Appendix II

MEDICAL TREATMENT

Appendix II presents a general summary of the medical treatment of the three patients. Annexes I and II provide nutritional reports specific to the treatment of the patients in Mexico City. The information presented in this appendix and in Annexes I and II was provided by the medical teams at the Primero de Mayo Hospital in San Salvador and the Angeles del Pedregal Hospital in Mexico City. It is recognized that in some respects the data are incomplete. Nevertheless, it is considered important to present those that are available. This has been done with a minimum of editorial changes to the English translation of the text provided by the medical teams.

AII.1. INITIAL DIAGNOSIS AND TREATMENT AT THE PRIMERO DE MAYO HOSPITAL IN SAN SALVADOR

The first medical examination of Patient A took place in the Primero de Mayo Hospital in San Salvador at 03:55 on Day 1 (Sunday 5 February), when prodromal symptoms such as intense nausea, vomiting, total erythema, weakness and headache had developed. The patient was misdiagnosed as having food poisoning and nausea and discharged at about 06:00 the same day.

The first laboratory analyses of samples were carried out on Day 3 (Tuesday 7 February) and a severe lymphopenia was registered: the cell count was about 500 μL^{-1} (compared with about 2500 μL^{-1} normally).

In the first two to three days, Patient A's main complaints were weakness, nausea, headache, anorexia and pain in the feet. Total erythema showed up slightly. Dark hyperaemia of the skin on the legs and feet was strongly developed with oedema. A diagnosis of severe radiation lesions was consequently made. In this period the patient received appropriate symptomatical therapy.

It should be noted that prodromal symptoms in combination with deep lymphopenia could be an indication for acute radiation syndrome (ARS) in addition to radiation burns.

The prodromal phase of ARS is usually followed by a latency period. In the case of Patient A, however, the severe radiation damage to the mucosa of the mouth and oesophagus appeared on Day 4 (Wednesday 8 February) and developed with the occurrence of some ulcers. It was not possible for him to eat normally. The mouth pain was intense and almost continuous for two weeks.

Another symptom of acute radiation syndrome, radiation enteritis, began on Day 8 (Sunday 12 February). It was manifested by diarrhoea, vomiting and pain. Fever began at the same time.

The main syndromes of ARS cytopenia became evident at the same time: the number of leucocytes in the blood was 2900 μL^{-1} on Day 6 (Friday 10 February) and only 900 μL^{-1} on Day 10 (Tuesday 14 February). A typical abortive rise in the number of granulocytes was observed on Day 19 (Thursday 23 February), but this was not significant (maximum 1900 μL^{-1} leucocytes). The decreasing concentration of thrombocytes was evident after Day 10 (Tuesday 14 February) and a minimum level of about 20 000 μL^{-1} was observed after 20–25 days. There was no significant decrease in the concentration of erythrocytes, but a drop in that of haemoglobin was evident, to 86 $g \cdot L^{-1}$ (normally 160 $\pm$ 2 $g \cdot L^{-1}$).

After a latency period (from Day 4 to Day 14: Wednesday 8 to Saturday 18 February), the skin lesions began to cause difficulties and severe pain, and oedema of feet and skin followed by the development of ulcers was observed.

By Day 11 (Wednesday 15 February) the medical staff of the Primero de Mayo Hospital in San Salvador considered that the patient might require bone marrow transplantation. On Day 24 (Tuesday 28 February), Patient A was transferred to the Angeles del Pedregal Hospital in Mexico City. Similar documented clinical information in respect of Patients B and C was not available.

AII.2. TREATMENT IN THE ANGELES DEL PEDREGAL HOSPITAL IN MEXICO CITY

Upon arrival at the Angeles del Pedregal Hospital, the three patients were carefully examined and their medical histories were recorded. The patients were found to be exhibiting signs and symptoms of whole body irradiation (see Tables VI and VII) with acute injury to the legs and feet (Figs 18–20). The diagnosis was made of ARS in the latent period characterized mainly by severe pancytopenia, which occurs about 20 days after whole body irradiation.

