

## APPENDIX

### Acute radiation effects in victims of the Chernobyl nuclear power plant accident

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#### *Introduction*

1. This Appendix sets out the essential findings of the clinical observation of a group of patients suffering from acute radiation sickness following the accident at the Chernobyl nuclear power plant on 26 April 1986. The observations were conducted at the specialized treatment centre in Moscow over a period of two years.

2. An initial report on the accident was submitted by the Soviet representatives to the Post-Accident Review Meeting held at the International Atomic Energy Agency in August 1986 and was summarized in IAEA Safety Series Technical Report No. 75 [118] and in [G33]. The proposal to present this information in its present form was endorsed at the thirty-sixth session of UNSCEAR in March 1987.

3. The basic information on the radionuclide releases and the types of exposures of the irradiated persons coincided with the expected pattern for an accident at a nuclear power plant of similar type: as much as 100% of gaseous fraction of the noble gases and nuclides may have escaped from the plant; caesium, iodine and tellurium isotopes accounted for up to 10-20% of the nuclide inventory, and other radionuclides for up to 30% [118].

4. The plant personnel and auxiliary staff present at the industrial site in the immediate vicinity of the accident zone were subjected to the combined effect of radiation from several sources: (a) short-term external gamma/beta radiation from the gas emission cloud (in

the case of persons in the immediate area of the accident zone at the time of the explosion); (b) external gamma/beta radiation of decreasing intensity, from fragments of the damaged reactor core scattered over the industrial site; (c) inhalation of gases and aerosol dust particles containing a mixture of radionuclides; and (d) deposition of these particles on the skin and mucous membranes at the time of the intensive generation of steam or dust and the wetting of clothing (as a result of them being blown or washed off contaminated objects).

5. However, the most significant factor was the general, external and relatively uniform whole-body gamma-irradiation and the beta-irradiation of extensive body surfaces, coupled (except in two cases) with a very small intake of nuclides through inhalation, predominantly of radioiodine and caesium isotopes. Thus, the basic clinical picture was that of a distinctive acute radiation sickness caused by gamma-irradiation of the whole body and by beta-irradiation of extensive areas of the skin surface.

6. Direct and indirect dosimetry methods were used to determine the nuclide content in the body. A great many tests were carried out, both while the victims were alive and (in 28 cases) after they had died, so that it was possible to estimate the nuclide content in the body and the resultant dose levels. An example of these types of analyses is shown in Figure A.I., giving the distribution of various radionuclides in the lungs.

7. The iodine isotope content in the thyroid gland was determined repeatedly (as many as four to six

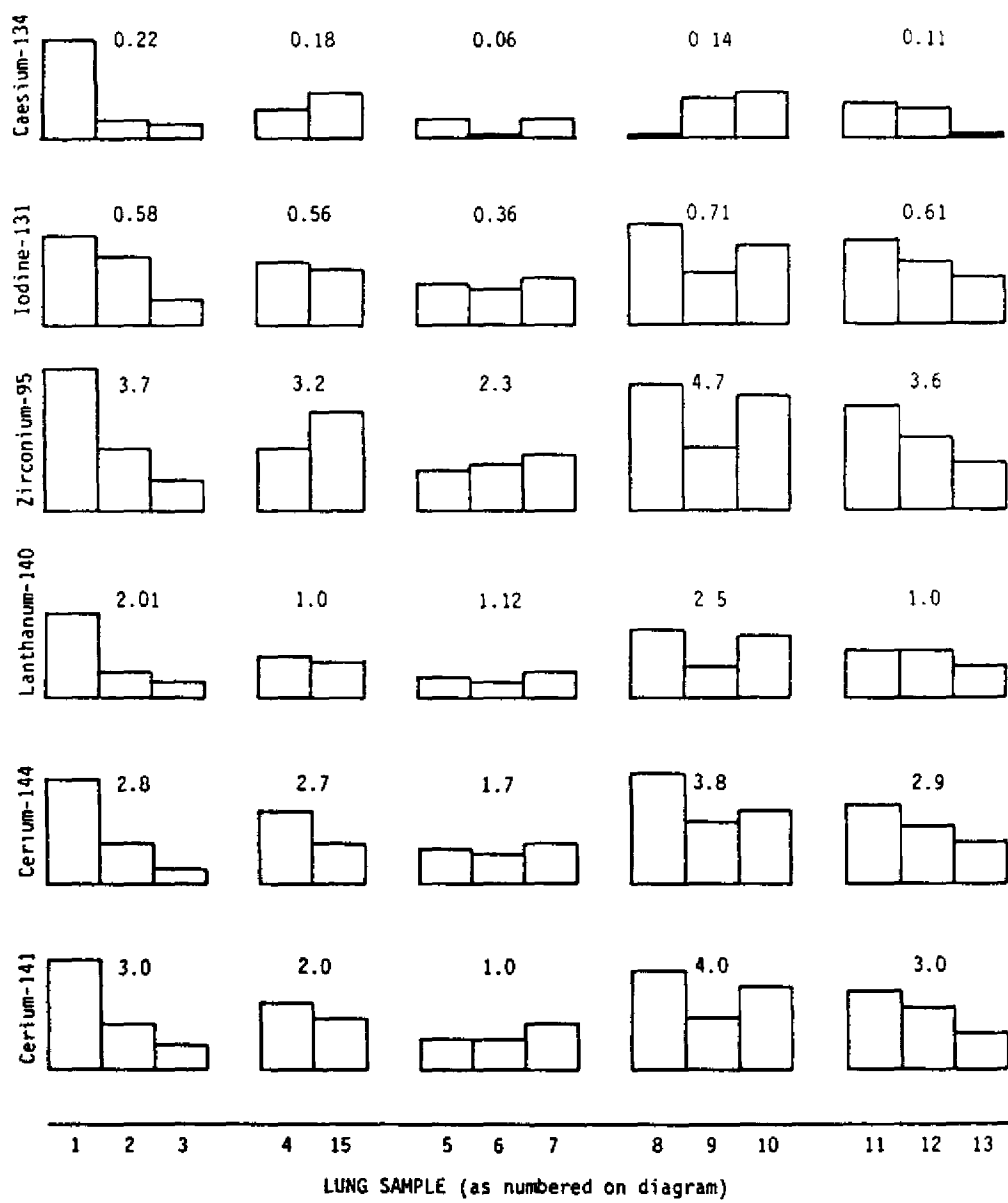
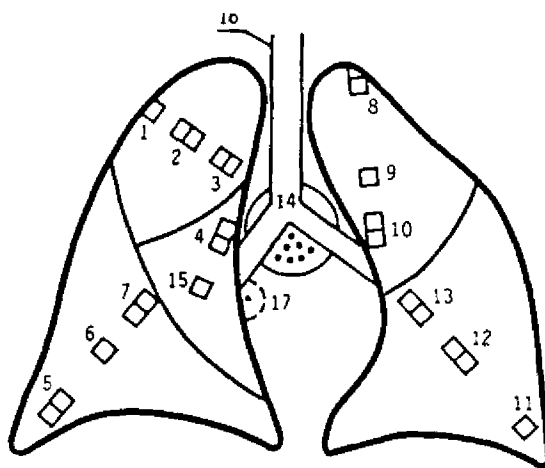


Figure A.I. Location of lung samples taken at the time of autopsy and distribution of the main radionuclides in lung samples. The number above each sample group indicates the approximate relative average value.

times) from the second day after the accident. These measurements showed that  $^{131}\text{I}$  accounted for  $80 \pm 20\%$  of the total activity of all iodine isotopes,  $^{133}\text{I}$  for  $15 \pm 10\%$ , and the remaining isotopes ( $^{123}\text{I}$ ,  $^{124}\text{I}$ ,  $^{126}\text{I}$ , and  $^{130}\text{I}$ ) for not more than 2%.

