Pergamon

European Journal of Cancer Vol. 33, No. 9, pp. 1413–1418, 1997

Printed in Great Britain
0959-8049/97 $17.00 + 0.00

PII: S0959-8049(97)00128-7

Original Paper

Carcinoma of the Stomach Following the Chernobyl Nuclear Accident

I.B. Shchepotin,[1,2] V.L. Valetsky,[2] V.A. Chorny,[2] M. Shabahang,[1] R.J. Nauta,[1] R.R. Buras[1] and S.R.T. Evans[1]

[1]Department of Surgery, Georgetown University Medical Center, 3800 Reservoir Road NW, Washington DC 20007, U.S.A.; and [2]Ukrainian Institute of Oncology and Radiology, Kiev, Ukraine

Medical consequences of many nuclear accidents on humans are well studied, but the results pertaining to gastric cancer patients who were exposed to radiation as a result of the Chernobyl nuclear accident have not been analysed. In this study, the outcome of the surgical treatment of 68 gastric cancer patients who were exposed to radiation as a result of the Chernobyl nuclear accident was compared with that of 117 consecutive gastric cancer patients from uncontaminated areas of the Ukraine. Patients in the study group was significantly younger than that of the control group. Comparative analysis showed the same frequency of regional metastases (65.7% versus 71.1%, $P > 0.05$), but a smaller number of distant metastases (23.8% versus 38.1%, $P < 0.05$) in the study group. 41.2% of patients in the study group underwent total gastrectomy compared to 19.6% of patients in the control group ($P = 0.002$). Postoperative complications developed in 13.2% of patients in the study group, while postoperative mortality in the study group was 7.3% compared to 1.7% in the control group. A significant decrease in CD16 cells was noted in patients from the study group following the operative procedure. Young age, invasive tumours with smaller number of distant metastases, frequent necessity for total gastrectomy and combined operations with adjacent organs, a higher level of postoperative morbidity and mortality and low levels of natural killer cells (CD16+) with a tendency to decrease after surgery are characteristic of patients with carcinoma of the stomach affected by the Chernobyl accident. © **1997 Elsevier Science Ltd.**

Key words: gastric cancer, surgery, Chernobyl, nuclear accident

Eur J Cancer, Vol. 33, No. 9, pp. 1413–1418, 1997

INTRODUCTION

MEDICAL CONSEQUENCES of major nuclear accidents on humans are relatively well studied and widely known. A comprehensive programme of medical follow-up of atomic bomb survivors in Japan has produced a quantitative analysis of cancer risk from exposure to ionising radiation [1–4]. The National Research Council report on Mortality of Nuclear Weapons Test Participants showed a 62% higher rate of cancer among soldiers involved in nuclear weapons testing who had exposures to fallout of 300 mrem or more [5]. The accident that occurred at the Chernobyl Nuclear Power Plant on April, 1986 had severe consequences, namely radioactive contamination of a significant land area and exposure of the population to measurable levels of radioactive fallout [6, 7]. On average, 17 million people, 2.5 million of these younger than 5 years of age, were exposed to some degree of radioactive contamination [8]. Currently, it is not clear what proportion of the 17 million people contaminated by Chernobyl developed gastric cancer. These numbers are currently not available. Approximately 90 000 citizens of the Ukraine were evacuated due to the heavy contamination of the environment and the average effective dose was retrospectively estimated to be 15 msv, although individual values vary in an extremely wide range from 0.1 to 383 mSv [9].

Correspondence to I.B. Shchepotin.
Received 6 Nov. 1996; revised 10 Mar. 1997; accepted 11 Mar. 1997.

Approximately 800 000 so-called liquidators who were involved in the clean-up operation were each exposed to radiation for an average of 2 months, often without proper safety equipment and dosimetry badges [10]. Given the long latency period for cancer induction exposure [11], it is still too early to fully assess the health risks of the exposed population and draw conclusions about pathogenesis and clinical peculiarities of radiation-related cancers [10]. However, beginning in 1989–1990, a definite increase in the incidence of thyroid cancer in childhood reported in the Ukraine [12] and the Republic of Belarus [13] was considered to be a direct consequence of the accident at Chernobyl. Another earlier report from the same institution, had concluded that even in the most highly contaminated areas of the Ukraine, no significant increase in malignancies, including thyroid cancer in childhood, occurred between 1986 and 1991 as a result of the Chernobyl accident [14]. A substantial increase was predicted over the next 50 years in the exposed population by other authors [15]. However, an International Atomic Energy Agency study showed that levels of environmental fallout contamination were insignificant [16] and no health disorders that could be attributed to the radiation exposure were identified among residents living within contaminated villages [17]. Despite the fact that no notable increase in the incidence of other malignancies has been reported, we believe that analysis of the consequences of Chernobyl, including continued medical follow-up along with clinical and epidemiological studies, is important [10] to prepare for any comparable events in the future [18].