Immediately after the patients' admission to the Angeles del Pedregal Hospital, it was decided to conduct the following studies:

(1) routine laboratory and X ray screening;
(2) bone marrow aspiration and bone biopsy;
(3) making of ABO blood group cultures and human leucocyte antigen (HLA) aspiration biopsy cytology (ABC) cultures, degeneration reaction (DR) cultures, complotype cultures and mixed lymphocyte cultures for Patients A and B and their brothers;
(4) calorimetric and nitrogen balance analyses;
(5) serology studies for Herpes I and II, cytomegalovirus, human immunodeficiency virus (HIV) and viral hepatitis profile;
(6) electrocardiogram, echocardiogram and cardiological evaluations;
(7) analysis of cultures of the feet obtained serially;

TABLE VI. SIGNS AND SYMPTOMS FOR PATIENTS A, B AND C UPON ADMISSION TO THE ANGELES DEL PEDREGAL HOSPITAL

Signs and symptoms	Patient A (On Day 24)	Patient B (On Day 26)	Patient C (On Day 33)
Nausea	Moderate	Mild	None
Vomiting	Moderate	Mild	None
Diarrhoea	Severe	None	None
Weight loss	10 kg	4–5 kg	None
Meatal obstruction[a]	Severe	None	None
Foot pain	Severe	Severe	None

[a] Secondary to mucous plug.

TABLE VII. RESULTS OF PHYSICAL EXAMINATIONS FOR PATIENTS A, B AND C UPON ADMISSION TO THE ANGELES DEL PEDREGAL HOSPITAL

	Patient A (Day 24)	Patient B (Day 26)	Patient C (Day 33)
Karnovsky score	30%	30%	80%
Pallor	Severe	Moderate	Moderate
Bleeding	Gingival and epistaxis	No	No
Petechia and echymosis	In venipuncture sites	In venipuncture sites	No
Mucositis	Severe	Moderate	No
Body temperature	39.5°C	39.0°C	Normal
Xerostomy	Present	Present	Absent
Alopecia	Total	Partial	Minimal, biparietal

TABLE VIII. VITAL HAEMATOLOGICAL VALUES FOR PATIENTS A, B AND C UPON ADMISSION TO THE ANGELES DEL PEDREGAL HOSPITAL

Patient	Haemoglobin ($g \cdot L^{-1}$)	White blood cells (μL^{-1})	Total neutrophil count[a]	Platelets (μL^{-1})
Patient A (Day 24)	60	200	0	20 000
Patient B (Day 26)	86	700	56	54 000
Patient C (Day 33)	84	2300	437	35 000

[a] Total neutrophil count is calculated as count per unit blood volume multiplied by estimated blood volume.

(8) computerized tomography of legs and magnetic nuclear resonance as well as Doppler studies of the legs;
(9) cytogenetic dosimetric studies of blood samples obtained.

For Patients A and B the positive results of laboratory studies were as follows:

(1) severe pancytopenia with life threatening neutropenia (see Table VIII);
(2) bone marrow aplasia in aspiration and bone biopsies;
(3) cultures of the feet were positive for *Staphylococcus saprophyticus* (coagulase negative) and *Staphylococcus aureus*;
(4) ABO blood groups and HLA:
Patient A: O positive. A3, A28, B35, B7, Bw6, Cw4 and MLC negative and identical HLA, ABC, DR and complement with four identical brothers.
Patient B: A positive. A1, A28, B35, BX, Bw6, Cw4 and MLC negative and identical HLA, ABC, DR and complement with one identical brother.

Treatment strategy

(1) *A multidisciplinary medical team.* A medical team and a paramedical team were established for a multidisciplinary approach, including specialists in: haematology; bone marrow transplantation; infectology and hospital infection control; clinical laboratory analysis; cytogenetics; cardiology; clinical nutrition; plastic and vascular surgery as well as general surgery; nuclear medicine; pathology; psychiatry; anaesthesiology; pain clinic; dermatology; and physiotherapy. Nurses with

extensive experience in the management of neutropenic patients were assigned to each patient. Consultations were established with advisers and experts from the Mexican National Commission for Nuclear Safety and Safeguards and from REAC/TS at Oak Ridge, USA.