8. The calculations for estimating intake quantities from the thyroid measurements were performed according to the recommendations of the International Commission on Radiological Protection [I19]. On the basis of the distribution of thyroid doses in exposed individuals (Table A 1), it may be stated that in the overwhelming majority of cases the thyroid doses were below the levels likely to cause direct injury to that organ ( $< 3.7 \text{ Sv}$ ) or of significantly influencing the clinical picture during the onset of acute radiation sickness. Low radioiodine dose levels were also suggested by the post-mortem nuclide measurements of the 28 persons who subsequently died.

9. Internal dose values according to post-mortem measurements for 6 patients are shown in Table A.2. The maximum amount of  $^{137}\text{Cs}$  and  $^{134}\text{Cs}$  incorporated activity was 7.4 MBq, except for two patients with extensive steam burns, which allowed intake of nuclides through the wound. The post-mortem dosimetry gave 40 and 80 MBq of  $^{137}\text{Cs}$  plus  $^{134}\text{Cs}$ , and 450 and 1,100 MBq of  $^{131}\text{I}$ , for these two patients, respectively. The whole-body internal doses in these two individuals from these nuclides were estimated as approximately 1 Sv and 2 Sv during the two to three weeks before they died, which are commensurable with their external gamma doses. This fact was taken into account during the interpretation of clinical data. Internal doses for other patients did not exceed 1-3% of the external irradiation doses.

10. The transuranic elements (e.g.,  $^{239}\text{Pu}$ ) were studied in urine specimens from 266 persons (635 analyses), including, in some of the cases, analyses conducted before and after the administration of pentacine. The urine activity values and a negative finding after chelation treatment confirmed the absence of a significant plutonium contamination of all the patients observed. Post-mortem tests by alpha spectrometry for transuranic elements showed their presence (74-300 Bq per organ) only in the lungs; curium accounted for as much as 90% of the specimen activity, and plutonium and americium for 10%.

11. Gamma-spectrometric analysis of the first specimens within 36-39 hours of the accident failed to reveal any sign of  $^{22,24}\text{Na}$  activation, which confirmed that neutron irradiation of the victims was not significant.

12. For most of the victims, the energy peaks of more than 20 radionuclides were detectable in the spectrum of their whole-body gamma measurements; however, apart from the iodine and caesium isotopes previously mentioned, the contribution to the overall dose from the others ( $^{95}\text{Nb}$ ,  $^{144}\text{Ce}$ ,  $^{140}\text{La}$  etc.) was negligible. These measurements, performed while the victims were still alive, were also confirmed through the analysis of autopsy specimens (approximately 35 specimens from each deceased person) (Figure A.I).

13. The dose levels from external irradiation were reconstructed from the indication of several measurements on the basis of previous experience. Subsequently, in three cases with a lethal outcome, these findings were refined using methods earlier proposed by Kraylor for clothing fabrics [B31] and according to the electron spin resonance technique for dental enamel [T16]. These measurements agreed within  $\pm 20\%$  with the dose estimates based on clinical and biological criteria.

14. The total number of affected individuals among the persons present at the reactor site in the early hours of 26 April 1986 was 203, as given in the report presented by Soviet representatives at the Post-Accident Review Meeting in August 1986 [I18]. Of these, 115 were treated, beginning on day 2, at the specialized treatment centre in Moscow, it was this group that provided most of the scientific analytical data discussed in this report. At other hospitals in Kiev there were only 12 patients with a clearly defined clinical pattern of second-degree acute radiation sickness and one person with fourth-degree acute radiation sickness, a fact that cannot in any substantial way alter the overall assessment of the data for the entire group of victims.

15. The increase in the total number of affected individuals from 203 to 237, announced in November 1986, was due solely to persons suffering from first-degree acute radiation sickness. There were 31 persons suffering from first-degree acute radiation sickness at the special treatment centre in Moscow and 109 persons in Kiev. The task of establishing a diagnosis distinguishing between first-degree acute radiation sickness and ordinary somatic diseases according to generally accepted criteria is a complex one, and one that continued throughout 1986. On the whole, a critical analysis of the data shows a decrease in the number of persons suffering from first-degree acute radiation sickness in comparison with the number given originally. At the time of writing this report, up to three quarters of these persons are for all practical purposes healthy. Their clinical signs of reaction to the accident during the first three months were neither individually significant nor typical of a reaction to irradiation. Table A.3 shows the distribution of patients with acute radiation sickness according to its degree of severity [B31] in the group selected for scientific analysis.

#### A. INITIAL DIAGNOSIS OF ACUTE RADIATION SICKNESS

16. The medical unit serving the plant was informed of the accident within 10-15 minutes of its occurrence. First aid to the affected individuals was provided by middle-level medical personnel and emergency teams over a time period from 30-40 minutes to 3-6 hours after the accident. First aid consisted in the evacuation of the victims from the industrial site, the simplest forms of medical attention, the administration of antiemetic and symptomatic (sedative, cardiotoxic) drugs, the distribution of potassium iodide and the transportation of persons suffering from a pronounced primary reaction to the medical unit. During the first

12-24 hours after the accident, other persons who were in satisfactory condition were urged to go to the medical unit for examination; a total of 132 persons were hospitalized there during the first 12 hours. One person with severe thermal burns died during the first hour. Another, a reactor operator, could not be found; his working station was located in the collapsed high-activity zone.

17. Within 12 hours, a specialized emergency team arrived at the site and began work. Within 36 hours, this team, together with the on-site medical unit, examined more than 350 persons and carried out approximately 1,000 blood tests, each person undergoing two to three such tests. The treatment with potassium iodide was continued.

18. Within the first three days, 299 persons suspected of suffering from acute radiation sickness were sent to the specialized treatment centre in Moscow and to hospitals in Kiev, and over the subsequent days some 200 additional persons were admitted for examination.

19. The primary diagnostic criteria for assessing the priority for hospitalization were the presence, time of onset and intensity of nausea and vomiting and of primary erythema of the skin and mucosae, and a decrease of the lymphocyte count in the peripheral blood to below  $10^9/l$  during the first days following irradiation.

