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● *Medical Aspects*

CLINICAL AND HEMATOLOGICAL ASPECTS OF ^{137}Cs :
THE GOIÂNIA RADIATION ACCIDENT

C. E. Brandão-Mello,* A. R. Oliveira,[†] N. J. Valverde,[‡]
R. Farina* and J. M. Cordeiro[§]

*Instituto de Radioproteção e Dosimetria/CNEN, Av. das Américas Km 11.5, Rio de Janeiro, CEP 22602, Brazil;

[†]Indústrias Nucleares do Brasil S.A., Rio de Janeiro, Av. Pres. Wilson 231, CEP 20030, Brazil;

[‡]Furnas Centrais Elétricas, Rua Real Grandeza 219, Rio de Janeiro, CEP 22283, Brazil;

and [§]Marcílio Dias Navy Hospital, Rio de Janeiro, Brazil

Abstract—Fifty persons involved in the ^{137}Cs accident in Goiânia showed symptoms of whole-body and local acute irradiation and also external or internal contamination mainly due to ingestion or absorption of ^{137}Cs . Fourteen of the 50 developed severe bone marrow depression characterized by neutropenia and thrombocytopenia. Eight of these 14 received GM-CSF intravenously. None were submitted to bone marrow transplantation. Four of the 14 died due to hemorrhage and infection. For those with significant internal contamination evaluated by *in-vitro* and *in-vivo* assays, Prussian Blue was administered with doses ranging from 1.5 to 10 g d⁻¹. Besides Prussian Blue, other measures were taken to increase decorporation of ^{137}Cs , including administration of diuretics, water overload, and ergometric exercises. From 50 to 100 persons are being followed in a medical protocol.

INTRODUCTION

ON 13 SEPTEMBER 1987, a shielded radioactive ^{137}Cs source that contained 50.9 TBq (1375 Ci) was removed by two scavengers from its protective housing in a teletherapy unit in an abandoned clinic in Goiânia, Brazil and was later broken open (IAEA 1988; Alves 1988; Oliveira et al. 1990; Valverde et al. 1990; Oliveira et al., this issue). From 13–29 September 1987, many people received large doses of external or internal radiation from the ^{137}Cs .

Approximately 112,000 people were monitored, of whom 249 were contaminated either internally or externally. One-hundred twenty had light surface or clothing contamination and were rapidly decontaminated. One-hundred twenty-nine had moderate to severe internal or external contamination, and 50 required close medical surveillance; 79 persons with low-dose total-body irradiation were managed as out-patients. Twenty persons out of these 50 were hospitalized at the Goiânia General Hospital (GGH), and 14 of these 20 that required intensive medical care were transferred to a specialized unit in Marcílio Dias Navy Hospital (MDNH) in Rio de Janeiro. Thirty remained under medical observation at a primary care level unit and other dispensaries.

Fourteen persons developed bone marrow failure, and eight of them experienced the prodromal phase of the acute radiation syndrome (ARS). All 20 patients with the most severe internal or external irradiation received clinical, biochemical, hematological, and radiological

evaluations, which consisted of routine and specialized evaluations (Brandão-Mello et al. 1988, 1989).

The main purpose of this paper is to analyze the most outstanding clinical, laboratory, and radiological manifestations of those hospitalized patients and to make some overall comments about diagnostic and therapeutic procedures.

PATIENT TREATMENTS

Twenty persons were admitted to both hospitals (GGH and MDNH) during the interval between 30 September and 15 January 1988. Fourteen of these were cared for at the MDNH in Rio de Janeiro; the remaining six patients were cared for in the GGH. At the end of November 1987, all surviving patients in Rio de Janeiro were returned to GGH where decorporation therapy and medical treatment of skin-radiation injuries continued until it was safe to discharge them from the hospital.

The male:female ratio was 4:1 (16:4) and the median age was 26.9 y (range 6 to 57). All of them were either relatives or neighbors of those who lived near the yard where the source had been broken, or employees of the owners of the two junkyards to which pieces of the ^{137}Cs teletherapy unit had been taken.

The routine evaluation consisted of clinical histories; blood counts including white and red blood cells, platelets, reticulocytes, hematocrit, and hemoglobin; biochemical analyses including glucose, BUN, and electrolytes (Na,

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K, Cl); liver function tests, total protein, albumin, globulin, cholesterol, uric acid, and creatinin; and urinalysis and stools for ova and parasites.