(2) *Intensive supportive care.* The patients were put in reverse isolation in single rooms. All medical and nursing staff and relatives as well as visitors in contact with the patients wore caps, gowns, sterile surgical gloves, face masks and sterile boots, and washed their hands with iodine solution before visits. Food was sterilized in microwave ovens. Strict precautions were taken in puncturing the skin and intramuscular injections were restricted. Vascular access for Patients A and B was with Hickman double lumen catheters for intravenous fluids, drug administration, total parenteral nutrition, and blood and component therapy transfusions, as well as for taking laboratory blood samples.

(3) *Transfusion.* Administration of packed red blood cells was indicated to maintain the haemoglobin level higher than 100 $g \cdot L^{-1}$. HLA compatible platelet concentrates donated by matched brothers were obtained by standard haematological techniques with an intermittent cell separator machine (Haemonetics 30S, Braintree, Massachusetts, USA). Transfusions were administered when the platelet count was below 20 000 μL^{-1} or when there were signs of bleeding with a platelet count of below 50 000 μL^{-1}. All blood cell products administered were first irradiated to 20 Gy in order to prevent acute graft versus host disease after the transfusion.

(4) *Clinical nutrition.* Nutritional conditions were carefully evaluated. Patient A was put on parenteral nutrition and Patients A and B on enteral nutrition. Supervision was on a daily basis; nitrogen balance and calorimetric estimates were made and potassium, calcium and albumin counts were performed, and diets were adjusted accordingly in an attempt to overcome the patients' calorie and protein malnutrition on admission. (A detailed description is given in Annexes I and II.)

(5) *Intestinal sterilization.* Oral and intestinal sterilization with nystatin and trimethoprim–sulphamethoxasole was indicated for Patient A; likewise for Patients B and C but in the neutropenic period only.

(6) *Treatment of infectious complications.* Systemic administration of amikacin, vancomycin and cephtazidime IV was used successfully to treat staphylococcal infections in Patients A and B, with fever remission after three days of therapy. Only Patient A received amphotericin B for oral, oesophagal and urinary infection by *Candida albicans*, demonstrated by signs and symptoms as well as by direct identification and cultures.

(7) *Treatment of haematological disturbances.* The three patients met the established criteria for bone marrow depression of differing severities. They were referred to the medical staff in the Angeles del Pedregal Hospital for inclusion in the

bone marrow transplantation programme. However, bone marrow transplantation was considered not to be indicated in view of the poor clinical condition of Patients A and B and well known complications of the treatment (high risk of infection due to long term immunosuppression, graft versus host disease, drug toxicity) and uncertainties about the follow-up and treatment in San Salvador.

Treating the bone marrow depression

Since the precise indications for bone marrow transplantation in patients who have received high radiation doses due to whole body irradiation in accidents remain uncertain, it was decided to use recombinant human GMCSF (rHuGMCSF; supplied by Scheramex Laboratories, Mexico City) on the basis of its ability to reduce the interval of life threatening neutropenia associated with chemotherapy, as demonstrated in various clinical trials.

For all three patients, the administration of rHuGMCSF was commenced at a daily dose of 240 $\mu g \cdot m^{-2}$ body surface area by intravenous infusion for two hours until the total neutrophil count (TNC) had increased to at least 1500 μL^{-1}. The numbers of days required for TNC and for haematological recovery are indicated in Table IX. The medical team at the Angeles del Pedregal Hospital considered that the

TABLE IX. HAEMATOLOGICAL RECOVERY FOR PATIENTS A, B AND C

Patient	Number of days for recovery[a] of total neutrophil count (TNC)		Number of days for recovery of platelets		Number of days for recovery of haemoglobin	
	Since accident	Since first intake of GMCSF[b]	Since accident	Since first intake of GMCSF[b]	Since accident	Since first intake of GMCSF[b]
Patient A	44	20	132	108	—	—
Patient B	36	10	42	16	80	56
Patient C	43	9	41	7	48	14

[a] The criterion for recovery of the total neutrophil count is defined as an increase in the count of 1500 μm^{-1} over the lowest value recorded.