20. The diagnosis of acute radiation sickness was subsequently confirmed in 99 of the 128 persons (firemen, Unit 4 operators, turbine-room duty officer and auxiliary personnel) admitted to the specialized treatment centre in Moscow during the first two days and in six of the 74 victims hospitalized during the following three days. This is an indication of the high specificity of the screening methods used. An additional 10 cases of minor acute radiation sickness were diagnosed among persons present at the site at the time of the accident, who were later admitted to the hospital facility for a variety of reasons. In the reception area the patients were monitored again for contamination and, if necessary, subjected to decontamination measures (washing under a shower with ordinary soap and change of underwear). Blood and urine samples were taken for a quick test of the presence of radionuclides; the patients also underwent measurements (repeated a further 4-6 times during the first 6-10 days) of the radioactive iodine content in the thyroid. Measuring devices consisting of a scintillation detector or a semiconductor detection unit were used for the whole-body counting of radionuclide activity.

## B. THE BONE MARROW SYNDROME AND ITS TREATMENT

21. Dosimetric data, together with an analysis of the circumstances of the accident and the presence in a considerable number of the victims of obvious primary reaction symptoms (nausea, vomiting, diarrhoea, hyperaemia of the mucosae and skin, lymphopenia), confirmed that the principal modes of irradiation had been: (a) by external, relatively uniform gamma-radiation; and (b) by deposition of beta/gamma-emitting nuclides

on the skin. Radionuclide ingestion was below the level likely to cause acute radiation injury. As already noted, two patients suffered from all three of these irradiation modalities, in combination with extensive steam burns.

22. The important diagnostic task during the first few days after the accident was the assessment of the degree of severity of the bone marrow syndrome resulting from the external gamma-irradiation dose. This was possible through the use of previously devised methods, which are based on the number of lymphocytes and on chromosome aberrations in peripheral-blood lymphocytes or on the incidence of chromosome aberrations in bone marrow cells [B31, B50, G24]. These data were later transformed into a prognosis of the overall dynamics of the blood picture. A subsequent re-assessment of dose levels involving a larger sample of cells scored revealed not more than 5-10% changes in the estimated doses.

23. Dose-effect relationships for these indicators had been derived earlier through the analysis of relatively uniform accidental or therapeutic irradiations of human subjects having normal initial haematological characteristics and exposed to well established doses [P22]. Figure A II shows the curves (and analytical expressions) for the relationships between the dose and the blood lymphocyte count for each of the first nine days and the average lymphocyte count on days 4-7 and days 1-8 after irradiation. The radiation dose received by each person was estimated according to the number of chromosome aberrations (dicentric) in a blood-lymphocyte culture, using a dose-effect curve for 100 first-mitosis cells that had been obtained after whole-body gamma-irradiation to treat acute leukaemia patients during a period of full clinical and haematological remission [P23]

24. The formula for calculating of the dose is as follows:

$$D = (-a + \sqrt{a^2 + 4by})/2b$$

This assumes that the yield of dicentric shows a linear-quadratic dependence on dose:

$$y = (a \pm 2.24)D + (b \pm 0.56)D^2$$

where D is the average gamma-irradiation dose in the body (Gy), y is the dicentric count per 100 cells; a = 8.36; b = 5.70.

25. Up to day 7 after the accident, the estimates of the average dose of total gamma-irradiation were refined, mostly on the basis of the peripheral-blood lymphocyte counts but also, in the more severe cases and to a lesser degree, on the chromosome aberration count. This made it possible to divide the patients into various prognostic groups [B31], according to the severity of the bone marrow syndrome as follows (see Table A.3):

(I)	slight	(1-2 Gy)
(II)	intermediate	(2-4 Gy)
(III)	severe	(4-6 Gy)
(IV)	extremely severe	(6 Gy and above)

It was also possible to separate those persons who received doses of less than 1 Gy.

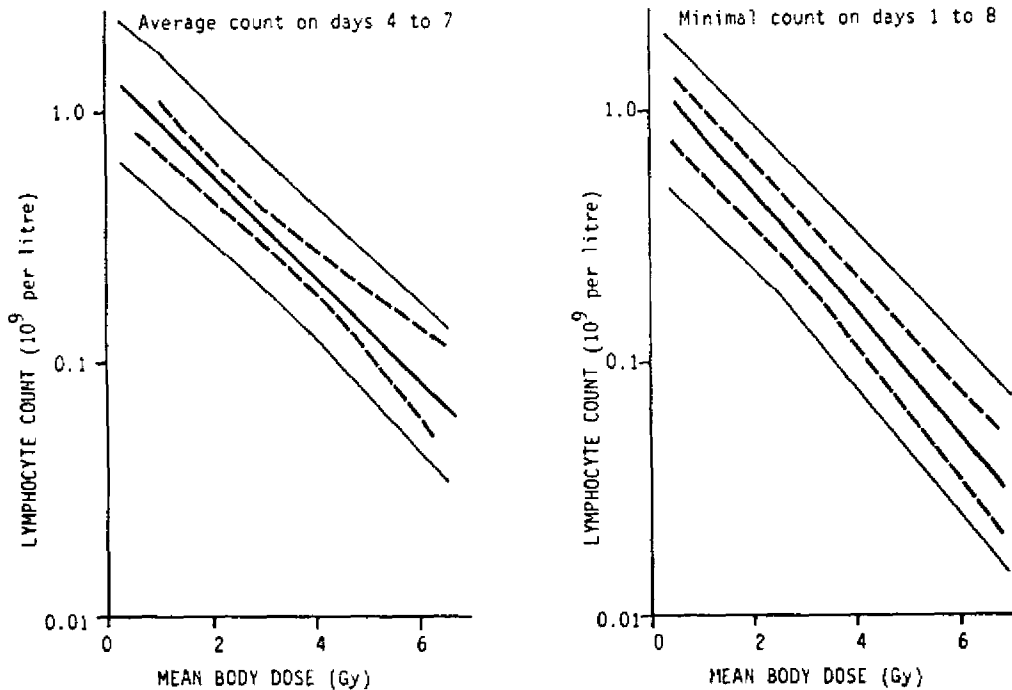
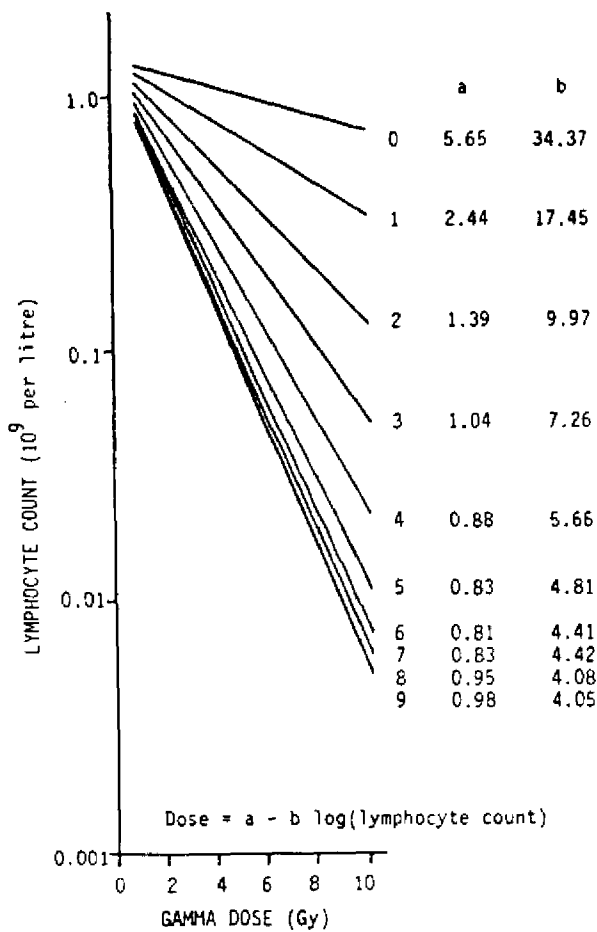