The specialized examination consisted of:

- tests intended to evaluate skin-irradiation injuries including x-ray examinations of extremities, computerized tomography, magnetic resonance imaging studies, and ^{99m}Tc red blood cell pool imaging;

- tests intended to assess bone marrow depression including bone marrow aspiration (sternal puncture) or bone marrow biopsy (from iliac spines anterior and posterior);

- specialized evaluations to assess ophthalmological and endocrine gland abnormalities, such as slit lamp, fluoresceinogram, and sperm counts;

- tests intended to assess internally deposited ^{137}Cs body burden and to monitor the efficacy of Prussian Blue that was given to patients in both hospitals to promote decorporation of ^{137}Cs , as well as other therapeutic measures like administration of diuretics, water overload, and ergometric exercises. *In-vitro* bioassays with radiochemical analyses of urine and fecal samples collected daily from patients with internal contamination and *in-vivo* assay with a whole-body counter that was set up in GGH were performed;

- dose assessments by cytogenetic dosimetry of chromosomal aberrations.

Medical interviews were conducted 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, weight loss, bleeding, and epilation.

Blood samples were obtained daily from each patient to evaluate the degree of bone marrow depression and immunodepression. In those patients in whom bone marrow depression was suggested, bone marrow aspiration and biopsy were performed by standard techniques and submitted to specialized hematologists. Biochemical tests representative of human metabolism were conducted bi-weekly or as indicated by routine assays. Analysis of urine and feces and *in-vivo* whole-body counting were performed and are discussed elsewhere in this issue (Farina et al.; Oliveira et al.).

Dose assessments by cytogenetic dosimetry were performed by standard techniques and methods as specified in IAEA Technical Report No. 260 (IAEA 1986). Whole blood samples were cultured, and after 48 h the lymphocytes were harvested and processed for chromosomal analysis. Since no calibration curve for ^{137}Cs was available, a calibration curve generated for ^{60}Co γ rays at a dose rate of 0.12 Gy min^{-1} was used for the dose estimates (Ramalho et al. 1988).

RESULTS

The major clinical, laboratory, and radiological features of these 20 patients are shown in Table 1. Also shown

are cytogenetic-estimated doses and internal contamination data based on total-body counting and urinary and fecal excretion of ^{137}Cs (Brandão-Mello et al. 1988).

Fourteen out of 20 persons developed moderate to severe bone marrow depression, characterized by bone marrow aplasia or hypoplasia at bone marrow aspiration (sternal puncture) or bone marrow biopsy. Blood smears and peripheral blood counts indicated leucopenia (leucocytes lower than $3.0 \times 10^9 \text{ L}^{-1}$), granulocytopenia (neutrophils lower than $1.5 \times 10^9 \text{ L}^{-1}$), and thrombocytopenia (platelet counts lower than $60 \times 10^9 \text{ L}^{-1}$). Ten of these 14 patients developed the most severe degree of bone marrow impairment. Eight of them developed the classical signs and symptoms of ARS, characterized by gastrointestinal tract symptoms such as nausea, vomiting, watery diarrhea during the prodromal phase, followed by the latent period, the critical phase, and finally the recovery.

One patient belonged to group III of bone marrow depression (estimated dose ranging from 2.0–4.0 Gy), five to group IV (cytogenetic estimated dose ranging from 4.0–6.0 Gy), and the two others from group V (higher than 6.0 Gy). There were six patients who developed moderate bone marrow depression but did not exhibit the prodromal phase of ARS and for that reason were not considered, at the time of this paper, to be suffering from classical ARS (Table 2).

The median interval from initial exposure to granulocytes lower than $1.0 \times 10^9 \text{ L}^{-1}$ was 23 d (range 11–41) and to granulocyte lower than $0.5 \times 10^9 \text{ L}^{-1}$ was 20 d (range 15–30) (Valverde et al. 1990).

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 fat 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.

Infectious complications of ARS were documented in the 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, probably acquired prior to initiating treatment, were responsible for sepsis and shock, unresponsive to antimicrobial drugs and vasopressors (dopamine). It is worth mentioning that due to the immunodepressed status secondary to the ARS, most of these patients developed opportunistic infections caused by fungal agents, like oral, esophageal, and vaginal candidiasis, which were responsible for complaints of dysphagia and odynophagia (Table 3).

Bleeding diathesis manifestations were recognized in four of eight patients hospitalized in Rio de Janeiro and, in at least two cases, the proximal cause of death was diffuse hemorrhage in the gastrointestinal tract and central

Table 1. Clinical and hematological evaluations of 20 patients.