[b] rHuGMCSF was first administered to Patients A, B and C on Day 24 (Tuesday 28 February), Day 26 (Thursday 2 March) and Day 33 (Thursday 9 March) respectively. The figures given are the number of days for which rHuGMCSF was administered.

increase in TNC was due to the administration of rHuGMCSF in view of the following observations:

(a) The nadir of cytopenia after whole body irradiation was evident in the three patients upon admission to the Angeles del Pedregal Hospital, with spontaneous recovery expected only after at least three weeks.
(b) The number of days required for the TNC to increase to 1500 was 20 for Patient A, ten for Patient B and nine for Patient C from commencement of the course of rHuGMCSF. The haemoglobin and platelet values were 80 $g \cdot L^{-1}$ and 11 000 μL^{-1} for Patient A; 90 $g \cdot L^{-1}$ and 76 000 μL^{-1} for Patient B; and 78 $g \cdot L^{-1}$ and 133 000 μL^{-1} for Patient C. The patients were dependent on transfusions at this time.
(c) The spontaneous recovery of haemoglobin and platelet counts was greater than that of TNC, which bears out the fact that rHuGMCSF stimulates granulocyte precursors only.
(d) Bone marrow aspiration when TNC reached 1500 μL^{-1} showed increased granulocyte mass and decreased red blood and megakaryocyte precursors.
(e) The increase in eosinophils in Patients A and B also suggested indirect effects of rHuGMCSF.

In early June the bone marrow aspiration showed dishaematopoietic morphological changes despite normal serum levels of iron, folic acid and vitamin B12 and this was the reason for the persistence of anaemia 172 days after admission.

Acute local radiation injury

Severe radiation injuries to the skin and underlying tissues of the lower extremities of Patients A and B were manifested by swelling, erythema, hyperpigmentation, epilation, and dry and wet desquamation. Radiodermatitis was observed in the anterior abdominal wall and chest in Patient A, and swelling of the lower legs after three days. Significant oedema and erythema were seen after a week in Patient A. Epilation with dry and wet desquamation was evident by a week after the accident (see Figs 18–20). The patterns of epilation and desquamation as well as the degree and extent of local skin injury reflect each person's position in relation to the source at the time of the exposure.

Treatment of acute local radiation injury consisted of daily surgical debridement with the use of antiseptic and analgesic solutions and topical antibiotics. Areas of dry desquamation were observed and were allowed to evolve through an expected clinical course of sloughing and epithelialization. By early June the extensive dry desquamation experienced by Patient A had evolved its clinical course and, with the exception of the hands, the skin appeared normal. His hands were partially depigmented and covered with thin, fragile epithelium. They were fully functional and not painful.

By early June only partial healing was evident of the parts of the body that had sustained high doses, namely the feet and lower legs. The patients were unable to stand and were experiencing severe pain from which almost no analgesic drugs or narcotics gave any relief. A mild response was found only with meperidine IV. Amniotic membranes were used to cover the plantar surfaces of the patients' feet. The blood flow to the lower extremities was evaluated by blood pool imaging, Doppler tests and magnetic resonance imaging. No significant circulatory embarrassment or deep tissue necrosis was revealed.

Nevertheless, a progressive dry gangrene occurred in the right foot of Patient A which ultimately necessitated amputation above the knee on Day 132 (Friday 16 June). A similar but delayed process was evident in Patient B, leading to amputation of the left leg on Day 161 (Saturday 15 July). Platelet recovery occurred; however, pain increased and there was progressive necrosis in the feet with no response to the antiaggregating agents used. After amputation, the general condition of Patients A and B improved and their requirements for drugs to reduce pain were less.

