63. At a relatively late stage, days 86-96, three patients died. One patient (case 6, dose about 7.5 Gy) died on day 86 of graft-versus-host disease complicated by cytomegalovirus (CMV) infection Cytomegalovirus infection was also the cause of death for another patient (case 16, dose about 10.1 Gy) on day 91. A female patient (case 33, dose about 4.1 Gy) died on day 96 displaying marked disruptions of cerebral blood circulation against a background of renal-hepatic insufficiency and foci of mycococcal infection (pneumonia) This patient suffered also skin injuries from beta-radiation which extended over one third of her skin surface and underwent a severe recurrent wave of erythema with oedema of the subcutaneous tissue.

5. Eye damage

64. Eye injuries were characterized by the early and subsequent involvement of all eye tissues in the pathological process (Table A.8) In this group of patients, damage to the skin and eyelid conjunctiva was caused, to a considerable degree, by beta-radiation.

65. At doses not exceeding 1 Gy there were no visible alterations in the structure of the eyes In the case of patients suffering from first-degree acute radiation sickness, changes were noted only in the front segment of the eye: there was in individual cases a slight erythema in eyelid skin during the first two to four days and an intensification of the vascular pattern in the lid and conjunctiva of the eyeball. In 40% and 100% of the patients suffering from second- and third-degree acute radiation sickness, respectively, the eyelid skin showed a first wave of of erythema within 6-12 hours of irradiation, and within 2-3 weeks there was a second wave. These cutaneous alterations disappeared without trace, leaving hyperpigmentation and scaling In all patients suffering from fourth-degree acute radiation sickness, the times to the appearance of the first and second wave of erythema were 1-2 hours and 8-10 days, respectively.

66. Microscopy of the bulbar conjunctiva revealed a number of alterations in the microcirculation: there was a dilation of the venules and capillaries (more rarely the arterioles), and an increase in the number of functioning vessels coupled with a reduced blood flow.

67. Two patients suffering from combined radiation and thermal second-degree lesions on the lid skin and conjunctiva experienced ulcerations on the skin around the eye that did not re-epithelialize for a long time. Epilation of the eyebrows was noted at days 15-17 in 16% of the persons with second-degree acute radiation sickness, and in 67% and 100% of those with third- and fourth-degree acute radiation sickness, respectively. The epilation was partial and transient. Hair growth on the head was fully restored. All patients retained their eyelashes.

68. Corneal damage was manifested in an early reduction in corneal sensitivity coinciding with the first wave of erythema, although first-degree patients did not show such an effect. At later times (days 35-55), superficial radiation-induced keratitis was observed in patients suffering from second-, third- and fourth-degree radiation sickness in 5%, 52% and 100% of the cases, respectively. Also noted were focal defects on the superficial epithelium of the cornea, these defects, which often merged, stained with fluorescein. The radiation keratitis regressed over a period of 1-1.5 months, leaving no opacification of the cornea.

69. Signs of disturbances in the haemodynamics of the retina were related to the dose and the degree of severity of radiation sickness. From a few days after irradiation, a reduction was observed in the level of diastolic pressure in the central retinal artery, followed later by signs of hypotonic angiopathy of the retina. Coinciding in time with the peak of the sickness, other injuries appeared, e.g., retinal oedema along the vessels and increased permeability of the retinal vessels (plasma discharge and haemorrhaging). The low diastolic pressure in the central retinal artery persisted over the entire acute phase.

70. In one severely ill patient (case 29, dose about 8.7 Gy) with fourth-degree acute radiation sickness, who survived the acute phase, the symptoms of angioretinopathy with haemorrhaging and plasma discharge recurred within 4.5 months, accompanied by a persistently low diastolic pressure in the central retinal artery (up to 5-10 mm Hg).

71. In the acute period, the treatment consisted in the topical application of ointments to the scaling surface of the eyelid skin and the instillation of 20% albucid, sophradex and vitamin solutions as eyedrops into the conjunctival cavity.