Figure A.II. Estimation of the total gamma dose according to the blood lymphocyte counts. Upper panel: Dose-effect relationships for lymphocyte counts at the days post irradiation shown on the curves; analytical expression and coefficients of these relationships. Lower panels: Curves showing the dependence of average lymphocyte counts on days 4-7 and the minimum lymphocyte count on days 1-8 as a function of the irradiation dose.

26. Particular attention during the first days was directed at identifying persons with an extremely severe and irreversible degree of myelodepression, for whom an urgent decision was required regarding a bone marrow transplant. Additional signs providing further evidence that a patient belonged to this group were (a) vomiting during the first half-hour and of diarrhoea during the first 1-2 hours from the start of irradiation; (b) a swelling of the parotid glands during the first 24-36 hours; and (c) the ascertainment of an irreversible degree of myelodepression using a diagnostic table previously devised (Table A.4).

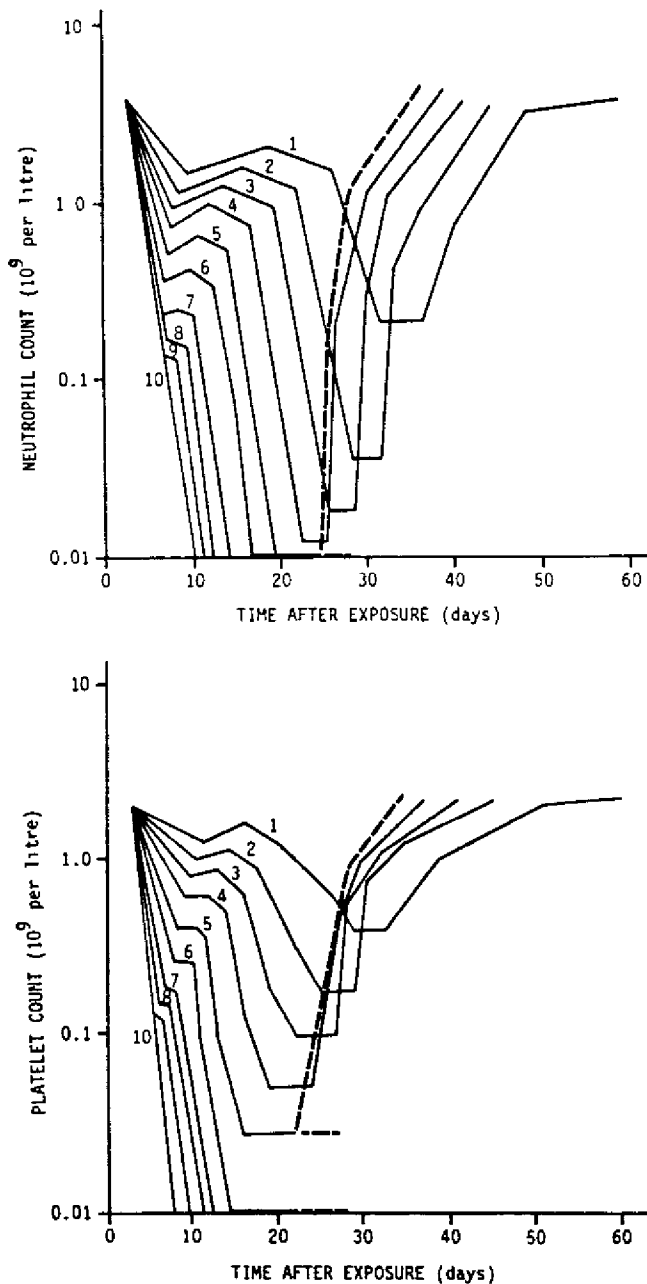


Figure A.III. Standard curves showing the changes of the neutrophil and platelet counts after various doses (numbers on the curves indicate the dose in Gy) in the case of relatively uniform whole-body gamma irradiation of human subjects. [B31]. (The broken segments of the curves at doses of 5-6 Gy indicate that recovery may not occur at these times in all patients.) Upper panel: Neutrophils. Lower panel: Platelets.

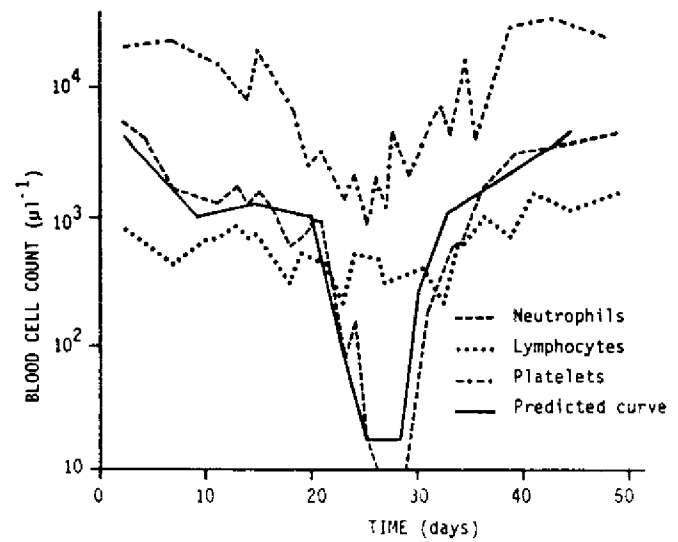


Figure A.IV. Example of the changes in neutrophils, lymphocytes and platelets observed in a patient (case 39) suffering from acute radiation sickness (estimated dose 2.4-3.3 Gy) and the predicted neutrophil curve for a total gamma dose of 3.0 Gy.

27 The results of numerous biochemical, immunological and biophysical indicators are undergoing processing and analysis at the time of writing this report. None of these indicators is as informative as the signs described above. However, it may be noted, for example, that hyperamylasemia was used as a supplementary prognostic test.

28 On the basis of the estimated dose, a prediction was made using standard curves [P22], of the overall trend with time in the neutrophil and platelet counts (Figure A.III). By way of example, Figure A.IV shows the real and predicted neutrophil curves for one patient (case 39). The total gamma-irradiation doses estimated according to the average lymphocyte count from day 4 to day 7 and according to the dicentric yield totalled 2.4 and 3.3 Gy, respectively. The patient's measured neutrophil curve almost coincided with the predicted neutrophil curve for 3.0 Gy of total gamma-irradiation.

