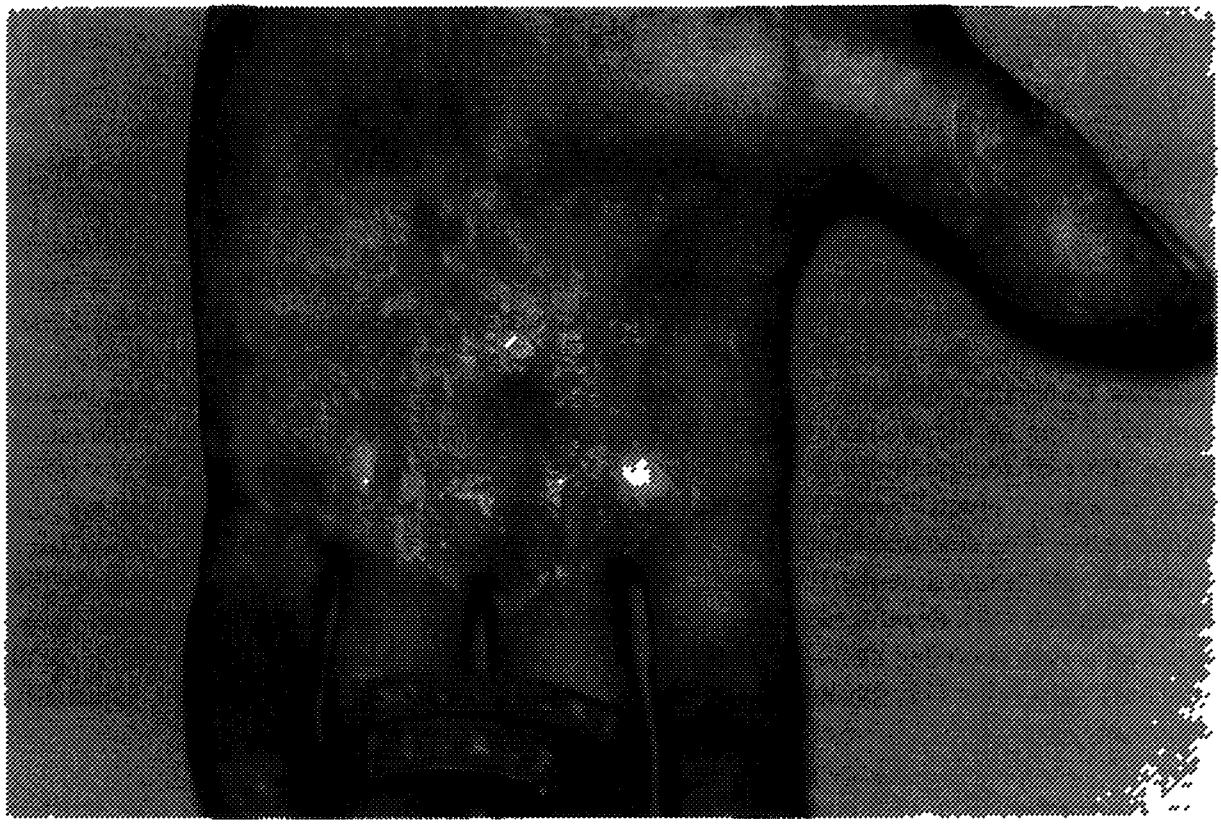

FIG. 9.5. 75 days after exposure. The wound, now limited to a superficial ulceration, is covered with a dense and firm fibrinous exsudate.

FIG. 9.6. 75 days after exposure. The fingers are thin, deformed and ankylotic. Note the shedding of nails.

Despite the somewhat arbitrary and debatable nature of any classification, like other researchers, we observed in the caesium patients two clinical evolutionary modalities of radiation lesions during the short and medium-term medical follow- up: exsudative epithelitis and vascular endothelitis. Exsudative epithelitis or moist (wet) desquamation, has four distinct phases: early transient erythema, sub-clinical or latent phase, typical or secondary erythema, which inaugurates the so-called exsudative process, and recovery phase, with or without sequelae. Generally, the whole process takes between eight to twelve weeks. Healing begins from the edges of the wound, with contraction of the ulcerated area and the appearance of sparse spots of reepithelialization on the naked dermis. Vascular endothelitis, on the other hand, is almost always associated with the occurrence of moist desquamation during the critical phase. The characteristic manifestation is a late erythema, which develops months later in an area which had apparently healed. This is followed by swelling and pain. Suddenly the wound reopens with development of a profound and deformed ulcer over an extensive area, which as a rule becomes necrotic (Fig. 9.7). The open lesion favors bacterial invasion with secondary infection. This evolution was most clearly seen in lesions of the hands, especially fingertips.

After irradiation with beta-emitters of high energy (^{137}Cs) or X or gamma rays, further changes can be observed such as pigmentary changes, atrophy, teleangiectasia, brittle and damaged hair and shedding of nails (Fig. 9.8).