No attempt has been made to identify a cause and effect relationship between the radiation exposure and gastric cancer. The Chernobyl accident released a lower dose of radiation over a longer period of time in contrast to any other nuclear accidents. As yet, researchers have not reached any conclusions about the impact of long-term, low-dose radiation on the risk of gastric cancer. To prove gastric cancer is related to radiation in observed patients, an extensive epidemiological study would be required. Instead, we tried to identify any differences in patients who developed gastric cancer and were previously exposed to radiation as a result of the Chernobyl accident. Comparative analysis of gastric cancer patients with an estimated radiation dose obtained as a result of the Chernobyl accident and in unexposed patients from uncontaminated regions of the country was performed to determine clinical differences. Specific changes in the immune system before and after surgery, which would be helpful in the understanding of the biology of the tumours, were also studied.

PATIENTS AND METHODS

Patient population

From January 1987 to January 1992, 68 patients with carcinoma of the stomach who were involved in the clean-up of the territory of the Chernobyl nuclear power station after the accident in April, 1986 or who inhabited contaminated zones were entered into this study. One hundred and seventeen consecutive gastric cancer patients from January 1987 to January 1992 who inhabited uncontaminated territories of the Ukraine and who were not involved in the Chernobyl accident clean-up were also entered into the study as a control group. All patients with gastric cancer were referred to the Department of Abdominal Tumours of the Ukrainian Institute of Oncology and Radiology at Kiev. There are 45 regional cancer centres in the Ukraine. Each centre receives referrals from the local clinics and hospitals within the geographical region of the Ukraine. Under the authority of the Ministry of Health, the Institute of Oncology is the leading Ukrainian organisation in charge of oncological research, developing protocols and techniques, training professionals, and the implementation of new methods. The institute also serves as the referral hospital for complicated and/or unusual cases of cancer. This institute receives referrals from 45 regional cancer centres throughout the Ukraine. In determining which patient in the Ukraine who develops gastric cancer goes to which cancer institute is purely based on geography.

Distribution of the patients by age and sex is shown in the Table 1. The study and control groups are from such extremely close geographic vicinities that the chance of an inherent difference in gastric cancer incidence is unlikely as was previously published [19]. All patients, including those in the study and control groups, underwent oesophagogastroduodenoscopy. The indications were the same for all patients admitted to the institute. No patients with multiple tumours were found despite a fairly aggressive clinical examination. Gastro-oesophageal junction cancers and distal oesophageal cancers were not included in this study. The study group included 18 'liquidators' (26%), workers who were involved in the clean-up of the contaminated territory on a contractual basis and 50 (74%) inhabitants of the controlled areas contaminated by the Chernobyl accident. Total doses obtained by 'liquidators' were not provided. Since many of the individuals involved in the clear-up were not directly monitored with radiation badges, but rather were given calculated doses, the accuracy of these estimates has been questioned [10]. Thirty-six patients were living on the territory with a level of ^{137}Cs contamination of 5-15 Ci/km^2 and 14 patients resided in the territory with a level of ^{137}Cs of 1–5 Ci/km^2. Patient distribution according to T, N, M

Table 1. Distribution of the patients based on age and sex

Age (years)	Study group			Control group		
	Men (n = 44)	Women (n = 24)	Total (n = 68)	Men (n = 66)	Women (n = 51)	Total (n = 117)
16–20	–	1 (4.2%)	1 (1.5%)	–	–	–
21–30	1 (2.2%)	–	1 (1.5%)	–	–	–
31–40	4 (9.0%)	3 (12.5%)	7 (10.3%)	1 (1.5%)	3 (5.9%)	4 (3.4%)
41–50	10 (22.7%)	3 (12.5%)	13 (19.1%)	6 (9.0%)	6 (11.8%)	12 (10.3%)
51–60	10 (22.7%)	8 (33.3%)	18 (26.5%)	28 (42.4%)	10 (19.6%)	38 (32.5%)
61–70	18 (40.9%)	7 (29.3%)	25 (36.8%)	24 (36.4%)	26 (50.9%)	50 (42.7%)
71–80	1 (2.2%)	2 (8.3%)	3 (4.4%)	7 (10.6%)	6 (11.8%)	13 (11.1%)