On Day 173 (Thursday 27 July), Patients A and B left the Angeles del Pedregal Hospital and were returned to the Medico-Surgical Hospital of the ISSS in San Salvador. Patient C, who experienced no severe localized radiation injury, returned to San Salvador on Day 55 (Friday 31 March), having recovered from his haematological depression.

Psychiatric treatment

Depression and anxiety were the main psychological disturbances suffered by the patients, and pain in the feet contributed to their emotional upset, especially for Patient A. Psychological and emotional support given by medical staff, nurses and family members were essential to the care of all three patients. Psychiatric consultations were made when necessary, and therapy was given to counter depression and anxiety arising as a result of prolonged confinement, incapacitating pain, fear of amputation, fear of dying, and separation from family and friends. Antidepressant medication was given when necessary.

AII.3. FURTHER TREATMENT IN SAN SALVADOR

Patient A

After returning to San Salvador on Day 173 (Thursday 27 July), Patient A remained at home until Day 177 (Monday 31 July) and was then transferred to a special room prepared for him in the Medico-Surgical Hospital. The follow-up treatment could not be fully carried out, mainly owing to the unavailability of prescribed

medicaments. On Day 187 (Thursday 10 August), a few days after his readmission to hospital in San Salvador, Patient A's condition began to deteriorate. By Day 191 (Monday 14 August) his condition had become critical, with high fever, rapid breathing, pneumonia, infection of his other (left) leg, poor circulation and low blood pressure, and he was moved to the intensive care unit. On Day 192 (Tuesday 15 August) he sustained a pneumothorax as a consequence of the perforation of the lung membrane by a catheter. His haemoglobin count fell from 100 to 50 $g \cdot L^{-1}$, and the concentration of thrombocytes dropped to 20 000 μL^{-1}. The treatment plan prescribed was for blood transfusion, administration of antibiotics and albuminum infusion. Nevertheless, it was considered that he might still recover from this condition after the planned amputation of his other (left) leg.

Patient A died at 07:00 on Sunday 20 August, 197 days after the accident. Since his family did not give the permission necessary for a post-mortem examination to be performed, no definite cause of death can be stated. Radiation induced pneumonitis complicated by traumatic perforation of the lung membrane may be considered to be the main cause of death.

Patient B

After returning to San Salvador on Day 173 (Thursday 27 July), Patient B also remained at home until a special room was set up for him in the Medico-Surgical Hospital. His general condition continued to improve, but the condition of his other (right) leg worsened, with poor circulation, infection and extreme pain. Wide antibiotic coverage was prescribed before amputation was performed on Day 202 (Friday 25 August). Subsequently, Patient B was recovering and was in good physical and mental condition. However, his risk of developing cataracts is high.

Patient C

Patient C returned home to San Salvador on Day 55 (Friday 31 March) and from Day 58 (Monday 3 April) he was under observation as an outpatient by the ISSS. Except for residual but less evident effects in his left foot, the prognosis for his full recovery is good. On Day 199 (Tuesday 22 August) he returned to work at the plant and on Day 220 (Tuesday 12 September) he commenced physiotherapy for his left foot.

Annex I

PATIENT A: A NUTRITIONAL REPORT BY THE ANGELES DEL PEDREGAL HOSPITAL IN MEXICO CITY

Patient A entered the Angeles del Pedregal Hospital with a diagnosis of exposure to ionizing radiation resulting in secondary dermatomucositis and medullary hypoplasia. In the first evaluation of his condition, on Day 25 (Wednesday 1 March), a body weight of 50 kg was noted, representing 82% of the theoretically appropriate weight for his height (1.65 m) and average build. Patient A had lost 10 kg in the previous month. The tricipital cutaneous fold measured 6 mm (50% of the theoretical value), 23 mm being the sum of the four standard folds and 220 mm the mesobrachial circumference. The laboratory reported serum albumin of 34 $g \cdot L^{-1}$, which became 23 $g \cdot L^{-1}$ once the patient had undergone hydration; serum globulins were 24 $g \cdot L^{-1}$. Indirect calorimetry indicated an energy consumption of 1800 kcal (7530 kJ) with oxidation of 130 g in lipids, 95 g in carbohydrates and 60 g in proteins, a pattern suggesting the presence of sepsis. This evidence indicated the following body composition: brachial muscular area about 22 cm^2; muscular mass 14 kg; fat mass 4 kg; lean mass 46 kg; total body water 34 kg; this pointed to a weight deficit of 10 kg in muscular mass and a diagnosis of second grade protein denutrition.