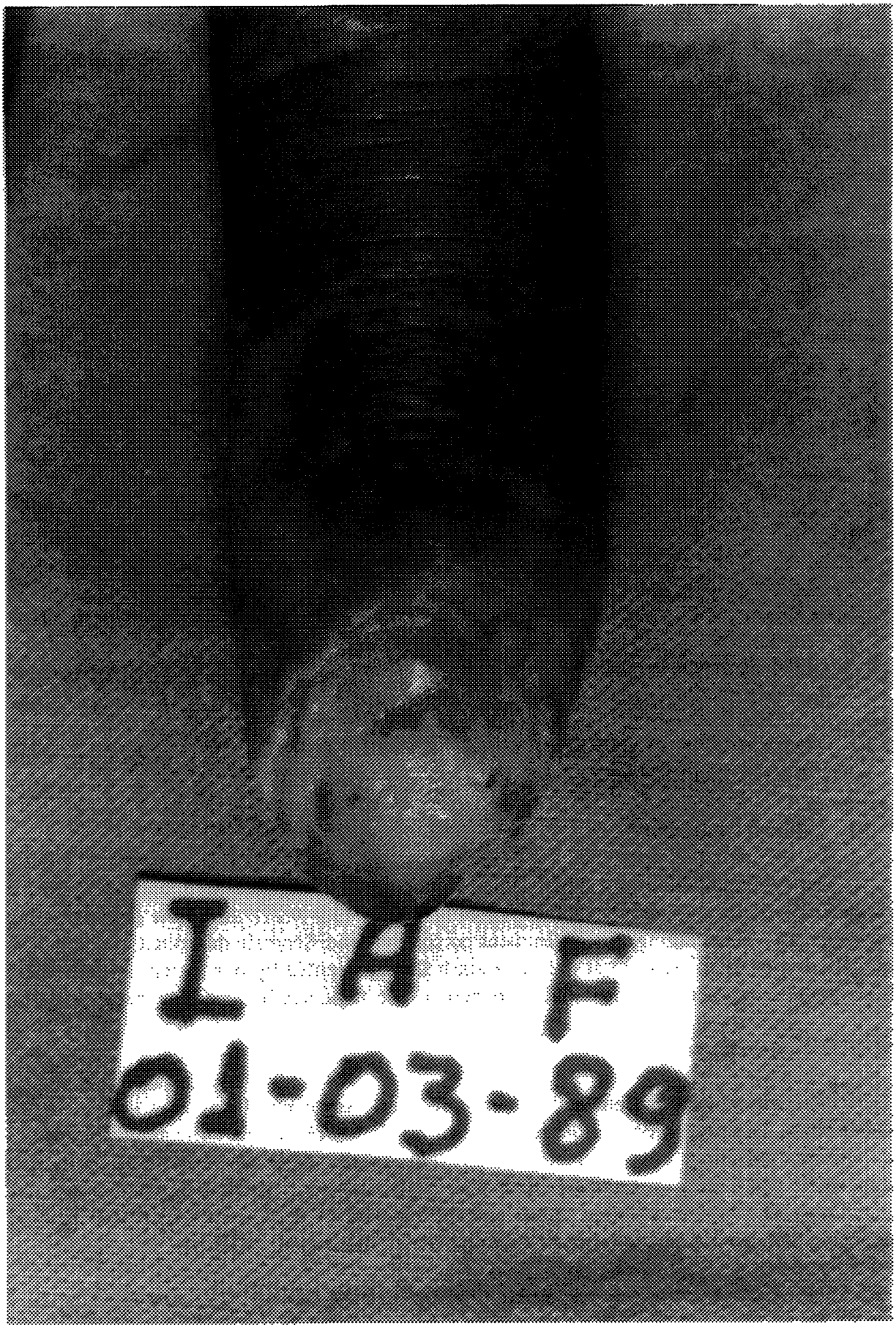

FIG. 9.7. Reoccurrence of finger injury 1 year and half after exposure.

FIG. 9.8. Hyperpigmentation of skin. The nail of the forefinger is darkish and broken.

9.3. THERAPEUTIC MANAGEMENT OF LOCALIZED RADIATION INJURIES: THE GOIÂNIA EXPERIENCE

9.3.1. Clinical treatment

The systematization of a therapeutical protocol proved to be a hard task owing to the limited experience in handling such a type of pathology [9.9–9.11]. A review of the existing literature was discouraging, since treatment procedures were scarcely described in detail. The guidelines we rested on to treat the radiation lesions presented by our patients were mainly based on previous accident cases and the experience accumulated by the Curie Institute [9.7].

9.3.1.1. Pain management

Pain was always present and accompanied early erythema, being less intense in the latent phase, and severe, continuous and unrelenting during blistering. Patients complained of a burning, pulsating, continuous and deep pain. In the most severe lesions, pain was unbearable and largely unresponsive to analgesics, leading some patients to manifest suicidal intentions. The rupture of large bullae and the removal of dead tissues increased pain by exposing the naked derme to ordinary stimuli, even air movement.

Pain was not completely responsive to drugs. In most cases it was necessary to remove the ulcerated and necrotic tissues. As long as it was not possible to clearly delineate unviable tissues for resection, patients were kept under rigorous analgesia. Generous and continuous use of central-acting analgesics, given either orally or parenterally, were indicated as soon as pain appeared. Intense pain called for the use of opioid analgesia. In the absence of a good response, extradural opioid analgesia was performed [9.12, 9.13]. To avoid excessive

administration of narcotics, ice water was sprinkled around the lesion, which relieved the pain temporarily.

9.3.1.2. Reduction of inflammatory reaction

It is known that inflammation is mediated by chemical metabolites which can produce local vasodilatation (heat and hyperemia), an increase in vascular permeability (tumor), which can provoke pain, and indirectly influence the fibrotic process which will develop later. Thus it is essential to delay or reduce this condition. Various therapies have been tried out clinically and experimentally for this purpose: antihistamines, aspirin, corticoids, epsilon-amino-caproic-acid (EACA), anti-inflammatory drugs and drugs to protect the vascular endothelium, among others.

