

Accidental Radiation Exposure

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We report a radiation accident in which a technologist was in close proximity for 40 seconds to a source containing 7,700 curies of cobalt 60. The average bone marrow dose was estimated at 118 rads. Within the first 24 hours postexposure, lymphopenia developed and after two weeks, the platelet and granulocyte count began to fall and reached nadir at approximately four weeks. During the phase of granulocyte depression, the protective environment of a laminar airflow facility was believed to have lessened the risk of infection. This patient's hematological recovery was complete in six weeks.

After exposure to higher doses of radiation than this patient received, recovery can occur if appropriate supportive care, ranging from rest and observation to marrow transplantation, is employed. The clinical course, laboratory data, and estimated dose-exposure will dictate what type of therapy is needed. Each case must be individually evaluated.

Life-threatening radiation accidents are exceedingly rare, hence it is worthwhile to report each one. A summary of data on previous accidents can be found in a publication by Lushbaugh.¹ A recent accident resulting in an essentially whole-body exposure at a high-dose rate is the subject of this report.

Methods

The following procedures were used for the hematological studies: hemoglobin determination in a photometer by cyanmethemoglobin methods,² volume of

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packed red cells in Wintrobe hematocrit tubes,³ white blood cell counts (WBCs) done in triplicate in an electronic cell counter, and phase microscopy for enumeration of platelets by the Brecher-Cronkite method.⁴ Differential counts were performed on 200 cells per blood smears (Wright stain). Chemical determinations included: Oliver's method for creatine phosphokinase (CPK)⁵ and the method of Goodwin et al for serum iron and binding capacity.⁶

Report of a Case

Exposure.—A 32-year-old man, a research technologist, was accidentally exposed to the gamma rays from an unshielded cobalt 60 source of 7,700 curies which was located in a shielded room provided with interlocks and various safety devices. Unaware that the source was outside its shield, the technologist walked close to where he changed samples that were located 17 cm from the source. Soon after the technologist left the room, the operator of the irradiation facility realized that the sources might have been unshielded and that a serious exposure had possibly occurred, but was uncertain about it. A description of the facility and a discussion of the cause of the accident are given by Wade.⁷ The exposed man was brought 6 km by car to the Oak Ridge Associated Universities (ORAU) Medical Division and admitted to the hospital one hour after exposure. The thermoluminescent dosimeter worn at waist level was sent to the supplier for processing; when the results became available 28 hours later, an exposure of 260 roentgens was established. Reconstruction of the accident victim's path and actions showed that he had probably been in close proximity to the source for about 40 seconds. Studies carried out with a phantom provided information about the dose distribution.⁸ It was deemed best to assume that the dosimeter worn by the patient was the most accurate basis for estimating the exposure; therefore the absorbed doses, and the doses to

different parts of the body, as derived from the phantom studies, were normalized to this basic value (Table 1). The radiation distribution was rather uneven because of the positions of source and patient (Fig 1). Average midline dose for the torso was estimated to be 127 rads and to the marrow, 118 rads. It was conjectured that the right hand might have received 800 to 1,200 rads and the left hand 500 to 600 rads.

Clinical Course.—When first examined two hours after the accident, the patient appeared apprehensive but not ill. Results of a general physical examination were normal. The hands showed no redness, swelling, or tenderness. Episodes of vomiting, occurring suddenly without preceding nausea, began 2¼ hours postexposure and recurred ten times during the next 24 hours. Diarrhea and fever were absent.

About 24 hours later, he complained of itching and burning of his eyes and the sclerae were reddened. These manifestations, not present on admission, lasted for about 24 hours, then cleared. On the seventh hospital day he was allowed to go home to avoid exposure to nosocomial bacteria. He returned daily for blood counts. On day 25 he was readmitted and placed in a sterile laminar airflow unit where his exposure to infection would be reduced. No prophylactic antibiotics were given. Food was not sterilized.

No bleeding or temperature elevation occurred during the period of hematological depression that lasted from days 25 to 34 postexposure. On day 36 an infection in his mouth, diagnosed as Vincent angina, was treated with hydrogen peroxide mouth washes and orally administered penicillin for five days. On day 48, after the recovery of all his cellular blood elements was nearly complete, he was sent home. Out-patient visits were continued.