72 Within observation periods of up to one year, no obvious radiation-induced alterations of the lens were noted.

6. Treatment of radiation burns and other injuries

73. The treatment of radiation burns and other non-bone-marrow syndromes and their complications posed complex and multifaceted problems [J18]. From day 2 through day 8, 15 haemosorption sessions (purification using activated charcoal) were conducted for 13 patients suffering from the most severe skin lesions. Three patients who had been exposed to a total dose range of 2.0-4 6 Gy survived; they underwent haemosorption on a single occasion at days 5-8, i.e., considerably later than the time at which this might have affected the treatment of the bone marrow syndrome. This method of treatment did not change the outcome of the illness by modifying the haemocytopenia.

74. During the haemosorption process, and particularly towards the end of the session, many patients experienced a short-term improvement (lasting from a few hours to a single day), a reduction or disappearance of the pain in the extremities, and also a decrease of the oedema in their tissues. In this connection, contributory effects from the medication accompanying the procedure cannot be totally excluded.

75. A more widely used technique to combat the development of renal-hepatic insufficiency and fatal encephalopathic coma was plasmapheresis. Lesions induced by beta-irradiation over 30-40% and more of the body surface served as an indication for the application of this procedure. Plasmapheresis sessions were conducted for 17 patients from days 18-37. For a number of patients, daily sessions were conducted, up to six times

76. The positive effect of repeated plasmapheresis was shown by a reduction of bilirubinemia and transaminasemia and a lowering of the nitrate level in patients suffering from renal-hepatic insufficiency caused by skin burns. On occasion, the plasmapheresis sessions were accompanied by reactions of minor severity such as chills and fever; there were no fatal complications. Another method used to treat toxicosis due to skin injuries was the injection of 1,000 ml of freshly-frozen plasma, accompanied by round-the-clock administration of heparin (1,000 active units/hour) with a liquid load (2-6 litres/day) and forced diuresis adequate to the intake volume. A pre-condition for this treatment was the presumption of disseminated intravascular clotting (DIC) syndrome (no typical anomalies in respect of coagulation were present) as a possible cause of encephalopathy and renal-hepatic syndrome. In its most strictly applied form, the heparin treatment method was used with two patients over a period of 7-15 days. The impression was that these patients survived longer than did patients whose condition was similar in terms of severity and extent of their burns Their renal-hepatic insufficiency was less pronounced, however, a death due to encephalopathic coma was not averted

77. The topical treatment of the burns required the involvement of a group of surgeons and nurses. A broad range of preparations and agents having an anti-inflammatory, bacteriostatic and regeneration-stimulating effect was used Good results were achieved with lioxanol aerosol, an anti-burn ointment based on hydrocortisone with locally acting antibiotics, as well as BALIZ-2 solution and collagenous coatings. In each individual case the treatment varied in accordance with the stage of the lesions. Experience gained in the use of bactericidal fabric, both as a dressing material and for supplementary bedding, for patients with extensive burns deserves a particularly favourable comment in this connection [Z2].

78. Treatment of pain, as is typical of radiation injuries, was rather ineffective. At present, there are clearly no suitably effective local anaesthetics.

79. In patients suffering from severe radiation-induced inflammation of the oral mucosa, and enteritis, total parenteral nutrition had a positive effect; this was based on alvesin hydrolysate or an aminoacid mixture, aminone and a 40% glucose solution as the energy material. The treatment was carried out according to the principles and rules described by Dudrick et al. [D18]. This method was tested over a number of years with good results in patients receiving whole-body therapeutic gamma-irradiation at a dose level of 10 Gy for allogeneic bone marrow transplantation. The danger, which has possibly not been fully evaluated, is the probability that certain severely injured, comatose patients may enter a state of hyperosmolarity. Data on plasma osmolarity that would appear to be necessary in a programme of total parenteral nutrition were not provided for all patients.