From a strictly clinical point of view, based only on the observation of patients locally irradiated, we can not say that such drugs are therapeutically effective. On the other hand, every year new and extremely powerful non-steroidal anti-inflammatory drugs (NSAID), capable of quickly reducing inflammation, are available to doctors. It remains to be seen, in the specific case of severe localized radiation injuries, if it is possible to use such drugs over a long period, in view of the adverse effects they invariably provoke (gastric irritation, inhibition of platelet function). In such circumstances it would be advisable to use creams and ointments with local anti-inflammatory effect, that could be used for weeks. The extract of Aloe vera (Aloe barbadensis) much used in cosmetics, is supposed to be a good antagonist of prostaglandin E (the basis for its anti-inflammatory application). Acemannan, the active ingredient of this plant, also influences the proliferation of fibroblasts, endothelial cells and keratinocytes (the basis for its wound care application). It is also known to have a certain effect on cytokines Il-1, Il-6 and TNF. Our experience was limited to the Goiânia patients, who used this product over a long period without any side effects. Healing improvement and diminishing of inflammation were observed in less severe injuries, nonetheless not modifying the outcome of severe lesions.

9.3.1.3. Healing acceleration

Occlusive dressings were applied on open wounds to protect lesions against infections, to reduce pain and to accelerate healing. We know little about the mechanisms by which they act but they probably are based on the migration of epithelial cells from healthy areas surrounding the wounds. An effect on the partial pressure of oxygen and induction of epidermal growth factors is also possible [9.14].

Creams and ointments with fibrinolytic and proteolytic properties (fibrinolysin) were applied on the raw surfaces of the injured dermis. Such use was based largely on favorable results obtained in conventional skin ulcers and was applied only during a short period.

9.3.1.4. Cleaning of wounds and use of antiseptics — Prevention of infection

It was imperative to keep the wound clean and aseptic by repeated bathing with antiseptic solutions, which also provided analgesic, antipruritic and moistering effects. Hands and fingers were immersed in boric acid solution which succeeded to reduce skin dryness, pain and itching.

When blisters and vesicles ruptured, the dermal naked surfaces were protected with non-adherent dressing coated with neomycin. Although the majority of lesions presented bacterial

colonization, only in few instances infections developed during hospitalization. However, non-observation of basic hygienic rules by some patients during outpatient care resulted in late and painful secondary infections that required topic and systemic antibiotics.

9.3.1.5. Improvement of local microcirculation

It is well established that radiation damages small vessels, especially capillaries, inducing death of endothelial cells, loosening or displacement of basement membrane, which in turn induces platelet aggregation and consequent deposit of fibrin. Theoretically, the use of vasodilators could be justified to improve local circulation and reduce ischemia, delaying thrombosis and tissue anoxia. However, a potent vasodilator (nafthydrofuril), when used in patients with extensive lesions showed discouraging results. Nevertheless, systemic vasodilators should be considered in the case of pedicle grafts, to assure blood flow between the host tissues and graft.

A drug capable to improve the flow properties of blood by decreasing its viscosity, with action at the microcirculation level (pentoxifylline) was used in two patients, reducing the risk of early formation of microthrombi, thus improving blood flow in the injured tissues.

In one patient hyperbaric oxygen therapy (HOT) was indicated before grafting to reduce anoxia resulting from ischemia, The measures of transcutaneous pO2 in thigh wound showed values well below the contralateral limb, which indicated compromise of local microcirculation. HOT (20 sessions, 90 minutes, 2.4 atmospheres) hastened granulation at wound edges, reduced the ulcerated area and considerably increasing the local pO2, thus facilitating the integration of the graft with the damaged area.

9.3.2. Surgical treatment [9.15]

Extensive lesions involving thick fatty or muscular regions, required removal of all necrotic and infected tissues, until reaching an area of good blood supply, and only then could the bed of the wound be covered with a good quality split skin graft. In two cases, lesions on the palms of the hand required ample resection, practically to the level of the flexor mechanism, followed by coverage of the ulcer bed with an abdominal flap. The application of a flap gave the region a bulging look which was not esthetically desirable, and limitation of finger flexion was quite evident (Fig. 9.9). Nonetheless, it did eliminate pain and improved the patient's comfort. For cosmetic reasons, removal of excessive fatty tissue through lipoaspiration was suggested, but it was advisable to retain the original remnant, which would serve as a kind of shock-absorbing cushion for the area. After surgery, the region was immobilized with splint during 10 d, after which active and passive mobilization of the hand was begun.

Finger lesions developed very slowly, and sometimes quiescent injuries reopened. Surgical treatment consisted of resection of the lesions followed by coverage with a skin graft. In one case, microsurgery was performed. Transferring a segment of tissue with the intact vascular pedicle to be anastomosed to the finger vessels, thus preserving the most sensitive of the fingertips.

In two patients the development of necrosis and mumification of fingers required amputation as soon as the irreversibility of the damage was confirmed clinically by vascular scintigraphy. In these lesions, the pain, extreme discomfort, and poor evolution helped to