His right hand, which presumably received more radiation than any other part of his body, showed no visible signs of radiation damage, but beginning three days after exposure and continuing inter-

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FOLDER ACCIDENT FILE #3

COLLECTION MARKER FILES
BOX No. 3 OF 6

REPOSITORY DOE - FORRESTAL

Organ	Average Dose Rate, rads/min	Dose in 40 sec,* rads	Dose Normalized to Patient's Badge, rads
Bone marrow	157	105	118
Intestines	220	147	166
Kidneys	137	91	103
Lenses of eyes	206	137	155
Spleen	153	102	115
Stomach	217	145	163
Midline	169	113	127

* Patient's exposure time estimated as 40 seconds.

Day of Sample	Urine Excretion, mg/24 hr			
	Pseudouridine	Uracil	Hypoxanthine	Xanthine
1	75	...*	21.5	12.5
2	65	10.8	17.5	13.9
3	71.7	9.5	16.5	11.4
4	50.7	6.5	9.6	6.7
8	48.6	4.2	7.0	4.0
Normal values	42-64	7	6.8	2.8-8.7

* Elevated but not quantified because two peaks were not resolved.

mittently for some time, pain in the fingers and palm, described as a dull aching sensation, occurred after he had used the hand for prolonged periods, and sometimes woke him at night. About four months after the accident the pain subsided, only to recur several months later and then eventually to disappear. The consistency of his description made the pain seem quite credible. Radial pulses remained good and no ischemic changes were noted. Hair was always present on the backs of his hands with no detectable alteration. Thermistor readings of all fingertips showed variations of only 0.1 C, which were not considered significant. About four months after the accident the patient noted a faint, white horizontal line transversing the mid-part of all the nails of the right hand only. Having grown out with the nails, this line was no longer visible after six more weeks.

Examination of his eyes by an ophthalmologist on three occasions has revealed no abnormality.

For approximately four months after the accident he had easy fatigue; tasks formerly done with ease tired him quickly. However, work tolerance gradually increased until 11 weeks after the accident he returned to full-time employment in an area believed free of any abnormal radiation exposure.

Hematological Changes.—The blood count two hours postexposure was similar to pre-

employment blood counts; by four hours the leukocyte count had doubled and the absolute lymphocyte count had dropped from 2,840/cu mm to 948/cu mm. In 12 hours the total leukocyte count dropped to its admission level. At this time the only irregularity noted was the presence of abnormally large granulocytes on stained smears. Except for a rise to 1,900/cu mm at 16½ hours after exposure, the absolute lymphocyte count remained about 1,000/cu mm for the next four weeks.

Progressive depression of platelet and leukocyte values were followed by spontaneous recovery (Fig 2). The platelet count dropped from the normal range of 150,000 to 350,000/cu mm to 57,000/cu mm on day 25 and reached a nadir of 37,000/cu mm on day 29. On day 36 the WBC was lowest (2,000/cu mm).

Sternal marrow aspiration performed 29 hours after exposure revealed normal particles and minor morphological abnormalities including megaloblastoid changes of the erythroid series. The myeloid:erythroid (M:E) ratio was 4.8. On cytogenetic analysis of the direct marrow preparation, abnormalities were observed in 70% of the metaphases analyzed; the aberration most frequently seen was chromatid breaks. On day 5 a marrow aspiration yielded a hypocellular specimen, with a M:E ratio of 5.0 and hypersegmentation of mature granulocytes. Unsatisfactory preparations pre-

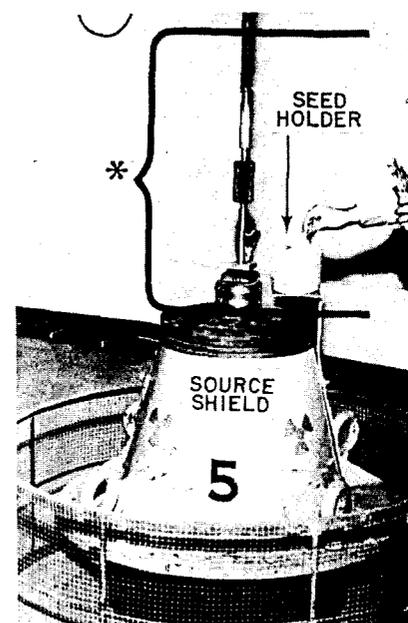


Fig 1.—Position of unshielded source in relation to accident victim. Bracketed area (*) indicates unshielded cobalt 60 source.

cluded cytogenetic analysis. On day 19 the marrow aspirate showed a moderate increase in cellularity, with relatively more erythroid elements (the M:E ratio was 1.1). On direct preparation for cytogenetic analysis, this marrow showed only one dicentric chromosome in 100 metaphases counted. More information on the cytogenetic findings is available elsewhere.⁹

Other Laboratory Changes.—The patient's endurance was tested by means of bicycle exercise monitored by ergometer. The day after these tests were begun, the CPK level in the patient's serum rose from normal (25 milliu/ml) level found on admission to 343 and 455 milliu/ml on days 4 and 5, respectively (Fig 3). Although daily exercise of increasing duration was continued, the CPK level returned to normal range within three more days.