Subject	Age (y)	Sex	Clinical evaluation	Hematol. evaluation	Cytogen. dosimetry (Gy)	GM-CSF	Estimated intake (Bq)	PB*
RSA	22	M	A,C,E,F,H,I,L,N,O	Q,R,S,T,U	6.2	No	1 × 10 ⁸	Yes
WMP	19	M	A,C,D,E,F,I,N,O	Q,R,S,T,U	2.7	Yes	5 × 10 ⁷	Yes
DAF	36	M	A,B,C,D,E,F,H,I,N,O	Q,R,S,T,U	7.0	No	2 × 10 ⁸	Yes
LNF	6	F	A,B,C,F,I,L,M,N,O	Q,R,S,T,U	6.0	Yes	1 × 10 ⁹	Yes
IBS	22	M	A,C,E,F,I,L,M,N,O	Q,R,S,T,U	4.5	Yes	5.5 × 10 ⁷	Yes
MGF	38	F	A,B,C,E,F,H,I,J,L,M,N,O	Q,R,S,T,U	5.5	Yes	2 × 10 ⁷	Yes
AAS	18	M	A,B,F,H,I,M,N,O	Q,R,S,T,U	5.3	Yes	1 × 10 ⁸	Yes
MGA	57	F	A,B,C,F,H,I,N,O	Q,R,S,T,U	4.3	Yes	1 × 10 ⁷	Yes
GGS	21	M	A,E,H,O	Q,R,S,T,U	2.9	Yes	1 × 10 ⁸	Yes
EF	42	M	O,P	Q,R,S,T,U	4.4	Yes	4.5 × 10 ⁷	Yes
EBS	13	M	O,P	Q,R,S,T,U	2.9	No	3.5 × 10 ⁷	Yes
LNF	14	M	O,P	Q,R,S,T,U	1.3	No	2 × 10 ⁸	Yes
OAFJ	12	M	O,P	Q,R,S,T,U	1.6	No	1 × 10 ⁸	Yes
LOMS	28	F	A,N,O	Q,R,T,U	1.0	No	4 × 10 ⁸	Yes
IAF	40	M	O,P	T	3.0	No	1 × 10 ⁸	Yes
EF	46	M	O,P	R,T	2.1	No	8 × 10 ⁵	Yes
KSS	30	M	O,P	V	1.1	No	5.5 × 10 ⁷	Yes
OAF	32	M	O,P	V	1.0	No	5.5 × 10 ⁶	Yes
MPG	33	F	O,P	V	0.6	No	4.5 × 10 ⁶	Yes
SPQ	13	M	O,P	V	0.6	No	8 × 10 ⁶	Yes

A. Anorexia
 B. Bleeding
 C. Vomiting
 D. Diarrhea
 E. Weight loss
 F. Fever
 G. Abdominal ache
 H. Epilation/hair loss
 I. Infection
 J. Jaundice
 L. Anemia

M. Death
 N. Nausca
 O. Radiodermatitis
 P. Asymptomatic
 Q. Bone marrow aplasia/hipoplasia
 R. Leukopenia
 S. Thrombocytopenia
 T. Lymphopenia
 U. Neutropenia
 V. Normal

* PB = Prussian Blue, administered in doses ranging from 3.0–10.0 g d⁻¹.

nervous system (Table 4) (Selidovkin 1989; Brandão-Mello 1989).

Biochemical tests

A number of biochemical tests were performed twice weekly or as indicated. Some of them covered a long period of time, and hypocholesterolemia (lower than 150 mg%) and hyperuricemia (higher than 7.0 mg%) were observed in eight patients. Other abnormalities were episodic; for instance, hypoproteinemia was observed in three patients during the deepest phase of bone marrow depression, when those patients were receiving antimicrobial and antifungal drugs. Hypocholesterolemia and hypoproteinemia have been described by Jammet et al. (1980) and hyperuricemia by Andrews et al. (1980).

Liver functions

Slight disturbances of liver function were found in a few cases at the time of hospitalization. These included mild elevations of aminotransferases (ALT/AST), neither persistent nor higher than 2.5 times the normal limit. One of the patients with the most severe bone marrow depression disclosed bleeding diathesis, jaundice, and anemia. This patient had a previous history of anemia, and at

autopsy chronic liver disease was suspected (macroscopic view) (Kumatori et al. 1980).

Electrolytes

Since Cs is a K analogue and is distributed predominantly intracellularly, the serum levels of K were evaluated twice a week and whenever there was a clinical indication to do so. The serum levels of K did not have a significant variation (3.4–4.6 mEq L⁻¹).

Sperm counts

The examination of spermatopoiesis was performed on nine of the 20 persons. The spermatozoa were reduced or absent in the semen (azoospermia) by November 1987. Reduced motility and abnormal spermatozoa were also observed. Testicular biopsies were not performed (Kumatori et al. 1980).