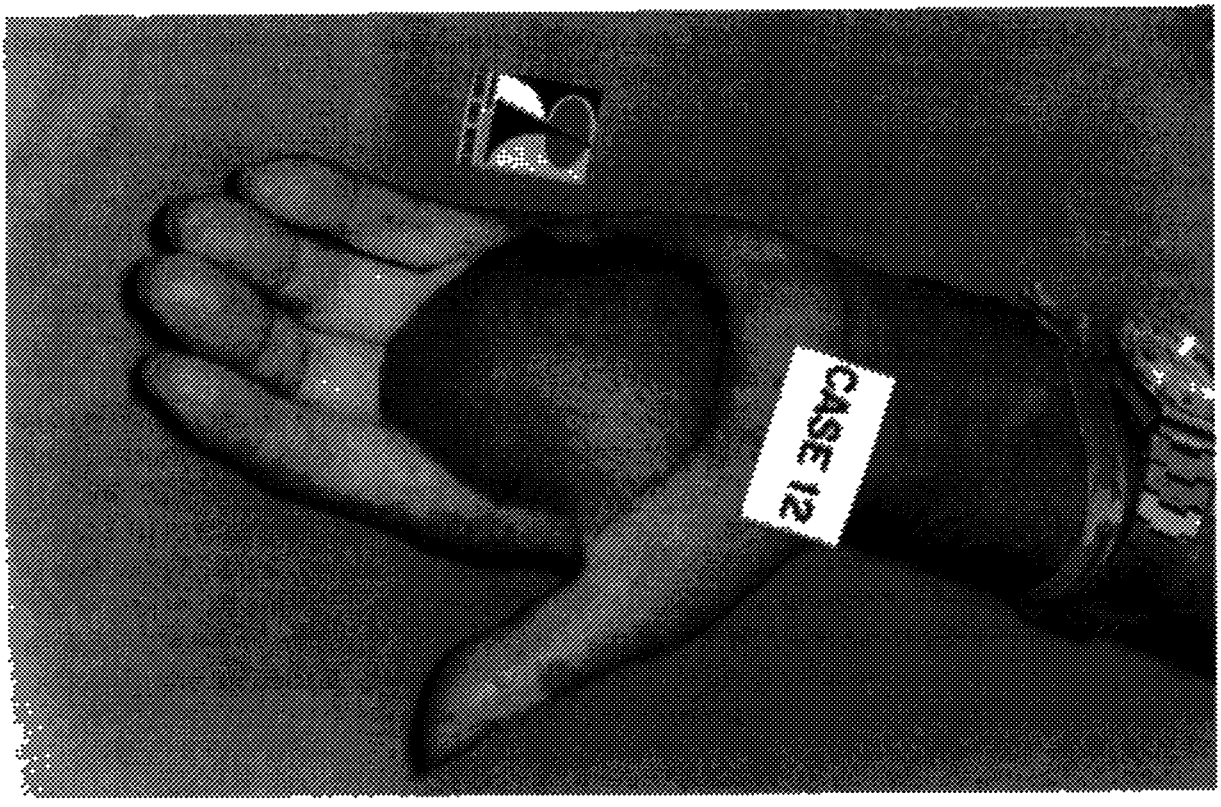

FIG. 9.9. The entire injury was excised and bed of ulcer covered with a full-thickness flap. Palm of hand shows a bulky appearance.

convince the patients of the need for amputation. Early intervention offered many advantages, such as reduction of infectious complications, a shorter period of hospitalization, and greater speed of rehabilitation.

In a patient with a severe radiation injury in the lateral aspect of the right thigh, excision was performed, followed by coverage of the wound bed with a skin graft from the contralateral limb one year after exposure. Aiming for esthetic improvement, a decision was made to use dermoexpander to increase skin area, which could facilitate closure of wound. Unfortunately, dehiscence and infection occurred during expansion, forcing interruption of the procedure.

Not all grafts were successful. In one case this became evident soon after surgery. This lesion comprising the sole of the foot at the level of the hallux, was covered with a skin graft obtained from the unaffected foot, and sutured to the perilesion area after resection of the ulcer. The graft did not "take", both because the patient did not follow instructions about rest and avoidance of trauma and because infection developed. There were additional doubts regarding the viability of the neighboring tissue, and consequently, a conservative approach was adopted with daily dressings changes and applications of antibiotics and topical healing drugs. The affected area became atrophic, deformed, and ankylotic.

9.4. LESSONS LEARNED

The initial treatment of any localized radiation-induced injury can be conservative. The extent of the damage should be clearly defined as soon as possible, when it is possible to

decide whether or not to opt for surgical intervention. Noninvasive procedures are indicated when there is an inflammatory reaction.

If dosimetry and laboratory data indicate that tissue damage is irreversible or that the tissue received doses above those that would respond favorably to any conservative therapy, the patient should be told that the only option is surgery, despite the fact that in most cases the external aspect of lesion offers hope to both doctor and patient of possible recovery. The experience gained recently and the lessons learned from the handling of severe lesions indicate early removal of irreversibly damaged tissue.

The two problems challenging physicians are: (1) determining the extent of the damage and deciding which tissue will inevitably become necrotic and (2) choosing the most suitable moment to perform surgery. If we consider data provided by magnetic resonance imaging, computerized tomography, vascular scintigraphy, hystochemical and immunocytochemical studies of biopsy material, as well as topographic dosimetry (including depth distribution of doses), and taking into account the pathophysiology of the irradiated tissue, then surgery will have great possibilities for success. Ignoring these aspects can lead the surgeon to perform successive and ever-increasing resections, thus delaying healing, increasing the period of disability and endangering the possibility of better future results.

Sometimes, it is difficult to determine the exact moment for surgery. In most cases, the patient reacts peremptorily to any suggestion of early surgery. However, with the failure of the lesion to heal, and the development of infections, algesic crises, functional incapacity, and vasculitis, patients finally recognize the futility of this attitude and even ask the surgeon to act [9.16–9.17]. In any case, it is clear that surgery must be performed only after the development of a necrotic ulcer. At this point, it is mandatory to select the surgical procedure which offers the best possibilities for success in each case.

The repair surgeon, because of the experience acquired with the treatment of conventional thermal burns and trauma, tends to remove only the tissue that appears to be macroscopically inviable. Copious bleeding can create the false impression that sufficient tissue has been removed, but it may only indicate the existence of rigid vessels affected by fibrosis, with little, if any, capacity to contract [9.16]. It is up to the radiation medicine specialist to alert the repair surgeon to the pathophysiology and evolutionary potential for progressively compromise of capillaries and small vessels. Complete excision of damaged tissue will inevitably relieve pain, which is in itself an indication of adequate removal. If not, the lesion will continue to progress, with tissue loss and risk of exposing vital structures such as nerves, tendons, and deep vessels.

9.5. CONCLUSIONS

It was evident that conservative treatment - use of vasodilators, anti-inflammatory and healing drugs - did not greatly modify the clinical evolution of severe radiation injuries. The decision for surgery was taken on the assumption that it would reduce the patient's suffering, preventing secondary infections, improve function, and bring psychological benefit.