Table 2. Distribution of the patients based on T, N, M, criteria

p TNM	Study Group	Control Group
p T_2,N_0,M_0	4 (5.9%)	6 (5.1%)
p T_2,N_1,M_0	1 (1.5%)	–
p T_3,N_0,M_0	12 (17.6%)	11 (9.4%)
p T_3,N_0,M_1	1 (1.5%)	2 (1.7%)
p T_3,N_1,M_0	3 (4.4%)	5 (4.2%)
p T_3,N_2,M_0	9 (13.2%)	9 (7.7%)
p T_3,N_2,M_1	–	2 (1.7%)
p T_3,N_3,M_0	1 (1.5%)	–
p T_3,N_3,M_1	1 (1.5%)	2 (1.7%)
p T_4,N_0,M_0	6 (8.8%)	7 (6.0%)
p T_4,N_0,M_1	–	2 (1.7%)
p T_4,N_1,M_0	2 (2.9%)	10 (8.5%)
p T_4,N_1,M_1	3 (4.4%)	5 (4.2%)
p T_4,N_2,M_0	9 (13.2%)	7 (6.0%)
p T_4,N_2,M_1	8 (11.8%)	12 (10.3%)
p T_4,N_3,M_0	4 (5.9%)	5 (4.2%)
p T_4,N_3,M_1	3 (4.4%)	12 (10.3%)
p T_x,N_x,M_x	1 (1.5%)	20 (17.1%)
Total	68 (100%)	117 (100%)

classification is shown in Table 2. No significant difference in the histological type of tumours in the study and control groups was noted.

Flow cytometry

The following monoclonal antibodies were used in the study: anit-Leu-12 (CD19), anti-Leu-4 (CD3), anti-Leu-3a (CD4), anti-Leu-2 (CD8), anti-Leu-11c (CD16) and anti-interleukin-2 receptor (CD25). Antibodies were obtained from Becton Dickinson (San Jose, California, U.S.A.).

Monoclonal antibodies labelled with fluorescein isothiocynate (FITS) were used for direct immunofluorescence. A suspension of *Staphylococus aureus* labelled with FITS was used for detection of phagocyte activity. Preliminary incubation of peripheral blood samples with phytohaemagglutinin (Difco, U.S.A.) at 37°C for 16 h was followed by two washings and used for CD15+ cell detection. Peripheral blood samples were incubated with monoclonal antibodies at 4°C for 30 min followed by a standard lysis procedure with FACS Lysing Solution (Becton Dickinson Immunocytometry Systems) and two subsequent washings. Peripheral blood and *Staphylococcus aureus* were incubated at 37°C for 30 min, the phagocytosis reaction was then stopped and washed twice. Cell fluorescence was analysed on a FACScan flow cytometer (Becton Dickinson). An argon laser power of 15 mW at 488 nm was used for excitation; FITS fluorescence was measured at 520–540 nm, with 5×10^4 cells measured in each analysis. The data were analysed with FACScan research software.

Statistical analysis was done using Pearson's chi-square test to compare proportions, the trend test to test for a linear trend in a $2 \times K$ table with ordered columns, and *t*-test to compare quantitative variables. All tests were based on the extract, finite sample tail probability. All tests were two-sided and *P* values less than 0.05 were considered statistically significant.

RESULTS

Comparative analysis of the two groups of patients showed a similar gender distribution. Men were slightly over-represented in the study group, but this difference was not significant ($P = 0.28$). This difference was explained by the exclusive involvement of men in the clean-up of the territory surrounding the nuclear reactor. In the study group, 32.3% of patients were between 16 and 50 years of age, while in the control group there were only 13.7% in that age group (Table 1, $P = 0.002$). Among patients from the study group, 13.2% were below the age of 41 years compared to 3.4% of those in the control group. Among gastric cancer patients who were living in the contaminated areas, the majority resided in more heavily contaminated zones.