80. For the majority of patients suffering from first- and second-degree bone marrow syndrome, the period of clinical convalescence was completed by the third or fourth month. A longer period of treatment was required by persons suffering from severe radiation burns and the sequelae of third- and fourth-degree bone marrow syndrome At the present time, the bulk of the patients have resumed work with the exclusion of any contact with radiation sources.

81. Over the period from the fourth month to one year after the accident, the specialized treatment centre was periodically visited by patients with skin lesions (dystrophic and ulcerated areas and also oedema of the subcutaneous tissues, mainly on the knees and feet). These patients are being treated with agents designed to improve local blood circulation and tissue trophism Five patients with deep and extensive ulcers on their arms and other areas of the body underwent repeated plastic surgery, and a number of them will require more extended treatment.

82 Immunological examination data, acquired 0.5-1.5 years after the accident, have shown that in the peripheral blood of the patient groups with a history of acute radiation sickness of the second, third and fourth degrees a decline was observed in the number of T-lymphocytes with helper activity along with an increase in the number of T-lymphocytes with suppressor activity. This led to a considerable reduction in the normal ratio between these immunoregulatory lymphocyte sub-populations. At the same time, there was no reduction in the general lymphocyte level or in their T- and B-sub-populations. As an average for the groups, the level of class A, M and G immunoglobulins in the patients' blood serum corresponded to the physiological norm. Similar changes were not observed in the case of patients with a history of acute radiation sickness of the first degree. During this time they experienced no severe or life-threatening infections. In a number of cases an effort was made at immuno-corrective therapy using T- and B-activin.

83. Within these same patient groups, an estimate of the number of respiratory illnesses over the same period of time was conducted retrospectively. It was found that the incidence of illness in the group of 19 patients with a history of first-degree acute radiation sickness did not differ from the incidence of illness for the group of persons for whom no acute radiation sickness diagnosis had been established, and that it averaged 0.3 cases per person per year. During the same period, this indicator approached 1 for 22 patients who had experienced second-degree acute radiation sickness, and 3 for 8 persons with a history of third- to fourth-degree acute radiation sickness.

84. This comparison underlines the importance of the immune system in maintaining anti-infection

resistance in radiation convalescents and raises the question as to the usefulness of conducting supportive immunomodulating therapy courses, long after the incident, for persons who have undergone severe forms of radiation sickness.

85 The experience of the specialized treatment centres in Moscow and Kiev in the organization of medical care of persons exposed in this nuclear reactor accident has been described [N16]. For the survivors, a plan of scheduled follow-up observation is in effect, and decisions as how best to arrange their living and working conditions are being taken.

D. CONCLUSIONS

86. The analytical data presented in this Appendix and derived from clinical observations of the victims of the accident at the Chernobyl nuclear power plant are in agreement with the data in Annex G

87 However, the fact that such a large group of 115 patients, who had all received uniform whole-body irradiation, was treated simultaneously for acute radiation sickness of varying degrees of severity, represents a unique event that makes it possible to clarify numerous aspects of early effects in man A complicating factor was the presence of severe and extensive beta-radiation skin injuries in 58 patients which aggravated the course of the sickness in 19 of the 28 who died. Two more patients died during the first days as a result of severe combined injuries (trauma plus thermal burns plus irradiation).

88. The analysis provides a basis for describing the principal clinical syndrome, the bone marrow syndrome, with various degrees of severity in all 115 patients. In the case of some of them the bone marrow syndrome was combined with intestinal and oropharyngeal injuries and radiation damage to the skin, the foreward segment of the eye (keratitis), and the lungs.

89. The treatment provided was in accordance with international practice and proved highly effective for the patient group exposed to doses of 2-4 Gy and for two thirds of the patients who received doses of 4-6 Gy. In the group of patients receiving 6-16 Gy, two patients who received doses of 8-9 Gy survived past 60 days

90 The average bone marrow dose and the prognosis regarding the further course of the illness were determined on the basis of biological criteria. During the early period, most information was obtained from the karyological analyses, the lymphocyte counts and the primary reaction periods, later, from the granulocyte counts. The remaining indications were of an auxiliary nature In three cases, the dose value coincided with the electron spin resonance study of dental enamel after death.