29. The calibration curves of neutrophil counts as a function of dose were also used for a final assessment of the magnitude of the total gamma-irradiation dose. The dose calibration curve was chosen that coincided with the measured second depletion phase. Also, use was made of the dose dependency of the second depletion phase, such as the time required for the neutrophil count to decrease to  $0.5 \cdot 10^9/l$  or the time to reach the minimum of the second depletion phase (Figure A.V).

30. For relatively low doses (1.0-1.5 Gy), the diagnosis was finally established over time periods of up to three months only in those cases that showed typical post-irradiation neutrophil and/or platelet time courses with distinct second depletion and restoration phases. The latter generally developed beginning in the fourth to the fifth week after irradiation. In order to determine these changes, it was necessary to carry out blood analyses not less than two or three times a week

over a period of two to three months. Examples of these curves are shown in Figure A.VI: (a) case 48: doses, estimated according to the lymphocyte count on days 4-7 and the dicentric yield were 1.1 Gy and 1.4 Gy, respectively; and (b) case 97: doses, estimated according to the lymphocyte count on day 9 (the first blood analysis was made at this time because of late arrival) and the dicentric yield were 0.3 Gy and 0.9 Gy, respectively. It should be noted that in the case of low doses, the minimum level for neutrophils occurred later (day 30-50) than for platelets (day 20-40), and the reduction in the number of platelets and their recovery were more clearly pronounced than for neutrophils.

31. On the basis of all these data, a diagnosis of acute radiation sickness with the bone marrow syndrome of the first, second, third and fourth degree of severity was definitively established for 31, 43, 21 and 20 patients, respectively (see Table A.3). The analysis of the observations carried out on these patients is the subject of the exposition that follows

32. Clinical manifestations of the bone marrow syndrome corresponded to the level and duration of post-irradiation pancytopenia (neutrophils  $0.1-0.5 \cdot 10^9/l$ , platelets  $10-20 \cdot 10^9/l$ ). The main signs were fever, infectious complications and petechial haemorrhages in the skin and oral mucosa.

33. Treatment was based on the principles of supportive therapy, including isolation, antimicrobial decontamination of the intestine, administration of systemic antibiotics and replacement transfusions of

blood cells. In cases in which there was a prognosis of irreversible myelodepression, transplantations of allogeneic bone marrow and embryonic human liver cells were performed

34. All patients suffering from a bone marrow syndrome of the second, third or fourth degree were individually accommodated in ordinary hospital rooms. These were adapted to ensure (a) barrier nursing; (b) air sterilization by means of ultraviolet lamps; (c) strict observance by the attending personnel of hand disinfection on entering and leaving the room; (d) mandatory use of individual or disposable gowns, masks, and caps; (e) antiseptic decontamination of footwear, (f) changes of underclothing for patients at least once a day; (g) use of antiseptic agents for washing the walls and floor of the room and the items of use; and (h) individual assignment of antiseptically treated nursing items in the room. This regimen made it possible to maintain the micro-organism population at less than  $500 \text{ m}^{-3}$  in the room air. Ordinary food was served, with the exclusion of raw vegetables, fruits and canned products.

35. Prophylaxis against endogenous infections was by means of the internal administration of bisepitol-480 and nistatin in amounts of six tablets and five million units per day, respectively, for one and 2-3 weeks prior to the development of agranulocytosis (leucocytes  $1.0 \cdot 10^9/l$ , neutrophils  $0.1-0.5 \cdot 10^9/l$ ).

36. With the onset of fever, intravenous administration of two or three broad-spectrum antibiotics was prescribed, one of them being from the aminoglycoside

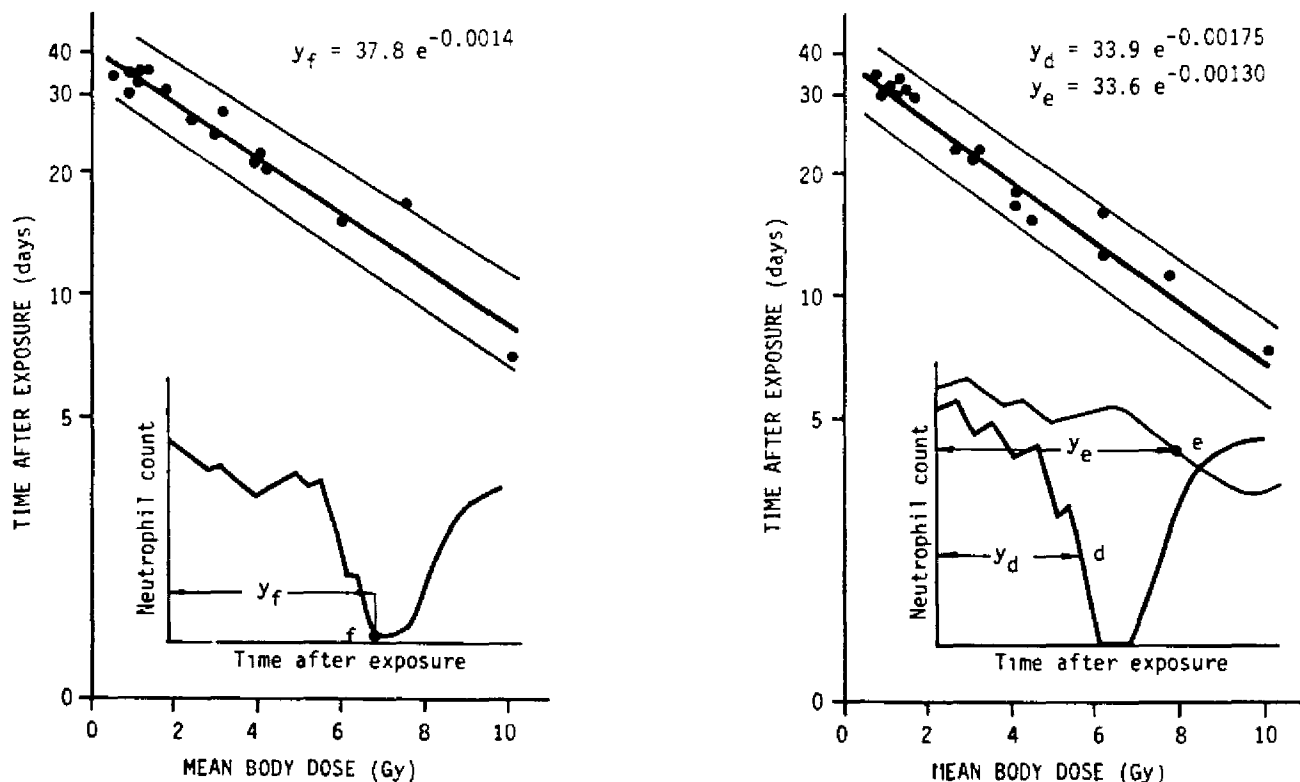


Figure A.V. Estimation of the total gamma dose according to two neutrophil counts: Left panel: time to the minimum of the second phase of depletion; Right panel: time to the "500 neutrophil day" or to the middle of the second depletion.