Comparative analysis of T, N, M indices in both groups showed the same frequency of regional metastases (65.7% versus 71.1%, $P > 0.05$), but a smaller number of distant metastases (23.8% versus 38.1%, $P < 0.05$) in the study group compared to the control group (Table 2).

All the presented data were collected in one institution where only one surgical philosophy existed regarding operative management of gastric cancer. The resectability level in the study group was 73.5% (50/68) in comparison with 46% (54/117) in the control group (Table 3, $P = 0.0004$). Total gastrectomies were performed in 63.6% of cases who had received radical surgery treatment in the study group and in 47.9% in the control group ($P < 0.05$). A greater number of total gastrectomies was performed in the study group in comparison with control (41.2% versus 19.6%, $P = 0.002$), while the same number of subtotal gastrectomies was done in both groups (23.5% versus 21.4%, $P = 0.85$). This was the lower result of a lower prevalence of tumours in middle and proximal locations in the study group (57.4%/control versus 44.4%/study, $P < 0.05$). A greater number of combined total gastrectomies with adjacent organs was noted in the study group when compared to control (50% versus 34.8%, $P < 0.05$) as well as the number of combined gastrectomies (31.3% versus 12%, $P < 0.05$). It was a result of a deeper level of invasion of the tumours into the adjacent organs which required resection in the majority of cases.

A higher level of postoperative morbidity and mortality was seen in the study group compared with the controls ($P = 0.01$). Postoperative complications developed in 13.2% of patients in the study group and 5.9% of the control group. Postoperative mortality in the study group was 7.3% compared to 1.7% in control group (Table 4). Four patients (14.3%) died after total gastrectomy and 1 (6.3%) after subtotal gastrectomy in the study group. Two patients (8.7%) died after total gastrectomy in the control group, while no

Table 3. Distribution of the patients based on type of surgery

Type of surgery	Study group	Control group
Total gastrectomies:	28 (41.2%)	23 (19.6%)
Standard	14 (50.0%)	15 (65.2%)
With adjacent organs	14 (50.0%)	8 (34.8%)
Subtotal gastrectomies	16 (23.5%)	25 (21.4%)
Standard	11 (68.7%)	22 (88.0%)
With adjacent organs	5 (31.3%)	3 (12.0%)
Palliative total gastrectomies	2 (3.0%)	2 (1.7%)
Palliative subtotal gastrectomies	4 (5.9%)	4 (3.4%)
Bypass surgery	10 (14.7%)	31 (26.5%)
Exploration	8 (11.8%)	32 (27.4%)
Total	68 (100%)	117 (117%)

Table 4. Postoperative morbidity and mortality

Complications	Study group ($n = 68$) Number	Died	Control group ($n = 117$) Number	Died
Intra-abdominal bleeding				
TG	1	0	1	0
SG	0	0	0	0
Subphrenic, subhepatic abscesses peritonitis				
TG	2	2	2	2
SG	0	0	1	0
Leakage of the oesophageal, gastric anastomoses				
TG	1	1	2	0
SG	1	0	0	0
Intestinal fistula				
TG	2	1	1	0
SG	1	0	0	0
Renal–hepatic failure				
TG	0	0	0	0
SG	1	1	0	0
Total	9 (13.2%)	5 (7.3%)	7 (5.9%)	2 (1.7%)
TG	6	4	6	2
SG	3	1	1	0

TG, total gastrectomy; SG, subtotal gastrectomy

deaths occurred after subtotal gastrectomy in the control group (Table 4).

Immunological status including lymphocytic subpopulations CD3+, CD19+, CD4+, CD8+, CD16+, CD25+ and the percentage of phagocytic neutrophils was studied in both groups of gastric cancer patients before surgery, and at days 7 and 15 after surgery. This was compared with results from the study of healthy donors. In gastric cancer patients from the control group, no significant differences in immune status was found in comparison with healthy donors (Table 5, $P > 0.05$). In gastric cancer patients from the study group, a significant decrease in the relative number of natural killer cells (CD16+) was noted in comparison to those from healthy donors– -8.4 ± 4.2 versus 15.9 ± 2.3 (Table 5, $P < 0.05$). On day 7 after surgery, the number of natural killer cells in the study group was still low (7.2 ± 3.9, $P < 0.05$) when compared with healthy donors and on day 15, this level had decreased (5.7 ± 3.4, $P < 0.05$). In patients from the control group, the level of CD25+ did not differ from that of healthy donors (Table 5, $P > 0.05$). In gastric cancer patients from the study group, the level of lymphocytes being interleukin-2 receptor (CD25+) was significantly lower than that of healthy donors, 11.0 ± 4.5 versus 23.9 ± 4.8, $P < 0.05$). After sur-