A diet was worked out containing 3000 kcal (12 550 kJ), with 100 g of protein, 410 g carbohydrates, 105 g lipids, 120 milliequivalent (mEq) sodium [one milliequivalent is the number of grams of solute contained in one millilitre of Normal solution], 140 mEq potassium, and 45 mMol phosphates and calcium. It was hoped that this diet would lead to a weight increase of 220 g per day.

To deal with anorexia and poor absorption, parenteral feeding was adopted from the time of Patient A's admission to the hospital on Day 25 (Wednesday 1 March) until Day 67 (Wednesday 12 April). His admittedly scant oral ingestion was continued at the same time in order to maintain trophic stimulus to the intestinal mucosa. During this period, twenty-four hour losses of uric nitrogen in urine were 20–37 g (daily average) with creatinine excretion of 0.97–1.00 $g \cdot d^{-1}$, indicating a serious catabolic state. During this period, the net nitrogen loss was between 3 $g \cdot d^{-1}$ and 6 $g \cdot d^{-1}$, equivalent to a loss of muscular mass of 180 $g \cdot d^{-1}$.

When parenteral feeding was started, the patient's energy consumption rose to 2440 kcal (10 210 kJ) with oxidation of 104 g of lipids, 207 g of carbohydrate and 138 g of protein. No mechanical, metabolic or septic complications that could have been attributed to the parenteral feeding were detected during the whole period (certain extreme laboratory results were explained by the fact that samples had been taken by catheter during the parenteral feeding).

When the cycle of parenteral feeding was finished, we noted a weight increase to 55 kg and an increase in the tricipital cutaneous fold to 7 mm, with the mesobrachial circumference remaining at 220 mm. Twenty-four hour urinary creatinine dropped to 0.71 g and serum albumin rose to 30 $g \cdot L^{-1}$. The ending of the parenteral feeding cycle, decided on since the malabsorption problem seemed to have been solved, coincided with the suspension of the administration of the medullary stimulation factor and a reduction in urinary excretion of nitrogen. This exceptionally important reduction led us to think of the medullary stimulation

factor as a catabolic agent for extramedullary tissue (as is reported in connection with other similar substances).

During the period from Day 68 (Thursday 13 April) to Day 87 (Tuesday 2 May), the patient's oral ingestion was carefully monitored; we noted, however, that there was no adequate acceptance of the diet owing to anorexia with a consequent loss of 6 kg in weight. During this period ingestion did not rise above 1200 kcal (5020 kJ) and 45 g of protein, whereas the measured energy consumption was about 1500 kcal (6280 kJ). A nasogastric probe was therefore inserted in order to cover the patient's nutritional requirements. At the outset there was a certain intolerance of the enteral feeding which manifested itself in nausea and steatorrheic stools, as a result of which high doses of pancreatic enzymes had to be administered together with loperamide up to 30 $mg \cdot d^{-1}$. In this way it was possible to restore adequate digestion and absorption, according to the clinical indicators, and the patient's weight increased by 2 kg within 40 days.