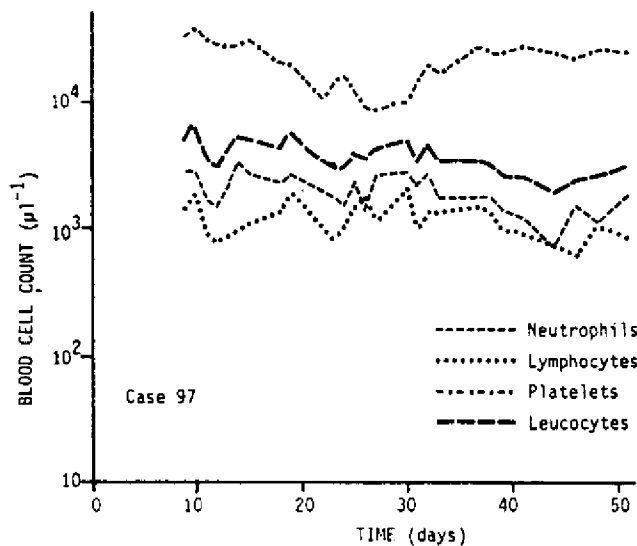
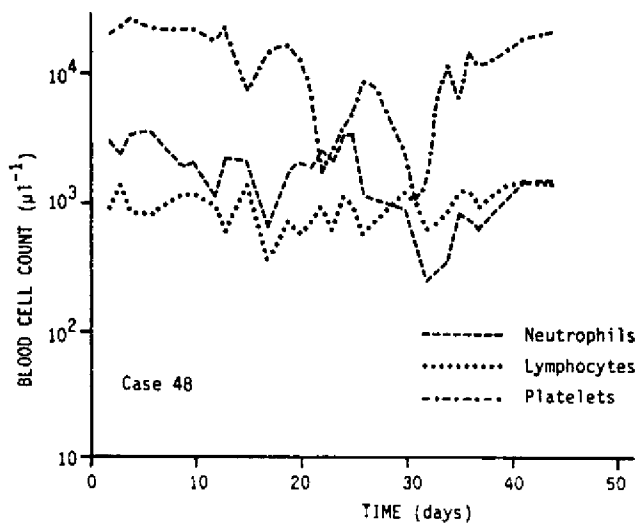


Figure A.VI. Changes in neutrophil, lymphocyte, platelet and leucocyte counts after whole-body gamma irradiation. Case 48, estimated dose 1.1-1.4 Gy. Case 97, estimated dose 0.3-0.9 Gy.

group (gentamicin or ampicillin), the cephalosporins (cephazolin, cephamecin, cephobide) and the semi-synthetic penicillins with activity against *Pseudomonas aeruginosa* (carbenicillin, piperacillin), all in maximum doses. This treatment reduced the fever in more than half of the patients. If within 24-48 hours there was no effect, extensive use was made of gamma globulin (Sandoglobulin), made available by the Sandoz Company (Switzerland). Six grams were administered intravenously every 12 hours, three or four times. The policy adopted was one of early empirical prescription of 1 mg/kg per day amphotericin-B given intravenously, if the fever had not disappeared within a week of the above mentioned antibiotics, in combination with the intravenous administration of gamma globulin.

37. In this situation, acyclovir was used for the first time, and with good effect, in the treatment of patients with acute radiation sickness suffering from a herpes simplex infection. Not less than one third of the patients with third- and fourth-degree acute radiation sickness were affected by this virus. Acyclovir was not

used prophylactically; experience has shown that this should be the case with high-dose whole-body irradiation. An ointment containing acyclovir proved effective in the treatment of skin lesions involving herpes virus.

38. The regimen described above for the empirical treatment to combat infection proved to be highly effective: there was no evidence that deaths were caused by bacterial infection alone in patients suffering from the bone marrow syndrome. This was so even among those with a severe or extremely severe form of acute radiation sickness, provided it was not complicated by burns, radiation-induced enteritis or acute secondary syndromes as a result of a bone marrow transplantation.

39. Blood screenings carried out while the patients were still alive or, in the case of those who died, posthumously, most often revealed epidermal staphylococcus. It will only be possible to evaluate the role of this form of bacteria as an agent of terminal septicaemia when these results have been compared with the histological data from analysis of various organs that have not yet been completed.

40. One of the undoubted successes in the treatment of the bone marrow syndrome in patients with acute radiation sickness was the rational use of fresh donor platelets for the prophylaxis and treatment of bleeding. To make these measures possible, the collection of the thrombocytes was organized on an urgent basis, using the method of fourfold thrombocytapheresis from individual donors at seven blood transfusion centres. For one transfusion, platelets obtained from a single donor (on the average  $300 \times 10^9$  platelets in 200-250 ml of plasma) were used. Transfusions were carried out when the platelet level in the blood fell to  $20 \times 10^9/l$  or lower, with appearance of the first signs of bleeding. The infusions were repeated every 1-3 days. As a prophylaxis against acute secondary syndrome, the thrombocytes as well as the other blood components were irradiated with 15 Gy before infusion in order to inactivate the immunocompetent cells originating from the donor.

41. Platelet transfusion prevented life-threatening bleeding, even in patients with protracted (more than 2-4 weeks) and severe thrombocytopenia. The majority showed no signs of bleeding at all, although autopsies disclosed microcirculatory failures and porosity of the capillaries in a number of organs. In this situation, successful use was made of cryo-preserved allogeneic and, what is particularly important, autologous thrombocytes. The latter were obtained from patients with second- or third-degree bone marrow syndrome during the first days following irradiation (1-2 sessions)—this had no effect on the post-irradiation behaviour of their platelet counts—and were used with great effectiveness when the patients developed critical thrombocytopenia. No cases of refractoriness to thrombocytes transfusion were observed. On the average, from three to eight transfusions of standard amounts of thrombocytes ( $300 \times 10^9$  cells) were required for the treatment of a single patient with second- and third-degree acute radiation syndrome. Leucocytes





43. The indication for an allogeneic bone marrow transplantation or an embryonic liver cell transplantation was the whole-body gamma-irradiation dose, estimated according to the peripheral-blood lymphocyte count and the chromosome aberrations at about 6.0 Gy and above. At these dose levels the prognosis expected was for irreversible or extremely protracted severe myelodepression.

44. A total of 13 allogeneic bone marrow transplantations and six embryonic liver cell transplantations were performed. The latter contains haemopoietic stem cells and a minimum of immunocompetent cells, which sharply lowers the risk of an acute secondary syndrome.

45. Seven patients who received allogeneic bone marrow transplant died between two and 19 days (15-25 days after irradiation) from acute radiation injuries to the skin, intestines and lungs.

46. Of six patients who did not suffer fatal skin burns and intestinal injuries and whose total doses had been estimated at between 4.4 and 10.2 Gy, two survived allogeneic bone marrow transplants (gamma-ray doses of 5.6 and 8.7 Gy). Both had haplo-identical female donors (sisters), rejected the partially functioning transplant (at days 32 and 35) and experienced a restoration of their own myelopoiesis, beginning at day 28.