Table 5. Lymphocytic subpopulations and percentage of phagocytic neutrophils in gastric cancer patients before, after 7 and 15 days after surgery

Parameters	Groups of patients: Study group N	Study group Mean ± S.D.	Control group N	Control group Mean ± S.D.	Healthy donors N	Healthy donors Mean ± S.D.
CD3+, %						
Pre-operative	13	71.4 ± 7.6*	14	61.7 ± 9.0	13	71.3 ± 4.8
POD 7	11	67.3 ± 9.4	15	61.2 ± 10.5	13	N/A
POD 15	9	68.3 ± 9.8	12	62.6 ± 8.3	13	N/A
CD19+,%						
Pre-operative	13	11.1 ± 4.2	14	15.5 ± 2.2	13	13.5 ± 3.2
POD 7	11	11.7 ± 3.9	15	11.8 ± 3.7	13	N/A
POD 15	9	9.6 ± 4.3	12	10.3 ± 6.4	13	N/A
CD4+,%						
Pre-operative	13	39.3 ± 8.8	14	42.6 ± 8.0	13	41.8 ± 4.0
POD 7	11	41.9 ± 8.4	15	46.6 ± 10.3	13	N/A
POD 15	9	43.3 ± 9.3	12	49.1 ± 7.5	13	N/A
CD8+,%						
Pre-operative	13	36.1 ± 13.3	14	31.5 ± 10.1	13	33.4 ± 4.5
POD 7	11	30.4 ± 11.8	15	28.4 ± 10.3	13	N/A
POD 15	9	33.0 ± 13.6	12	25.4 ± 8.0	13	N/A
CD16+,%						
Pre-operative	13	8.4 ± 4.2	14	10.7 ± 6.2	13	15.9 ± 2.3
POD 7	11	7.2 ± 3.9*	15	10.7 ± 4.4	13	N/A
POD 15	9	5.7 ± 3.4*	12	10.9 ± 6.8	13	N/A
CD25+,%						
Pre-operative	12	11.0 ± 4.5*	12	15.0 ± 6.9	13	23.9 ± 4.8
POD 7	11	15.4 ± 6.2	14	17.2 ± 6.8	13	N/A
POD 15	9	18.2 ± 6.8	12	17.5 ± 4.3	13	N/A
Phagocytic neutrophils, %						
Pre-operative	13	78.0 ± 15.2	14	74.7 ± 12.1	13	94.3 ± 7.3
POD 7	11	81.6 ± 13.7	15	80.7 ± 9.0	13	N/A
POD 15	9	81.6 ± 13.7	12	80.7 ± 9.0	13	N/A

POD 7, 7 days after surgery; POD 15, 15 days after surgery.
*$P < 0.05$ (study group versus healthy donors)

gery, the level of CD25+ normalised in this group of gastric cancer patients (Table 5, $P > 0.05$).

Before surgery, gastric cancer patients from the control group showed a significantly lower level of phagocytic neutrophils when compared to healthy donors (74.7 ± 12.1 versus 94.3 ± 7.3, Table 5, $P < 0.05$), whilst the percentage of phagocytic neutrophils in the study group did not significantly differ from that of healthy donors (78.0 ± 15.2 versus 94.3 ± 7.3, Table 5, $P > 0.05$). After surgery, the number of phagocytic neutrophils was normal in all arms of the study (Table 5, $P > 0.05$).

DISCUSSION

Currently, there are no reports in the literature pertaining to the treatment of gastric cancer in patients previously exposed to radiation as a result of nuclear accidents. A recent publication revealed no difference in the clinical symptoms of gastric cancer in theses patients, but found that the impairment of erythrocytic membrane function required correction [20]. Our preliminary data showed that there was a significantly larger number of young patients in the group of patients who received different doses of radiation as a result of the Chernobyl accident in comparison with the control group and with our previously published data regarding gastric cancer patients [21, 22]. As shown in other studies [18], we found that the highest incidence appeared to be in patients who were living in more contaminated areas.