Following supracondylar amputation of the right leg, the patient weighed 43 kg, and it was possible to maintain a daily weight increase of 40 g. On Day 157 (Tuesday 11 July) serum albumin was 27 $g \cdot L^{-1}$; anthropometry indicated a weight of 44 kg with a tricipital cutaneous fold of 3.5 mm, a mesobrachial circumference of 205 mm and the sum of the four folds 16 mm, indicating recovery of the brachial muscular area to 22 cm^2. Energy consumption was evaluated by calorimetry to be 1500 kcal (6280 kJ), whereas it was not possible for oral ingestion to rise above 1300 kcal (5440 kJ) and 65 g of protein. The possibility of malabsorption was evaluated by determining the fat content of the faeces once the administration of pancreatic enzymes and loperamide had been suspended, and the possibility of pancreatic insufficiency or other damage was investigated by tomography of the pancreas. These possibilities were thereby eliminated.

The nutritional diagnosis remained second degree denutrition with serious muscle wastage through disuse without malabsorption. During the patient's hospitalization it was impossible to carry out an intensive physiotherapy programme owing to his state of severe psychic depression. The nutritional plan for the following days required an energy input of 2500 kcal (10 460 kJ) with 120 g of protein, 300 g of carbohydrate and 90 g of lipids, in a fractionated oral diet including five meals (breakfast at 07:30, a mid-morning snack at 11:00, lunch at 13:00, tea at 17:00 and dinner at 21:00). Enteral feeding was to be resorted to if the anorexia persisted, with a nasogastric probe and infusions of 400 mL every three to four hours. This diet would need to be supplemented by calcium (2 $g \cdot d^{-1}$), orally administered multivitamins and zinc sulphate (25 $mg \cdot d^{-1}$). Among the factors responsible for the persistent denutrition in Patient A's case must be listed firstly anorexia and secondly the disuse of muscular function, both being secondary to the severely depressed state of the patient. There seemed to be no objective organic conditions that would have justified the anorexia.

It should be noted that throughout his hospitalization Patient A remained bedridden with very little activity, a situation which favours not only muscular but also bone catabolism, and it was not possible to reverse the latter even by administering high doses of calcium (1.5–3.0 $g \cdot d^{-1}$). Without supplementary calcium, a substantial rise in alkaline phosphatase was observed, which did not drop off completely even when the calcium supplement was resumed. For practical purposes, it might have been useful to try calcitonin, but not in the areas affected by radiation and osteomalacia. In the event that bone decalcification persisted, when active mobilization was recommenced it would have been important to test the response to calcitonin in vivo before administering this compound on a therapeutic basis.

The following points remained to be clarified:

(1) The question of whether a forced, intensive physiotherapy programme applied from the beginning would have modified the evolution of muscular wastage and improved the trophism of the affected muscle and skin.

(2) The question of whether the use of medullary stimulation factor played a decisive role in inducing the catabolic state observed in Patient A.

Annex II

PATIENT B: A NUTRITIONAL REPORT BY THE ANGELES DEL PEDREGAL HOSPITAL IN MEXICO CITY

Patient B was referred to Clinical Nutrition on Day 26 (Thursday 2 March) with a diagnosis of exposure to ionizing radiation and secondary dermatomucositis.

Physical examination revealed the following alterations: thin skin, conjunctival pallor, fissured lips, bleeding gums, hot tongue, xerosis of the skin, altered pigmentation and muscular hypotonia.

Patient B's weight on admission on Day 26 (Thursday 2 March) was 60 kg (84% of the theoretically appropriate value): his normal weight was 65 kg (91% of the theoretically appropriate value) and he had lost 5 kg over the previous month. His height was 1.77 m, the tricipital cutaneous fold was 8 mm (80% of the theoretical value), and the sum of the four principal folds was 26 mm. The patient was slight of build and showed poor physical autonomy. The laboratory reported serum albumin of 34 $g \cdot L^{-1}$, lymphocytes 500 μm^{-3} and twenty-four hour urinary creatinine 1.4 g.

These data enabled us to calculate the following body composition: brachial muscular area 36 cm^2; fatty mass 6 kg; lean mass 53 kg; muscular mass 23 kg; total body water 39 kg. This added up to a weight deficit of 4 kg, including 3 kg muscular mass.