One aspect to be strongly considered before surgery is the depth and the extent of injury. It is essential to define areas of poor blood supply caused by a gradual and irreversible obliterating process, which usually can mimic healthy tissue. Certainly, this process plays a very important role in the slow and troublesome injury recovery as well as the vulnerability of

the affected tissue to trauma, temperature, and pressure changes, with consequent reopening of the injury.

During the management of any individual with a severe, localized radiation-induced injury, it is necessary to emphasize the role played by the physician in transmitting sympathy and confidence to the patient. Far from rare, in these cases, is the development of a dependent relationship between the patient and the doctor from whom, in moments of depression, anxiety, and pain, the patient will demand total dedication. Some patients show personality alterations associated with changes in temper and extreme worry with their situation, which can outweigh all other social and emotional problems. The role of the physician at this moment is crucial, for only by both interacting with patients and their families and adopting a knowledgeable technical approach to the medical problems themselves can any meaningful treatment can be delivered.

9.6. FINAL REMARKS

The occurrence of radiation accidents in medicine, industry and research is, fortunately, a rare event. Nevertheless, they can affect members of the public, who inadvertently handle the material, as was the case in Goiânia. We cannot dismiss without comment the inadmissible carelessness of professionals who left a teletherapy source of ^{137}Cs abandoned and without protection [9.18]. It is regrettable, but accidents of this type still occur, particularly in countries where the population lacks information about the risks which uncontrolled radiation sources can represent. Although the Goiânia accident occurred in one of the so- called third world countries, the possibility of an event of this nature occurring in one of the developed countries can not be dismissed. Goiânia itself is a cosmopolitan, socially sophisticated city of more than a million inhabitants and is an important medical center in our country.

The future of the 28 victims, who developed between them more than 100 injuries on their bodies, will depend mainly on the medical attention provided by the multidisciplinary team, and the role of each of these professionals will only have a positive effect if it is performed within the context of the complex of measures necessary for the mental and physical well-being of the patients.

This multidisciplinary team includes specialists in radiopathology, plastic surgeons, psychologists experienced and sufficiently sensitive to understand the chronico-degenerative and incapacitating character of the lesions, and capable of freeing these people from the stigma to which they have been subject, thus enabling them to return to a normal life; a dosimetrist, whose challenge is to attempt a more accurate dose estimate through reconstruction of each victim's relation to the accident, and finally and most important, a medical practitioner, who will be responsible for following their treatment through the years.

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10. THE INFECTIOUS COMPLICATIONS AND HEMATOLOGICAL DISORDERS IN THE GOIÂNIA RADIATION ACCIDENT VICTIMS

10.1. INTRODUCTION

Many of the people (approximately 250) were exposed to large external and internal doses of radiation from the radioactive source. Fifty of them showed signs and symptoms of whole body exposure and/or local acute irradiation as well as external or internal contamination from ingested or absorbed ^{137}Cs [10.1–10.3].

Eight of those 50 developed moderate to severe bone marrow (BM) syndrome and required intensive medical care at a specialized unit in Rio de Janeiro. None were subjected to bone marrow transplants. Ultimately, 4 of these casualties died of bleeding and sepsis despite the administration of rHuGM-CSF (Recombinant Human Granulocyte Macrophage Colony Stimulating Factor) [10.2–10.4].

Internal contamination due to ingestion or absorption of ^{137}Cs was successfully treated by means of the administration of PB, in dosages from 3 to 10 g d^{-1} for adults and from 1 to 3 g d^{-1} for children [10.5–10.7]. Radiation induced skin injuries were observed in 28 patients requiring surgical and post-operative procedures [10.8, 10.9].

The aim of this chapter is to describe the major infectious and hematological disorders related to the acute radiation syndrome due to exposure to ^{137}Cs.

10.2. PATIENTS

Twenty patients were admitted to the Goiânia General Hospital (GGH) and the Marcílio Dias Navy Hospital (MDNH) during the interval between 30 September and 15 January 1988. Fourteen of them were cured at the MDNH in Rio de Janeiro; the remaining six patients were treated at the GGH.

The male:female ratio was 4:1 and the average age was 26.9 years (range 6 to 57). All of them were either relatives or neighbours of those who lived near the yard where the source has been broken, or employees of the owners of the two junkyards to which pieces of the ^{137}Cs teletherapy unit had been taken [10.3].

The routine evaluation consisted of: (a) medical interviews in order to determine whether medical histories were compatible with signs and symptoms of acute radiation syndrome (ARS) and skin radiation injuries. Special attention was devoted to prodromal signs and symptoms such as nausea, vomiting, diarrhea, fever, epilation, weight loss and bleeding; (b) blood counts; (c) biochemical analyses including glucose, BUN, and electrolytes (Na, K, Cl); (d) liver function tests; (e) analysis of urine and stool for ova and parasites [10.3].

Specialize testes consisted of those intended to assess bone marrow depression including bone marrow aspiration (sternal puncture) and biopsy (from iliac spines anterior and posterior). Oral, nose, ear, skin, rectum and vagina swabs and cultures as well as blood cultures were routinely performed and guided the administration of antimicrobial drugs.

10.2.1. Hematological syndrome

The critical phase of the acute radiation syndrome (ARS) in Goiânia was characterized by the hematological syndrome. Fourteen of the twenty severely injured patients developed bone marrow depression, characterized by bone marrow aplasia or hypoplasia. Blood smears and peripheral blood counts indicated leucopenia (leucocytes less than 3.0×10^9 L^{-1}), granulocytopenia (neutrophils less than 1.5×10^9 L^{-1}) and thrombocytopenia (platelet counts less than 60×10^9 L^{-1}).