Ophthalmological findings

A few patients complained in the first days postexposure of lacrimation, hyperemia and edema of the conjunctiva, and pain in the eyeball. There were a few cases of protracted reduction in visual capacity, and they were referred to the Goiânia Eye Institute (Dr. Marcos Avila

Table 2. Acute radiation syndrome and bone marrow depression.

Bone marrow depression (grade)	BMDS ^a	Hospitalized patients	ARS ^b	Deaths	Cytogenetic dose (Gy)
I	01	4	None	0	0.2-1.0
II	02	3	None	0	>1.0-2.0
III	03	5	1	0	>2.0-4.0
IV	06	6	5	4	>4.0-6.0
V	02	2	2	0	>6.0
Total	14	20	8	4	

^a Bone marrow depression syndrome, clinically characterized by leukopenia, lymphopenia, granulocytopenia, and thrombocytopenia on peripheral blood counts and bone marrow aplasia or hypoplasia at bone marrow aspiration or biopsy.

^b Acute radiation syndrome, clinically characterized by prodromal phase, latent period, critical phase, and recovery.

et al.) in March 1988 to perform slit lamp, fluoresceinography, indirect ophthalmoscopy, tonometry, and refraction exams. No change in the lens transparency of the patients examined was recorded, but retinal abnormalities with radiation injury could be noticed and were documented (Kumatori et al. 1980).

DISCUSSION

The radiation accident in Goiânia was one of the most serious radiation accidents in the world and pointed out several difficulties to medical and health care workers. It was particularly unique in that whole body and local irradiation occurred at the same time and in the same patient associated with internal and external contamination.

The critical phase of ARS was represented by the hematological syndrome. We could not identify any case of gastrointestinal tract or CNS involvement as the critical phase in Goiânia, except for GI and CNS bleeding due to thrombocytopenia seen at autopsy. Fourteen patients developed bone marrow failure. Four of them died during the first month after the accident from complications of ARS, including bleeding diathesis and infection (sepsis) (Oliveira et al., this issue; Valverde et al. 1990).

Patients with severe bone marrow failure were treated in a specialized unit at MDNH in Rio de Janeiro with radiation protection precautions. They remained in isolation rooms with diets free of raw vegetables and uncooked foods. Infection prevention consisted of gut sterilization with oral trimethoprim-sulfamethoxazole and nystatin if neutrophils were lower than $1.5 \times 10^9 \text{ L}^{-1}$. Persons with fevers greater than 38.5°C and granulocytopenia (neutrophils lower than $0.75 \times 10^9 \text{ L}^{-1}$) were treated with empirical antibiotic regimen consisting of IV Gentamicin, Cephalothin, and Carbenicillin changed to Cefoperazone, Imipenem, and/or Piperacillin as a result of the evolution and/or cultures. Persons with a fever for more than 48-72 h received Vancomycin and/or Amphotericin B.

Parenteral nutrition, red blood cells, and platelet transfusions from voluntary unrelated blood donors were given to maintain hemoglobin higher than 10.0 g dL and platelets higher than $20 \times 10^9 \text{ L}^{-1}$. Blood products were irradiated with 15-25 Gy to prevent engraftment and graft vs. host disease. Acyclovir to prevent herpes virus activation and antihelmintics, such as Thiabendazole and Mebendazole, were given (Valverde et al. 1990; Butturini et al. 1988).

Despite these precautions four patients died, all of them with resistant *Klebsiella* sp. sepsis unresponsive to antibiotics and vasopressors. We cannot assume that they were colonized or infected prior to treatment with *Klebsiella* sp.; however, the pathogen isolated was resistant to all antibiotics tested except Polimixin B (Butturini et al. 1988).

The first two patients to die developed diffuse and severe hemorrhage to the GI tract and CNS, the probable cause of death despite red and platelet-packed cell transfusion. The clinical course and laboratory findings indicated that bone marrow transplantation was not required for any patient (Gale and Reisner 1988).

Eight victims in the hospital in Rio de Janeiro received a recombinant human granulocyte-macrophage-colony stimulating factor (GM-CSF), a molecularly cloned hematopoietic growth factor that stimulates granulocyte progenitor cells (Butturini et al. 1988).

GM-CSF was given as a 24-h continuous intravenous infusion at a dose of $500 \text{ mg m}^{-2} \text{ d}^{-1}$ in 0.9% NaCl with 0.9% albumin. Treatment was continued until granulocytes were higher than $2.0 \times 10^9 \text{ L}^{-1}$ for 3 d. The dose was then decreased to 50% for 3 d, to 25% for 3 additional d, and then discontinued (Butturini et al. 1988).