47. Four patients who received allogeneic bone marrow transplantation died between 27 and 79 days (34-91 days after irradiation) from mixed viral-bacterial infections. Two of them had effectively functioning HLA-identical transplants (cases 6 and 28: total gamma-ray doses 5.2 Gy and 6.4 Gy, respectively), and two had early rejection (day 16 and 42) of "haplo + 1" and haplo-identical transplants, but during times when their own myelopoiesis was restored (cases 5 and 16: gamma-ray doses 4.4 and 10.2 Gy).

48. Similarly, all the patients who received embryonic liver cell transplants died from skin and intestinal injuries within a brief period (14-18 days after irradiation), with the exception of one woman of 63 years (case 8, embryonic-liver cell transplant from an 18-week male donor), who lived 30 days, having received a dose of 8-10 Gy. At death (17 days after transplant), numerous mitoses were discovered, against a background of severe marrow pancytopenia, and all the cells had a female karyotype, i.e., regeneration of the host bone marrow had begun.

49. This experience confirms that in an emergency situation like the one described, the group of persons for whom bone marrow transplants would be indicated with a reasonable prospect of success is extremely limited. Seven of 13 patients died as a result of skin and intestinal injuries before bone marrow engraftment could be expected. In Table A.5 a comparison is given of survival or cause of death of patients receiving bone marrow transplantations and of patients in a control group.

### C. OTHER INJURIES AND THEIR TREATMENT

50. The extensive skin lesions caused by beta-radiation represented a distinctive feature of the injuries suffered in this emergency situation. Radiation-induced skin burns in firemen and personnel from the plant were observed only in combination with radiation injury to haemopoiesis and were therefore an integral part of the general acute radiation sickness.

51. This situation may be regarded as one in which there is an extremely non-uniform distribution of dose as a function of the depth of penetration within the body; the skin doses are estimated to be 10-20 times greater than the bone marrow doses. There was a definite correlation in the severity of the injuries in both tissues.

52. Table A.6 and Figure A.VIII show the distribution of cases involving radiation-induced skin burns of various degrees in patients with acute bone marrow syndrome of different severity. Skin injuries were observed in more than one half of the patients and in virtually every patient suffering from third- or fourth-degree bone marrow syndrome.

53. The aggravating contribution of radiation-induced skin injuries to the overall clinical picture arose not only from their severity, but also from the duration of the injuries, characterized as they are by recurrences of the pathological process. As a rule, the burns occurred at different times on various parts of the body. The most frequent locations during the early period were the wrists, the face, the neck and the feet; later, lesions appeared also on the chest and back, and still later on the knees, hips and buttocks. Exceptions to this sequence were encountered in individual cases.

54. The development of the injury was similar to that described by Cronkite et al. [C16], but in a more severe form. The diffuse hyperaemia in the first few days (primary erythema) was followed after 3-4 days by a period of latency. Secondary erythema in the more severe cases developed after 5-6 days and in the majority of patients from day 8 to day 21. Depending on the degree of the injury, it reached a level of dry (first-degree radiation burn) or moist desquamation with the development of blisters (second-degree burn), or the formation of vesicular-ulcerated and ulcerated-necrotic dermatitis (third- to fourth-degree burn). The re-epithelialization of the desquamated surfaces continued for two or three weeks from the occurrence of the visible injury to the skin. In six patients, the healing of the burns over skin areas involving deep necrosis did not begin until the end of the second month. A characteristic feature in the time course of the burns, and one which could be monitored throughout in this group of victims, was the appearance of recurrent waves of erythema, beginning by the end of the fourth week and continuing up to days 45-60. These changes were characterized by hyperaemia on the previously unaffected skin areas or by the increase in clinical signs of injury at the foci of the primary lesions then in the process of healing. For example, late secondary erythema appeared in the area of the

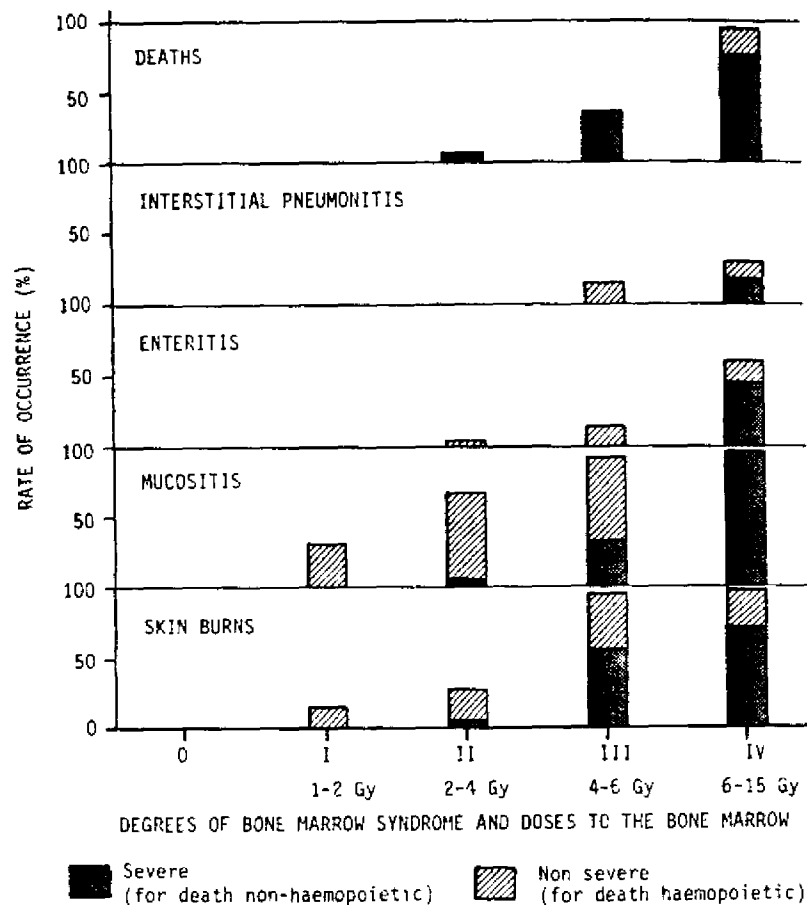


Figure A.VIII Frequency of deaths and non-bone marrow syndromes for various degrees of bone marrow syndrome in accident victims suffering from acute radiation sickness.

ankles and feet, or on the hips and buttocks, of those patients who during the first three weeks displayed "flowering" burns on their knees. By the time of appearance of this late erythema, the lesions that had occurred earlier in many instances had already been repaired. As a rule, late erythema was accompanied by oedema of the subcutaneous tissues, which was particularly noticeable when located on the knees: pain was experienced in walking, palpation of the skin and underlying tissues (muscles, tendons) caused discomfort. The most severe cases involved fever and a general worsening of the patient's condition. Late secondary erythema was successfully resolved within two weeks by purely topical treatment, although in the more severe cases it was necessary to resort to additional therapeutic means, such as the prescription of glucocorticoids, a form of treatment that fairly rapidly eliminated all manifestations of epidermatitis and subcutaneous oedema, both general and local.