As a result of a comparison of T, N, M indices and surgery, one may conclude that patients who were exposed to radiation after the Chernobyl accident were prone to have invasive tumours with smaller numbers of distant metastases. A significantly higher percentage of postoperative complications and level of postoperative mortality was noticed in the study group when compared with the control group and with our previously published results of gastric cancer management [21, 22]. This could be the result of a larger number of total gastrectomies and combined operations with adjacent organs or a consequence of immune system depression in patients exposed to radiation.

The causative factors for a large number of invasive tumours along with a smaller number of metastases in patients exposed to radiation as a result of the Chernobyl accident were not well defined. Previous analysis of other heavily exposed sites such as Hiroshima and Nagasaki [1–4], or the radiation test fields in the United States [5] offer no clear explanations related to alterations in the clinical manifestations of solid epithelial tumours. One may speculate that the inhibition of CD16+ cells may be a marker for immunological deficiency and may lead to more locally invasive tumours. Of course, this speculation does not explain the existence of fewer distant metastases. Additional studies will be necessary to attempt to elucidate these two intriguing questions.

Four decades after the explosion in Hiroshima, a uniform decrease in CD5+, CD4+ and CD8+ cell numbers and their functions has been shown [23]. During the first year after the Chernobyl accident, patients who developed acute radiation sickness had a decreased number of T cells [24], but persons who were engaged in clean-up operations (liquidators) had normal or slightly increased levels of T cells in their blood [25]. After five years, the total T cell number, cell thymic activity and α_1-thymosin concentration were decreased in all affected persons and it was speculated that radiation alters the function of thymic epithelial cells by direct action and/or through indirect mechanisms, causing immune system ageing [26, 27]. In our study, there was no significant difference in lymphocytic subpopulations CD3+, CD4+, CD19+ and CD8+ between healthy donors or gastric cancer patients from both study and control groups. A lower number of natural killer cells (CD16+) before surgery was very characteristic of gastric cancer patients who were exposed to radiation as a result of the Chernobyl accident. Due to the fact that CD16+ counts in gastric cancer patients from uncontaminated areas of the country did not differ from that of healthy donors, we speculated that natural killer cell status could play a significant role in gastric cancer pathogenesis of the affected persons and could have an impact on short- and long-term prognosis of the disease. Prevention of natural killer cell deficiency may play an important role in gastric cancer management. Changes in the CD25+ subpopulation and in phagocytic neutrophils count do not appear to be characteristic for gastric cancer in patients who were exposed to radiation after the Chernobyl accident.

In conclusion, we believe that young age, invasive tumours with a smaller number of distant metastases, frequent necessity for total gastrectomies and combined operations with adjacent organs, a higher level of postoperative morbidity and mortality, and low levels of natural killer cells (CD16+) are characteristic of patients with carcinoma of the stomach affected by the Chernobyl accident. We suggest that these results can be used for determining follow-up strategies for the population affected by Chernobyl or by any comparable event and can be helpful in the management of disease in these patients.

1. Putnam FW. Hiroshima and Nagasaki revisted: the Atomic Bomb Casualty Commission and the Radiation Effects Research Foundation. *Perspect Biol Med* 1994, **37**, 515–545.
2. Shimizu Y, Schuii WJ, Kato H. Cancer risk among atomic bomb survivors. The RERF Life Spann Study. Radiation Research Foundation. *JAMA* (5) 1990, **264**, 601–604.
3. Shigematsu I, Mendelsohn ML. The Radiation Effects Research Foundation of Hiroshima and Nagasaki. *JAMA* (5) 1995, **274**, 425–426.
4. Land CE. Studies of cancer and radiation dose among atomic bomb survivors. *JAMA* (5) 1995, **274**, 402–407.
5. Bross ID, Bross NS. Do atomic veterans have excess cancer? New results correcting for the healthy soldiers bias. *Am J Epidemiol* (6) 1987, **126**, 1042–1050.
6. Ginzburg HM, Reis E. Consequences of the nuclear power plant accident at Chernobyl. *Public Health Rep* (1) 1991, **106**, 32–40.
7. Likhatarev IA, Chumack VV, Repin VS. Analysis of the effectiveness of emergency countermeasures in the 30-km zone during the early phase of the Chernobyl accident. *Health Phys* (5) 1994, **67**, 541–544.
8. Holowinsky IZ. Chernobyl nuclear catastrophe and the high risk potential for mental retardation. *Ment Retard* 1993, **31**, 35–40.
9. Likhtarev IA, Chumack VV, Repin VS. Retrospective reconstruction of individual and collective external gamma doses of population evacuated after the Chernobyl accident. *Health Phys* (6) 1994, **66**, 643–652.
10. Weinberg AD, Kripalani S, McCarthy PL, Schull WJ. Caring for the survivors of the Chernobyl disaster. *JAMA* (5) 1995, **274**, 408–412.
11. Shimizu Y, Kato H, Schull WJ. Life span study report 11, II: cancer mortality in the years 1950–1985 based on the recently revised doses (DS86). *Radiat Res* 1988, **121**, 120–141.