Four patients who received GM-CSF subsequently died with complications of hemorrhage and infection as a result of their radiation doses (4.0-6.0 Gy). Two patients died of radiation toxicity and hemorrhage and two of bacterial sepsis with resistant *Klebsiella* sp. infections acquired prior to GM-CSF treatment despite increasing granulocytes. It is difficult to establish whether the bone marrow response was due to GM-CSF or due to infection, since both GM-CSF and infection (sepsis) rapidly increase the leukocyte count with an important shift to the left and immature forms.

The four surviving patients treated with GM-CSF included two treated early and who never developed infections. It is worth mentioning that reduction in GM-CSF dose resulted in rapid decrease in granulocytes followed by recovery, and that side effects were mild in most instances. These included rare fevers, malaise, phlebitis, and pulmonary infiltrate. Three persons developed respiratory failure while receiving GM-CSF. Bacterial sepsis was the likely cause, but GM-CSF toxicity cannot be excluded (Butturini et al. 1988). Two persons who received high doses (6.2-7.1 Gy) and exhibited severe bone marrow depression but who did not receive GM-CSF spontaneously recovered and survived (Fig. 1).

Use of GM-CSF was based on the assumption that residual progenitor cells existed and that a factor able to

Table 3. Clinical manifestations and infectious complications of acute radiation syndrome.

Clinical manifestations and infectious complications				
Subject	Site	Cultures	Antibiotics	Bone marrow depression (grade)
RSA	Right forearm	Negative	Gentamicin, Amikacin, Cephalothin, Cefoxitin	V
	Oral	<i>Candida</i> sp.	Nystatin, Amphotericin B, Parenteral Nutrition	
WMP	Tip of a subclavia Catheter	<i>Staphylococcus</i>	Vancomycin	III
	Blood (sepsis)	<i>Pseudomonas aeruginosa</i>	Cefoperazone, Imipenem	
DAF	Unknown	Negative	Gentamicin, Carbenicillin, Cephalothin	V
	Oral	<i>Candida</i> sp.	Amphotericin B, Parenteral Nutrition	
LNF ^a	Oral and esophageal	<i>Candida</i> sp.	Amphotericin B	IV
	Blood (sepsis)	<i>Klebsiella</i> sp.	Gentamicin, Carbenicillin, Cephalothin, Piperacillin, Cefoperazone, Parenteral Nutrition	
JBS ^a	Perineal	<i>Candida</i> sp.	Ketoconazole (topical)	IV
	Skin	<i>Klebsiella</i> sp.	Carbenicillin, Cefoperazone, Gentamicin, Piperacillin, Cephalothin, Vancomycin	
	Blood (sepsis)	<i>Klebsiella</i> sp.		
MGF ^a	Oral and esophageal	<i>Candida</i> sp.	Amphotericin B	IV
	Vagina	<i>Klebsiella</i> sp.	Cefoperazone, Piperacillin, Carbenicillin, Gentamicin, Cephalothin	
	Blood (sepsis)	<i>Escherichia coli</i> <i>Klebsiella</i> sp.		
MGA	Oropharynx	<i>Candida</i> sp., <i>Klebsiella</i> sp.	Nystatin	IV
	Vagina	<i>Candida</i> sp., <i>Klebsiella</i> sp.	Cefoperazone, Piperacillin	
	Rectum	<i>Klebsiella</i> sp.	Parenteral Nutrition	
AAS ^a	Blood (sepsis)	<i>Klebsiella</i> sp.	Cefoperazone, Piperacillin, Amphotericin B	IV

^a Subject died.

Table 4. Clinical manifestations and bleeding diathesis of acute radiation syndrome.

Clinical manifestations and bleeding diathesis				
Subject	Type/site	Platelet level	Therapy	Bone marrow depression (grade)
LNF ^a	Hematemesis	$25-50 \times 10^9 \text{ L}^{-1}$	Platelet transfusions Red packed cells GM-CSF	IV
	Melena			
	Epistaxis			
	CNS and intestine ^b			
MGF ^a	Skin and palatal petechiae	$27.7 \times 10^9 \text{ L}^{-1}$	Platelet transfusions Red packed cells GM-CSF Oral contraceptives	IV
	Orbital hematomas			
	Rectal bleeding			
	CNS and intestine ^b			
MGA	Plantar areas/petechiae	$21.0 \times 10^9 \text{ L}^{-1}$	Platelet transfusions Red packed cells GM-CSF	IV
	Hematomas			
	Rectal bleeding			
AAS ^a	Bruises on scleris	$11.0 \times 10^9 \text{ L}^{-1}$	Platelet transfusions Red packed cells GM-CSF	IV
	Hemorrhagic spots in GI tract ^b			

^a Subject died.