Indirect calorimetry indicated an oxygen consumption of 325 $mL \cdot min^{-1}$ and carbon dioxide production of 277 $mL \cdot min^{-1}$, with a respiratory quotient of 0.85, corresponding to a consumption of 2300 kcal (9620 kJ), with oxidation of 204 g glucose, 89 g lipids and 130 g protein.

The nutritional diagnosis was first grade protein denutrition. The nutritional recommendations were as follows: energy input 3300 kcal (13 810 kJ); protein 130 g; carbohydrates 530 g; lipids 98 g; sodium 70 mEq; potassium 130 mEq; calcium and phosphorus 49 mMol. With this prescription it was hoped to bring about a daily increase of 200 g in body weight. The feeding path initially recommended was oral, but in view of the patient's poor oral ingestion of the recommended diet and his rejection of an enteral probe, it was decided to supplement the diet by parenteral feeding since a central catheter was available. The parenteral feeding was started on Day 27 (Friday 3 March) and continued until Day 49 (Saturday 25 March), providing 85 g amino acids, 200 g glucose, 100 g lipids and 2100 kcal (8790 kJ) in total by this path. In conjunction with oral ingestion, the parenteral feeding succeeded in arresting the patient's intense catabolic decline and in improving the nitrogen balance from $-20\ g \cdot d^{-1}$ to $-1\ g \cdot d^{-1}$, which reduced muscle loss to approximately 30 $g \cdot d^{-1}$. At the end of the parenteral feeding period (22 days) the serum albumin level had risen slightly to 36 $g \cdot dL^{-1}$; the anthropometric values remained constant. There were no mechanical, metabolic or infectious complications in the administration of parenteral feeding.

When the parenteral support was suspended, oral ingestion remained within acceptable limits during the first two weeks, then dropped successively to values of 1500 kcal (6280 kJ) and 1200 kcal (5020 kJ) and 40 g protein, which meant a progressive weight loss of 100–150 $g \cdot dL^{-1}$. The reason for the reduced oral ingestion in the following three months was anorexia due to depression and poor acceptance of the standard meals provided by the hospital.

On Day 169 (Sunday 23 July) a new evaluation was made, revealing twenty-four hour creatinine excretion in the urine of 1.05 g; weight 49 kg (68% of theoretical); tricipital cutaneous fold 8 mm (80% of theoretical); sum of the four folds 28 mm; a mesobrachial circumference of 243 mm (90% of theoretical); brachial muscular area 28 cm^2; fat body mass 5 kg; lean mass 43 kg; muscular mass 19 kg; total water 31 kg; and a deficit of 10 kg of muscular mass. The albumin value was 41 $g \cdot L^{-1}$ and the oncotic pressure was 32 mmHg.

In view of the albumin value and the absence of sepsis or a critical state, a diagnosis of second degree protein–muscle malnutrition of the marasmic type was then made. On many occasions it was planned to try the enteral path to supplement the patient's scant oral ingestion, using a nasogastric probe, but in consequence of the patient's rejection of this probe it was finally decided to use strictly supervised oral feeding, which had variably satisfactory results.

From Day 150 (Tuesday 4 July) onwards it was possible to maintain oral ingestion above 2000 kcal (8370 kJ), as compared with a measured energy output of 1600 kcal (6690 kJ), with oxidation of 177 g carbohydrates and 45 g protein. This permitted a daily weight increase of approximately 100 g, and the patient's weight rose to 50.5 kg by Day 159 (Thursday 13 July). Following amputation, in order to alleviate the intense trauma induced catabolism, peripheral parenteral feeding was applied for two days with an input of 1900 kcal (7950 kJ), 100 g lipids, 85 g amino acids and 180 g glucose. Once oral ingestion had been completely restored, this parenteral support was suspended. The nutritional recommendations as of Day 166 (Thursday 20 July) were 2700 kcal (11 300 kJ), 420 g glucides, 67 g lipids and 100 g protein, with 100 mEq potassium, 40 mMol calcium and orally administered vitamin supplements, the diet being without restriction and divided into four meals per day.

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San Salvador
24–28 July 1989

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