91. There is a need for further analysis of the time course of the early effects for a more accurate understanding of the nature of lung and neurological injuries, and for more detailed data on the relevance of biological dose indicators and the reasons for disparities between them. It is hoped that these data will be of use in the preparedness to respond in the event of an accident of a similar type in the provision of medical treatment.

Table A.1

Thyroid doses received by exposed persons

Range of thyroid doses (Sv)	Number of persons
0 - 1.2	173
1.2- 3.7	18
3.7- 6.1	4
6.1- 8.6	4
8.6-11.0	2
11.0-13.4	2
13.4-15.9	0
15.9-18 3	2
18.3-20.8	0
20.8-23.2	1

Table A.2

Doses of victims receiving higher internal exposures

Case number	Thyroid dose a/ (Gy)	Lung dose a/ (Gy)	Whole-body dose (Sv)	
			Internal	External
24	30	2 5	2.0	1.7
25	6	2.0	1 0	4 7
17	1	0 4	0 2	10 0
3	0 3	0.3	0 2	12 0
4	1.2	0.4	0.1	11 0
26	0 5	0.3	0.1	12.0

a/ Doses accumulated until time of death

Table A 3

Distribution of patients with acute radiation sickness treated at the specialized treatment centre

Degree of severity	Number of patients	Bone marrow dose range (Gy)	Number of deaths	Time to death (days)
I	31	0.8-2.1	-	-
II	43	2.2-4.1	1	96
III	21	4.2-6.4	7	16,18,21,23,34,48,48
IV	20	6.1- 16	20	10,14,14,15,15,17,17, 18,18,18,20,21,23,24, 24,25,30,32,86,91
	115		28 a/	

a/ In addition to the patients who died of acute radiation sickness, one person died at the plant site and another within the first 12 hours following the accident, as a result of thermal burns, at the in-patient clinic in Pripyat where he had been given first aid.

Table A.4

Assessment of irreversible myelodepression according to diagnostic scores in cases of acute radiation sickness

Sign			Diagnostic score a/
Time to the onset of vomiting	(hours)	0.00- 0.4	+ 8
		0.41- 0.8	+ 4
		0.81- 1.2	+ 2
		1.21- 1.6	- 2
		1.61- 2.0	- 6
		> 2.01	-10
Lymphocyte count on the second day	(10^9/l)	0.00- 0.2	+ 6
		0.21- 0.4	+ 2
		0.41- 0.6	- 2
		0.61- 0.8	- 8
		> 0.81	-15
Lymphocyte count on the third day	(10^9/l)	0.00- 0.1	+ 8
		0.11- 0.2	+ 2
		0.21- 0.3	- 2
		0.31- 0.4	- 9
		> 0.41	-10
Lymphocyte count on the fourth day	(10^9/l)	0.00- 0.1	+ 4
		0.11- 0.2	+ 2
		0.21- 0.3	0
		0.31- 0.7	- 2
		0.71- 0.8	- 3
		0.81- 0.9	- 8
Lymphocyte count from day 4 to day 7	(10^9/l)	0.00- 0.1	+ 5
		0.11- 0.2	+ 2
		0.21- 0.3	- 1
		0.31- 0.4	- 5
		0.41- 0.5	-13
		> 0.51	-15
Average reticulocyte count from day 3 to day 5	(10^9/l)	0.0 - 8.0	+ 2
		0.1 -10.0	0
		10.1 -14.0	- 4
		14.1 -18.0	- 6
		18.1 -20.0	-10
Minimum neutrophil count for day 6 to day 7	(10^9/l)	0.00- 0.3	+12
		0.31- 0.6	+ 5
		0.61- 0.9	0
		0.91- 1.2	- 3
		1.21- 2.4	- 6
		2.41- 3.0	- 8

a/ The diagnostic signs are used to determine the diagnostic scores, which are then added together. A sum of +10 is the basis for a prognosis of irreversible myelodepression; a sum of -10 for a prognosis of no irreversible myelodepression. If after the diagnostic coefficients of all the available signs have been added no positive value has been reached, the answer is indeterminate (the available information is insufficient for a differential diagnosis, with an error probability of not more than ± 10%)