^b Discovered at autopsy.

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stimulate their proliferation and differentiation might play an important role in rejuvenating the natural defense mechanism of the irradiated patients. Although in the present case GM-CSF administration began when bone marrow recovery is expected to begin spontaneously, it seems clear to us that some patients, showing severe depression, responded promptly to GM-CSF with a remarkable increase in peripheral blood circulating cells. Was that coincidental? This does not seem to be the case. The myeloproliferative effect of the GM-CSF can also be estimated even when doses were reduced. Reduction in GM-CSF doses resulted in rapid decrease in granulocyte curves. When the drug was stopped at least for one patient, the granulocyte count dropped, and when treatment was resumed, it rose immediately (Fig. 2). On such occasions, a clear dose-dependent effect was noticed (Oliveira et al. 1989; Butturini et al. 1988).

The fact that four patients did not present a satisfactory response to the drug does not invalidate the possible and further use of GM-CSF or other hematologic

growth factors in patients with bone marrow failure caused by exposure to ionizing radiation. These data suggest a possible role for molecularly cloned hematopoietic growth factors to treat victims of radiation or nuclear accidents. Further studies of the experimental and clinical usage are required to identify which factors are most effective, what optimum dosage is, and how and when they are best given before future application in actual radiological accidents (Gale and Butturini, in press; Butturini et al. 1988).

It is worth mentioning that one female patient out of four from group I (doses ranging from 0.2-1.0 Gy) developed a moderate bone marrow depression. This woman had a high internal contamination at the first whole-body count ($31.7 \pm 5.4 \times 10^6$ Bq; $857 \pm 146 \mu\text{Ci}$) in November 1987 (estimated intake, 4.0×10^8 Bq). Two patients from group II (doses from 1.0-2.0 Gy) also developed bone marrow depression syndrome. One of them was heavily contaminated internally (estimated intake, 2×10^8 Bq). These data show that high body burdens were also responsible for internal irradiation. Two patients from