55. As may be seen in Table A.6, the burns suffered by the patients with acute radiation sickness covered from 1% to 100% of the body surface. It may be noted, in this connection, that if there were relatively early (from day 5-6) second- or third-degree burns over an area of even 30-40% of the body, followed by the spread of hyperaemia, these burns were life-threatening. In 19 of the 56 patients suffering from burns, the burns proved fatal (Figure A.VIII). It was found that patients with early secondary erythema over a body area of more

than 40% first developed a febrile-toxic syndrome, followed by renal-hepatic insufficiency and encephalopathic coma with cerebral oedema, resulting in death at 14-48 days after irradiation. A causal link connecting the fatal renal-hepatic insufficiency and the encephalopathic coma to the skin injuries is confirmed by the fact that a similar development of such fatal syndromes was observed in several patients who had neither severe bone marrow syndromes nor intestinal syndromes. However, in the majority of cases, burns were combined with an extremely severe bone marrow syndrome and severe acute enteritis, and in some cases the burns may have been the primary cause of death.

### 1. Intestinal syndrome

56. The intestinal syndrome was one of the more threatening manifestations of acute radiation sickness. In 10 patients, diarrhoea was observed from day 4 to day 8. This suggested that these persons had received total gamma doses of about 10 Gy or above; all these patients died during the first three weeks following irradiation. The occurrence of diarrhoea after eight days in seven other persons was an indication that they had received lower doses. The presence of radiation-induced enteritis lasting from day 10 to days 18-25 in spite of intensive water-electrolyte-protein supportive treatment suggests that the intestinal syndrome was not the main cause of death.

## 2. Oropharyngeal reactions

57. Acute radiation-induced inflammation of the oral and pharyngeal mucosa was observed in 82 patients. Its more benign manifestations (first and second degree of severity) were characterized by desquamation and oedema of the mucosa in the area of the cheeks and tongue and by tenderness of the gums. These were observed in 42 persons (dose range 1.7-4.0 Gy) from days 8-9 to days 20-25. The basic signs of a more acute oropharyngeal reaction were observed in 40 patients with third and fourth degree acute radiation sickness (dose range 4.5-16.0 Gy), and these were erosions and ulcers of the oral mucosa, sharp pain, and a large production of rubber-like mucus occasionally blocking the throat and causing breathing problems. The first signs appeared as early as days 3-4, attained their maximum intensity by day 10 and then subsided after days 18-20, when there was also granulocytopenia. The process involved no selective localization, as is characteristic of the ulcerated lesions in the area of the tonsils and gums when there are infectious complications. However, in a significant number of cases, the radiation-induced inflammation of the mucous membranes was complicated by secondary microbial and viral infection, which prolonged its course.

58. Another typical finding was the early (days 3-4) appearance of herpes-like rashes forming massive crusts on the lips and facial skin; this was observed in nearly 30% of the patients with severe bone marrow syndrome. Within this group of patients, primarily those suffering from fourth-degree acute radiation sickness, a pronounced radiation-induced parotitis was observed, coupled with an inability to salivate and a high level of amylase in the blood from days 1-4. The swelling of the parotid glands disappeared without special treatment, whereas recovery of salivary gland secretion was slower.

## 3. Lung reactions

59. Lung reactions were observed in seven patients suffering from third- and fourth-degree acute radiation sickness. Its characteristic signs were a rapidly intensifying dyspnoea together with respiratory insufficiency progressing over a period of two to three days culminating in death. Autopsies revealed large, blue lungs with pronounced interstitial oedema, without destruction of the mucous membranes of the trachea and bronchi. As a rule, interstitial pneumonitis developed several days before death, generally in combination with extremely severe lesions of the skin and the intestine. The times to death were 14-30 days after irradiation.

## 4. Causes of death

60. The frequency of non-haemopoietic injury increased as a function of total dose (Figure A.VIII). Clinical observations indicated the essential role of skin injuries in pathological processes prior to death. Among the patients that died, in two thirds of them there was extensive and severe radiation and thermal skin burns, which were considered life-threatening. In

five cases skin injuries were the sole cause of death, because there was neither radiation enteritis or irreversible myelodepression. Deaths were observed between 10 and 96 days after exposure. The clinical picture in all fatal cases was characterized as following a difficult course, because in every case two or three radiation syndromes had occurred with complex toxicity, infection and circulation disorders. A summary listing of patient identification and causes of death is given in Table A.7.

61. A detailed clinico-morphological analysis made it possible to identify the predominance, within specified time periods, of particular lethal syndromes. Up to day 24, a total of 19 patients (65%) died. In one half of these patients the competing causes of death were skin and intestinal reactions (cases 3, 4, 10, 14, 15, 17, 20, 23, 26, 2097, in all the cases the gamma-radiation dose in the bone marrow was estimated to be greater than 10 Gy). Four patients showed acute radiation injury in the lung (cases 2, 9, 12 and 27; the doses were, respectively, 9.2, 9.7, 9.3 and 8.3 Gy), and, of these, two (cases 2 and 9) suffered also severe injuries to the skin. Two patients died of combined thermo-radiation burns (cases 24 and 25; the gamma-radiation doses in the bone marrow were estimated to be 3.7 and 5.7 Gy, respectively, in combination with internal irradiation doses. Within this time-frame, one patient (case 62, dose about 6 Gy) died almost exclusively from severe radiation burns at a time when haemopoiesis had begun to be restored. Three cases (cases 17, 26, 62) had involvement of mycobacterial sepsis. One patient (case 30, dose about 5.5 Gy) died of bleeding caused by mechanical injury to the subclavicular vein during catheterization, and another (case 7, dose about 4.7 Gy), suffering from severe radiation injury to the skin, died of post-transfusion shock. Characteristics of the deaths on days 11-24 were marked circulatory problems during the terminal period. This was shown by the relatively high frequency of signs indicating cerebral oedema and focal haemorrhaging into the brain and spinal cord.

62. Six patients died during the period from days 25-48. All six cases were characterized by extremely severe complications of a toxic or infectious nature. Two patients (cases 31 and 34) involved sub-total skin injuries (bone marrow doses about 6.7 and 5.8 Gy, respectively, with death occurring on days 32 and 48, respectively), coupled with practically restored haemopoiesis. The immediate cause of death in these cases was severe respiratory insufficiency and cerebral oedema. In one patient (case 28, dose about 6.4 Gy; death on day 48) the cause of death was severe, graft-versus-host disease and fungal and viral infections. One additional patient (case 5, dose about 4.4 Gy) died on day 34 of severe pulmonary and renal insufficiency, caused, most likely, by the transplantation of HLA-non-identical bone marrow and by post-transplant immunosuppression using cyclosporin and methotrexate. Two patients (cases 1 and 8, doses about 6.6 and 8.3 Gy) died on days 25 and 30, respectively, with symptoms of severe toxicity and pulmonary insufficiency. In nearly all six cases there were marked circulatory disorders in the lungs, intestines, brain and myocardium.