Eight of these fourteen patients developed the most severe degree of bone marrow impairment, characterized by the classical signs and symptoms of the ARS, such as nausea, vomiting, and severe diarrhoea [10.2, 10.3]. One out of the eight patients belonged to group III of bone marrow depression (estimated dose from 2.0–4.0 Gy), five to group IV (cytogenetic estimated dose 4.0–6.0 Gy), and two to group V (dose higher than 6.0 Gy).

The bone marrow aspirate and biopsy performed in the most critically exposed patients indicated moderate to severe bone marrow hypoplasia, with lower than 30% cellularity and proportional increase in fatty tissue. Another remarkable feature was the moderate to severe degree of eosinophilia in some patients. At least six patients had severe granulocytopenia but only transient and mild thrombocytopenia. A small increase in the mitosis number was found in cells from the bone marrow biopsy in a few cases.

Bleeding diathesis manifestations were recognized in four out of the most eight affected patients hospitalized in Rio de Janeiro and, in at least two cases was responsible for the diffuse hemorrhage in the gastrointestinal tract and central nervous system, despite red and platelet-packed cell transfusion and oral contraceptives [10.3].

The eight most affected victims received a recombinant human granulocyte-macrophage colony stimulating factor (rHu GM-CSF), a molecularly cloned hematopoietic growth factor that stimulates granulocyte progenitor cells [10.9]. GM-CSF was given as a 24 hours continuous intravenous infusion at a dose of 500 mg m^{-2} d^{-1} for 3 d in 0.9% NaCl with 0.9% albumin. Treatment was continued until granulocytes were higher than 2.0×10^9 L^{-1} for 3 d and then decreased to 50% for more 3 d, to 25% for 3 additional d, and then discontinued [10.10].

Four patients (of those eight) who received GM-CSF subsequently died with complications due to hemorrhage and infections resulting from radiation doses (4.0–6.0 Gy). Two patients died of radiation toxicity and hemorrhage and two of the bacterial sepsis with resistant *Klebsiella* sp. infections presumably acquired prior to GM-CSF treatment despite increasing granulocytes counts. Administration of GM-CSF was followed by rare and mild side effects, which included fever, malaise, phlebitis and pulmonary infiltrate. Two patients who received high doses (7.0 and 5.5 Gy) and exhibited bone marrow depression but were not treated with GM-CSF spontaneously recovered and survived.

We consider that the use of GM-CSF was pertinent and we would not hesitate to indicate it in future radiation accident cases, particularly because of its low toxicity and as it does not alter the capacity of the bone marrow to maintain the intricate self-replication and differentiation process of progenitor cells [10.10].

Since February 1988, the most severely exposed victims have been examined quarterly with blood counts. Bone marrow aspirate and biopsy have been made yearly. From the hematological point of view all but four patients have normal blood cell counts. These four patients have mild and transient leukopenia and no clinical and infectious complications. Bone marrow aspirate and biopsy show normality in all three patients, in which a striking eosinophilia was observed. None have developed hematological malignancies until now. Bone marrow aspirate and smears are being collected for cytogenetic purposes, looking for mutation and oncogene markers and chromosomal aberrations.

10.2.2. Infectious complications

The infectious complications of acute radiation syndrome (ARS) caused by exposure and/or contamination with ^{137}Cs had been documented in eight patients with the most severe degree of bone marrow failure and were responsible directly or indirectly for the lethal outcome of four of them. In those persons who died, resistant *Klebsiella* sp. infections, presumably acquired prior to initiating treatment, were responsible for sepsis and shock, unresponsive to antimicrobial drugs and vasopressors.

Due to their imunossupressed status, developed opportunistic infections caused mainly by fungal species (*Candida* sp.) affecting oral, oesophageal, perineal and vaginal mucosae. Neither herpes virus and cytomegalovirus (CMV) were recorded, although preventive measures with anti-viral drugs were undertaken [10.3 and 5].

Patients with severe bone marrow failure were treated in a specialized unit at the MDNH in Rio de Janeiro with all universal radiation protection and microbiological precautions. They remained in isolated rooms, receiving diets free of raw vegetables and uncooked foods.

Infections prevention consisted of gut sterilization with oral sulphamethoxazole-trimephoprim, later changed to Norfloxacin and Nystatin if neutrophils were lower than $1.5 \times 10^9\ L^{-1}$. Patients with fever greater than 38.5° C and granulocytopenia (neutrophils lower than $0.75 \times 10^9\ L^{-1}$) were treated with empirical antibiotic regimen consisting of intravenously Gentamicin (80 mg kg^{-1} every 8 hours), Cephalotin (30 mg kg^{-1}, every 4 hours) and Carbenicillin (75 mg kg^{-1} body weight, every 4 hours) changed to Cefoperazone, Imipenem (1.5 to 3.0 g d^{-1}) and/or Piperacillin (40 mg kg^{-1} body weight, every 4 hours) as a result of cultures and clinical response. Patients with a fever for more than 48–72 hours received Vancomycin and Amphotericin B. Oral candidiasis was prevented by use of Nystatin and for unresponsive cases Ketoconazole or Amphotericin B were administered [10.11, 10.12].

Parenteral nutrition, red blood cells and platelets packed cells transfusions from voluntary blood donors were given to maintain hemoglobin higher than 10.0 g d^{-1} and platelets higher than $20 \times 10^9\ L^{-1}$. Blood products were irradiated in a linear accelerator with 15–25 Gy to achieve sterility and prevent engraftment and graft versus host disease. To accelerate the process for obtaining platelets concentrates, a Fenwall 2922 separator was employed. Acyclovir to prevent herpes virus activation and antihelmintics, such as Thiabendazole and Mebendazole were given [10.2, 10.3, 10.5].