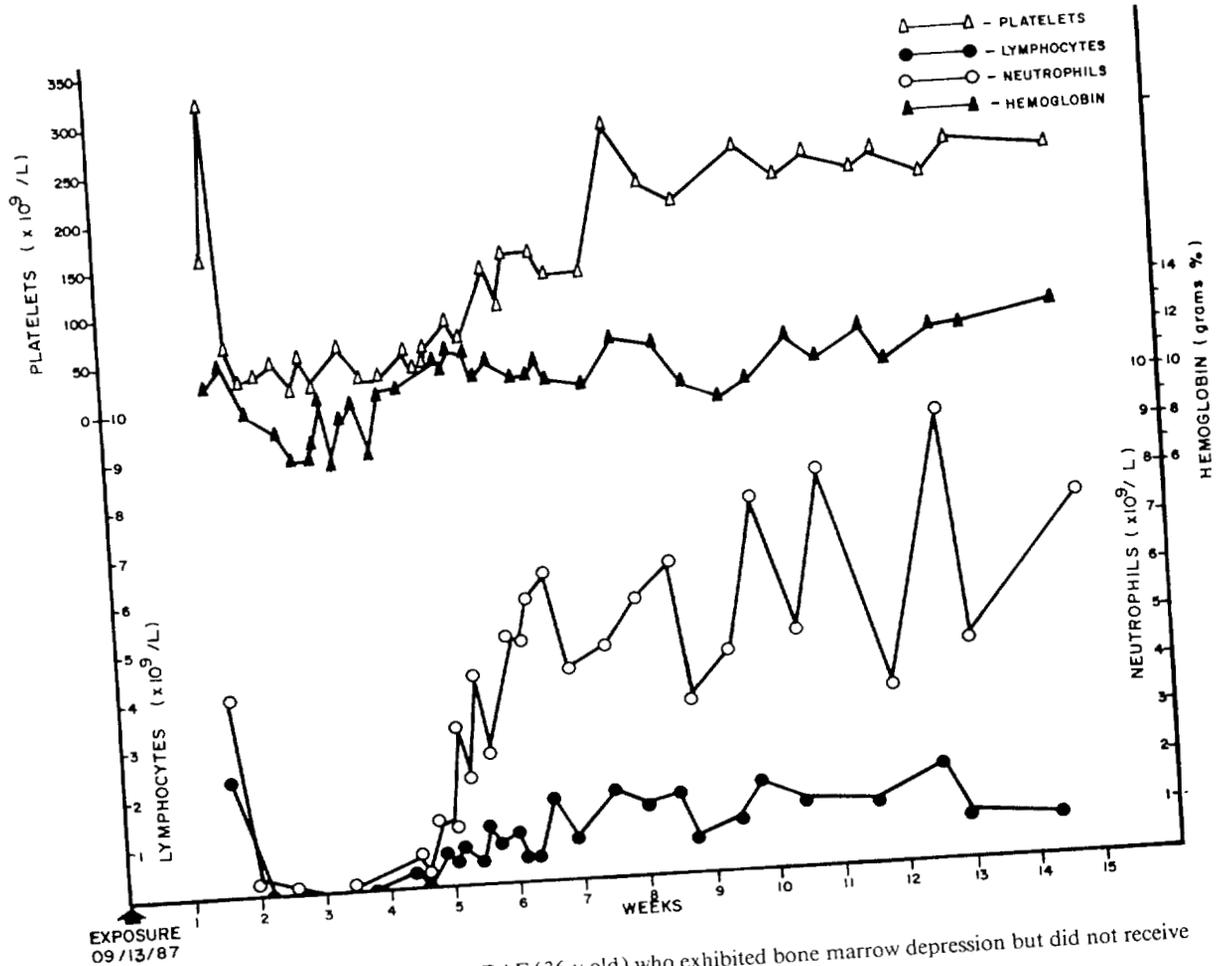


Fig. 1. Hematological curve of patient DAF (36 y old) who exhibited bone marrow depression but did not receive GM-CSF.

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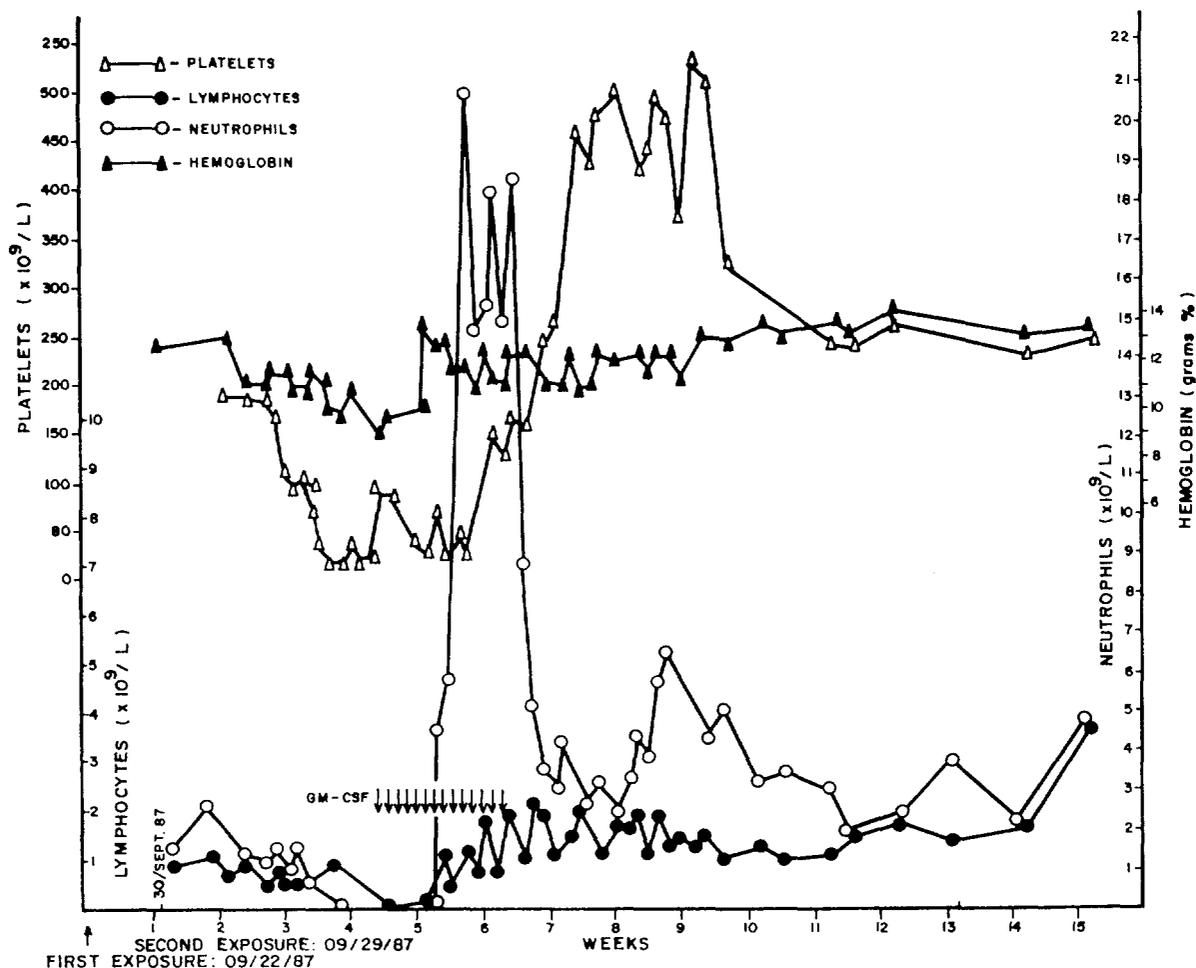