12. Nikiforov Y, Gnepp DR. Pediatric thyroid cancer after the Chernobyl disaster. Pathomorphologic study of 84 cases (1991–1992) from the Republic of Belarus. *Cancer* (2) 1994, **74**, 748–766.
13. Likhtarev IA, Sobolev BG, Kairo IA, *et al.* Thyroid cancer in the Ukraine. *Nature* 1995, **374**, 365.
14. Prisyazhiuk A, Pjatak OA, Buzanov VA, *et al.* Cancer in the Ukraine, post-Chernobyl. *Lancet* 1991, **338**, 1334–1335.
15. Baverstock KF. Thyroid cancer in children in Belarus after Chernobyl. *World Health Stat Q* (3) 1993, **46**, 204–208.
16. Henrich E, Steinhausier F. Dose assessment for recent inhabitants living adjacent to zones heavily contaminated from the Chernobyl. *Health Phys* (5) 1993, **64**, 473–478.
17. Ginzburg HM. The psychological consequences of the Chernobyl accident: findings from the International Atomic Energy Study. *Public Health Rep* 1993, **108**, 184–192.
18. Williams D. Chernobyl, eight years on. *Nature* 1994, **371**, 556.
19. Analysis of Cancer Distribution in Ukraine and Activity of Cancer Institutions in 1991–1993. Kiev, Ukrainian Ministry of Health, 1994, 120 pp.
20. Korobko VB, Kaban AP, Gunina LM, Fedorenko EA. The clinical and biochemical characteristics of the status of stomach cancer patients who were exposed to ionizing radiation as a result of the accident at the Chernobyl Atomic Electric Power Station. *Lik Sprava* 1995, **5 6**, 19–22.
21. Shchepotin IB, Evans SRT, Chorny V, *et al.* Intensive preoperative radiotherapy with local hyperthermia for the treatment of gastric carcinoma. *Surg Oncol* 1994, **3**, 37–44.
22. Shchepotin IB, Evans SRT, Chorny V, *et al.* Pre-operative superseletive intra-arterial chemotherapy in the combined treatment of gastric carcinoma. *Oncol Rep* 1995, **2**, 473–479.
23. Kusunoki Y, Akiyama M, Kyoizumi S, Bloom ET, Makinodan Y. Age-related alteration in the composition of immunocompetent blood cells in atomic bomb survivors. *Int J Radiat Biol* 1988, **53**, 189–198.
24. Bebeshko VG, Chumak AA, Bazyka DA, *et al.* Immunological monitoring of patients with acute radiation sickness 12-36 month after disaster on Chernobyl NPP. *Meditsinskaya Radiologiya* 1990, **35**, 27–30.
25. Petrov RV, Oradovskaya IV, Pinegin BV. Program of long-term immunological monitoring of population group exposed to risk factors at the Chernobyl accident. *Meditsinskaya Radiologiya* 1991, **1**, 39–42.
26. Yarlin AA, Belyakov IM, Kusmenok OI, *et al.* Late T cell deficiency in victims of the Chernobyl radiation accident: possible mechanisms of induction. *Int J Radiat Biol* (4) 1993, **63**, 519–528.
27. Oradovskaia IV, Ruzybakiev RM, Prokopenko VD, *et al.* Clinico-immunological characteristics of people who worked within the 30-kilometer zone of the accident at the Chernobyl Atomic Power Plant 4 years after the accident. *Radiat Biol Radioecol* (4-5) 1994, **34**, 611–619.

Acknowledgement—We thank Dr John Hanfelt, biostatistician at Georgetown University Medical Center, Lombardi Cancer Center, for helpful advice and for excellent biostatistical assistance.