Despite these precautions four patients died, all of them with resistant *Klebsiella* sp. sepsis unresponsive to antibiotics and vasopressors.

10.3. CONCLUSIONS

The Goiânia radiation accident was one of the most serious radiation accidents in the world, characterized by whole body and local irradiation, internal and external contamination.

Bone marrow depression was observed in fourteen victims, eight of them treated with GM–CSF. Six other patients received supportive care including prophylatic antimicrobial, antiviral and antifungal drugs, as well red and platelets packed cells transfusions.

Four patients died during the critical period of acute radiation syndrome due to hemorrhage and infectious complications.

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11. THE MEDICAL FOLLOW-UP (1990–1997)

11.1. INTRODUCTION

Large numbers of persons (approximately 250) were exposed to external and internal doses of radiation from the radioactive source; of these, 50 showed signs and symptoms of whole body exposure and local acute irradiation as well as external or internal contamination from ingested or absorbed ^{137}Cs. Fourteen of those 50 developed moderate to severe bone marrow (BM) syndrome and required intensive medical care at a specialized hospital in Rio de Janeiro. None were subjected to bone marrow transplants. Finally, four of these casualties died of bleeding and sepsis despite the administration of rHuGM-CSF (Recombinant Human Granulocyte Macrophage Colony Stimulating Factor). Internal contamination due to ingestion or absorption of ^{137}Cs was successfully treated by means of the administration of PB at doses from 3 to 10 g d^{-1} for adults and 1 to 3 g d^{-1} for children. Radiation induced skin injuries were observed in 28 patients requiring in some cases surgical and post-operative procedures.

Since March 1988, a medical follow-up protocol was established by CNEN and the Leide das Neves Ferreira Foundation of the State of Goiás, in order to follow-up more than 150 people involved in the accident. The aim of this Chapter is to describe the main after effects of the ^{137}Cs accident in the last 7 years, giving emphasis on clinical, hematological, radiological and psychological aspects.

11.2. PRELIMINARY TRIAGE OF THE RADIATION EXPOSED POPULATION

The initial assessment was carried out at the Olympic Stadium, a football stadium was used by the local authorities as a triage sorting centre. The individuals who handled the source received the highest level of contamination and irradiation. Those people living in houses adjacent to contaminated sites, or who had some type of contact with the victims, were also required to visit the triage centre. In addition, approximately 112 000 people were eventually monitored. In that first evaluation phase, a total of 249 people were identified as contaminated. Among them, 120 presented only clothing and shoe contamination; 129 showed external or internal contamination, and of these, 50 were subjected to direct medical surveillance on 30 September. a significant number were employees of the Sanitary Surveillance Division, members of the Police Department, Fire Department and close relatives of the victims. Of the total, 20 required specialized in-patient treatment because of their clinical and hematological symptoms as well as their local radiation injuries [11.1].

11.3. THE PLAN FOR LEVELS OF PATIENT CARE

Various types and degrees of injuries that may occur in a radiation accident call for a system of levels of patients care ranging from simple medical attention to more sophisticated hospital treatment. In the Goiânia accident, a system was established with the following levels:

Primary care level: The dispensary of the FEBEM (special housing centre); at the primary level were to be patients presenting external contamination and slight internal contamination.

Secondary care level: Goiânia General Hospital; at the secondary level were to be those patients with first and second degree local radiation injuries, or those who had received doses

capable of causing a slight-to-moderate impairment of the hematopoietic system, but who would not require special isolation measures or replacement therapy.

Tertiary care level: Navy Hospital, Rio de Janeiro; was to deal with those patients with severe impairment of the hematopoietic system, as well as those presenting third-degree local injuries.

11.4. CLINICAL AND LABORATORIAL EVALUATION

During the critical period, a significant number of clinical, biochemical and radiometric evaluations were performed on in-patients at Rio de Janeiro and Goiânia. These included peripheral blood smears and bone marrow aspirates; biochemical tests such as glucose, liver function tests, creatinine, electrolytes, cholesterol; evaluations of the immune system; serial microbiological analyses of immunossuppressed patients; cytogenetic analyses for biological dosimetry; electrocardiogram and electroencephalogram; CT scan, scintillography and MRI for local radiation-injuries; sperm counts; radiochemical analyses of feces and urine and whole body counts.

11.5. THERAPEUTIC MEASURES

The therapeutic procedures used during the critical period may be summarized as follows:

- those intended to overcome the critical phase of the acute radiation syndrome represented by bone marrow aplasia or hypoplasia;
- those intended to deal with local radiation injuries;
- those intended to accelerate ^{137}Cs removal from the body;
- those supportive psychotherapeutic measures.

11.6. HEMATOLOGICAL ASPECTS

The critical phase of the acute radiation syndrome (ARS) in Goiânia was characterized by hematological injury. Fourteen of the fifty severely injured patients developed bone marrow depression; and eight of them had classical signs and symptoms of the ARS. Four of them died due to bleeding diathesis and infection (sepsis) caused by Klebsiella resistant to antibiotics and vasopressors. None of them were recommended to have a bone marrow transplant.

Since February 1988, the most severely exposed victims have been examinated quarterly with blood counts, platelets counts, and retyculocytes. Bone marrow aspirate and biopsy were made yearly. From the hematological point of view, all but four patients have normal blood cell counts. These four patients have mild and transient leukopenia and no clinical infectious complications. Bone marrow aspirate and biopsy show normality in all three patients, in which an striking eosinophilia was observed.

Bone marrow aspirate and smears are being collected for cytogenetical purposes, looking for mutation and oncogene markers and chromosomal aberrations.

11.7. RADIATION SKIN INJURIES

Radiation induced skin injuries were observed in twenty eight patients who had handled the source housing or fragments of the source itself.