Fig. 2. Hematological curve of patient MGA (57 y old) who exhibited bone marrow depression but did receive GM-CSF.

group III (2.0–4.0 Gy) did not develop bone marrow failure as they were almost exclusively irradiated locally, disclosing severe skin-irradiation injuries, which required surgical debridements and skin grafts.

More than 110 blood samples from persons affected by the accident were analyzed by cytogenetic methods. The frequency of chromosomal aberrations in cultured lymphocytes was determined, and the doses were estimated using *in-vitro* calibration curves. This analysis, however, was complex. The protracted vs. acute exposure, the nonuniform distribution of doses, the lack of an ideal calibration curve (^{60}Co was used), and the continuous radiation from internally deposited ^{137}Cs all complicated the interpretation of cytogenetic dose estimates that were based on a chronic exposure model (Ramalho et al. 1988).

To surmount these difficulties, clinical dose estimates based on the interval from first exposure to the time when granulocytes were lower than $1.0 \times 10^9 \text{ L}^{-1}$, and $0.5 \times 10^9 \text{ L}^{-1}$, clinical course and time of onset of prodromal symptoms, and hematological curves were very useful to-

gether with the cytogenetic dose estimates in predicting the degree of bone marrow depression and the consequent degree of susceptibility to infection (Ramalho et al. 1988).

Decorporation of ^{137}Cs internal contamination was successfully achieved by Prussian Blue at doses ranging from $3.0\text{--}10.0 \text{ g d}^{-1}$ for adults and $1.0\text{--}3.0 \text{ g d}^{-1}$ for children. Diuretics, water overload, and ergometric exercises were also given to some patients who had high levels of internal contamination. Results are discussed elsewhere in this issue (Farina et al., this issue).

Radiochemical analysis for urine and fecal samples as well as total-body counting were very effective in detecting internal contamination with ^{137}Cs and very useful in monitoring the efficacy of drugs like Prussian Blue (see Farina et al., this issue).

CONCLUSIONS

1. The Goiânia radiation accident was one of the most serious radiation accidents in the world, character-

ized by whole and local irradiation, internal and external contamination, and skin-irradiation injuries.

2. Bone marrow depression was observed in 14 victims, eight of them being treated with granulocyte-macrophage-colony stimulating factor (GM-CSF). Six others received supportive care including prophylactic antibiotics, antiviral and antifungal drugs, as well as transfusions of red and platelet packed cells.

3. We consider that the use of GM-CSF on our patients was pertinent, if only because it enabled us to observe its potential effect in proliferating and differentiating progenitor cells of the hematopoietic system, as demonstrated in previous experimental studies (Metcalf 1985, 1986). We would not hesitate to indicate GM-CSF in future radiation accident cases, particularly because of its low toxicity during administration (fever, myalgia, phlebitis) and also because it has not, so far, altered the capacity of the bone marrow to maintain, within satisfactory limits, the intricate self-replication and differentiation process of progenitor cells.

4. Four patients died during the first month after

the accident from complications of acute radiation syndrome, including bleeding and infections.

5. Internal contamination due to inhalation, ingestion, or absorption of ^{137}Cs was assessed by *in-vivo* and *in-vitro* assays. Persons with substantial internal contamination received Prussian Blue at doses ranging from 1.0 to 10.0 g d⁻¹. Since Cs is a K analogue, diuretics, water overload, and ergometric exercises were also used.

6. Cytogenetic dose estimates were very helpful in providing useful information to the physicians responsible for diagnosis and prognosis and in anticipating medical management problems associated with bone marrow failure.

Acknowledgments—We are indebted to Drs. Adriana Ramalho and Ana Cristina Holanda de Nascimento for performing cytogenetic dose estimates. We are also indebted to Drs. Joyce Lipsztein, Carlos Alberto Nogueira, and Luiz Bertelli for performing *in-vivo* and *in-vitro* assays, Ms. Mara Lucia Lara for the computer analysis and generation of tables and graphs, and to Dr. Francisco Borges and Quimarcos from the Goiânia General Hospital for hematological and microbiological analysis.

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