Table A.5

Survival or cause of death of patients receiving bone marrow transplantations and of patients in control group

Dose range (Gy)	Bone marrow transplant patients				Control patients		
	Number of patients	Deaths a/	Deaths b/	Number of survivors	Number of patients	Deaths a/	Number of survivors
< 6.5	4	0	3	1	5	0	5
6.5-9	3	2 c/	0	1	4	3	1
> 9	6	5	1	0	5	5	0
Total	13	7	4	2	14	8	6

a/ Skin and intestinal injuries
b/ Bone marrow rejection (graft-versus-host disease) plus infection
c/ Positive graft-versus-host disease post-mortem histology.

Table A.6

Distribution of cases of radiation burns of different degree in the presence of acute bone marrow syndrome

Degree of severity of bone marrow syndrome	Total number of patients	Number of patients with radiation burns to various percentages of the body surface		
		0-10%	10-50%	50-100%
I	31	2	1	0
II	43	2	9	1
III	21	3	15	3
IV	20	1	10	9
Total	115		56	

Table A.7

Patient identification, estimated dose, cause and day of death

Degree of severity of ARS	Case number	Bone marrow dose (Gy)	Treatment a/	Day of death b/	Cause of death
II	33	4.1		96	Infection, renal-hepatic insufficiency and skin injuries
III	5	4.4	BMT	34	Infection, post-transplantation immunosuppression
	7	4.7		18	Skin injuries, post-transfusion shock
	24	3.7		23	Thermal and radiation burns
	25	5.7		16	Thermal and radiation burns
	28	6 4	BMT	46	Infection, graft-versus-host disease
	30	5 5	BMT	21	Bleeding from mechanical injury during catheterization
	34	5.8		48	Respiratory insufficiency, cerebral oedema
IV	1	6.6	BMT	25	Toxicity, respiratory insufficiency
	2	9.2	BMT	15	Skin and lung injuries
	3	12	BMT	17	Skin and intestinal injuries
	4	11.8	BMT	18	Skin and intestinal injuries
	6	7.5	BMT	86	Infection, graft-versus-host disease
	8	8.3	LCT	30	Toxicity, respiratory insufficiency
	9	9.7		23	Skin and lung injuries
	10	11.1	LCT	14	Skin and intestinal injuries
	12	9 3		24	Lung injuries
	14	10.9	LCT	18	Skin and intestinal injuries
	15	>10	LCT	14	Skin and intestinal injuries
	16	10 1	BMT	91	Infection, graft-versus-host disease
	17	10	BMT	18	Skin and intestinal injuries
	20	12 4	LCT	17	Skin and intestinal injuries
	23	13 7	LCT	15	Skin and intestinal injuries
	26	12.5		20	Skin and intestinal injuries
	27	8 3	BMT	24	Lung injuries
	31	6.7		32	Respiratory insufficiency, cerebral oedema
	62	6 1		21	Radiation burns (skin injuries)
	2097 (Kiev)	10.2		10	Skin and intestinal injuries

a/ BMT = bone marrow transplantation, LCT = liver cell transplantation.

Table A.8

Type of eye changes and per cent incidence in the victims of the accident

Nature of the changes	Degree of acute radiation sickness			
	I	II	III	IV
First wave of erythema	6.1	39.5	100	100
Second wave of erythema		20.9	80.9	100
Reduction in cornea sensitivity		18 6	100	100
Epilation of the eyebrows		16.3	66.7	100
Keratitis		4.6	52 4	100
Fundus				
Dilation of blood vessels		32.6	74.4	100
Decreased diastolic pressure of the central retinal artery		48.8	95.2	100
Retinal oedema		4.6	-	80
Haemorrhaging		13.9	23.8	80
Plasmorrhaging		4.6	23.8	80

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