Victims who handled the container received gamma radiation partly attenuated by the protective shielding material. Localized injuries caused by beta plus gamma radiations were observed in those who handled the unshielded source. Various parts of their bodies, including oral mucosa, had been in direct contact with the radioactive material. Local symptoms appeared a few hours after contact between the source and the skin surface. Pain, sensation of local heat, burning and pruritus, as well as changes in sensitivity were the most frequent complaints.

After the period of latency, a second wave of localized disturbances appeared, characterizing the critical phase, which was represented by secondary erythema, resembling a normal thermal burn. Soon afterwards, blisters or bullae developed, followed by rupture and drainage. Then a skin regeneration process began, characterized by tissue granulation at the outer edges of the injury, progressing toward the centre. As a rule, the recovery process started around 4–6 weeks after exposure in the less affected patients and, in those patients who received intense local irradiation, that recovery was never achieved.

In six cases, significant ulceration developed after a rapid period of erythema and blistering, and there was no latency phase. For the majority of patients, the injuries evolved favorably with complete or nearly complete, recovery within a few months after the accident.

Initially, the radiation skin injuries were managed conservatively by topical applications of antiseptic, anti-inflammatory and analgesic solutions, antibiotic creams (Neomycin) and cream containing substances with anti prostaglandin-like effects and anti-inflammatory actions (Aloe Vera, Allantoin).

The follow-up treatment was continued for patients having only desquamative epithelitis, superficial ulcers or local reactions of an inflammatory nature.

Twelve of the twenty eight victims had multiple injuries, affecting predominantly the upper limbs. Scars remained in eighteen patients after the critical phase of the accident and were managed with topical conservative measures. The injuries did not heal completely and relapsed in eight patients, who then required surgical debridments, amputation of the digital extremities and plastic skin grafts [11.2].

A prospective follow-up protocol of the skin radiation injuries was currently underway including angioscintillography with ^{99m}Tc, electromyography and CT scans in order to evaluate, identify and prevent relapses.

Recently one severely irradiated patient developed on his lower limbs a malignant skin lesion morphologically classified as a lentigo which was surgically excised.

Electromyography had been used to evaluate paresthetic abnormalities, hyperesthesia, hypesthesia, tingling and pruritus, with good results.

A clear limitation of the flexion (ankylosis) in the proximal and distant phalanges of the finger and toes was experienced by four patients due to fibrosis and tissue atrophy. Exercises and kinetic maneuvers were been encouraged.

11.8. CLINICAL ASPECTS — UPDATE (1990–1997)

From the clinical and hematological point of view, the great majority of the patients have been health for the last 5 years.

Gastrointestinal complains, such as heartburn, dyspepsia and nausea were relatively common. Upper gastrointestinal tract endoscopy was made in a significant number of patients, which revealed chronic gastritis, peptic ulcers, esophagitis, related directly or not to *Helycobacter piloris.* Adequate treatment was done with anti-acids H_2 blockers, Metronidazole, diet and psychotherapy support. At the same time, stools were analysed for ova and parasites and revealed intestinal parasites such as *Giardia lamblia, Entamoeba hystolitica* and *Strongyloides stercoralis.* These diseases are not radiation induced; they are not different from those present among the general population in Brazil. It must be borne in mind that the majority of the victims come from a very low social-economic and cultural stratum of the local population. Most of them are heavy smokers, consume high doses of alcohol and eat fatty seasoned food.

Recently (1993) one of the most severely exposed patient (7.0 Gy) developed a chronic liver failure characterized by ascitis, jaundice, gastrointestinal tract bleeding and malaise. he was admitted to the hospital and underwent a liver percutaneous biopsy which displayed alcoholic liver disease. In May, 1994, he was readmitted to the hospital with signs and symptoms of chronic liver failure, such as jaundice, ascitis, encephalopathy and upper gastrointestinal bleeding (melena). He developed hepato-renal syndrome, acute respiratory distress and died. An autopsy was made.

Cardiovascular abnormalities are mainly represented by moderate to light hypertension treated with diuretics and Betablockers.

The male population that received high doses if radiation (more than 1.0 Gy) are oligospermic or azoospermic. The female population displayed commonly gynecological infections due to candida and trichomonas.

At the beginning of 1992, a 32 years old woman, who had received 1.0 Gy of external exposure and a very high internal body burden (3×10^8 Bq), delivered a male baby with good health. Blood counts, cytogenetic dosimetry and whole body counting were performed and no significant internal contamination at time of birth, was noted.

Very recently two patients who received external doses lower than 0.2 Gy died, one of them due to complications of Chagas disease (megacolon and megaesophagus) accelerated by bacterial infection (*E. coli*) and the other due to breast cancer. Neither of them were internally contaminated at time of accident.

11.9. PSYCHOLOGICAL ASPECTS

During the four months the patients were hospitalized in Goiânia and Rio de Janeiro, a number of curious and unusual psychological reactions occurred. The major psychological and psychoneurotic effects of the twenty most severely exposed patients were summarized and presented in a recent paper [11.3]. Of the twenty patients, fourteen developed depression because of the prolonged confinement or because of the stress resulting from the accident itself. Time of confinement increased anxiety, irritability and emotional lability increased. Others displayed insomnia, nightmares and unexpected reactions to the news from the media.

Nowadays, the patients are in the stage of delayed effects. This period is basically represented by the difficult adaptation to a new mode of life and work, by negative attitudes about the sufficiency and equity of social assistance, and the desire to be compensated by the state and to receive secondary benefits.

Two patients, in particular, previously diagnosed as having psychotic syndromes, are still under close surveillance with psychiatrists and psychologists. Carbamazepine, Haloperidol, Amplictil and Phenytoin are being prescribed for these cases. very recently, one of them was once again admitted to a psychiatric hospital and experienced a reactivation of the psychotic syndrome.

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