On admission the serum iron was 180µg/100 ml and on day 5 was 310µg/100 ml; on day 12 it had returned to base line level, 170µg/100 ml (Fig 3).

Five 24-hour urine samples were analyzed by high-resolution liquid chromatography with an ultraviolet detector. Compounds quantified included β-pseudouridine, uracil, hypoxanthine, and xanthine (Table 2). Increased excretion of all four components during the first three days after radiation exposure had returned to normal range by the fourth day. The subnormal value for uracil excretion on day 8 remains unexplained.

Semen analysis six months after expo-

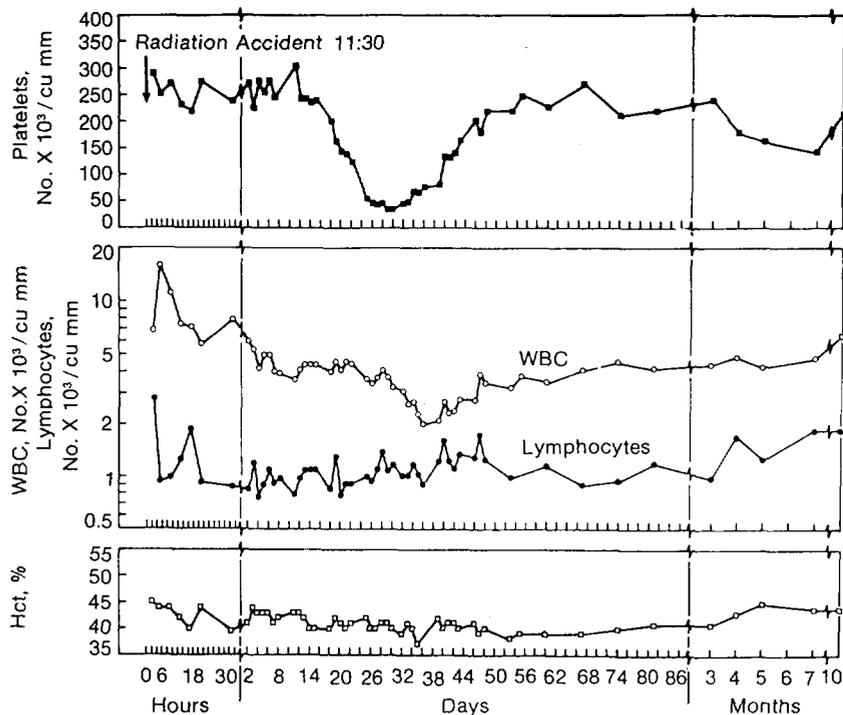
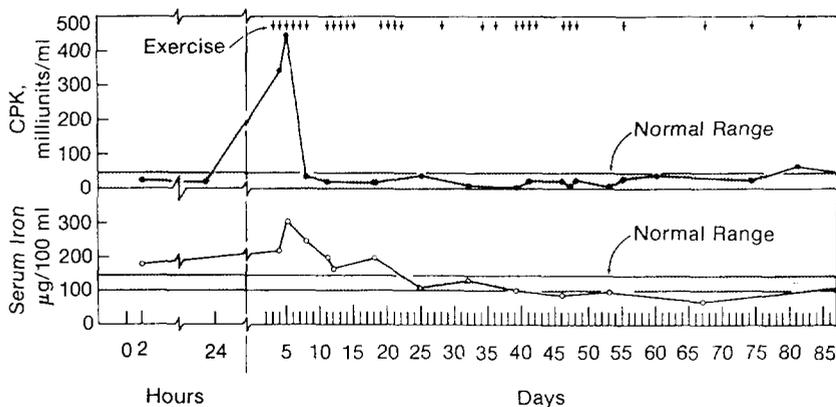


Fig 2.—Hematological changes of patient accidentally irradiated with 260 R at high-dose rate.

Fig 3.—Serum CPK value rose to nine times normal and serum iron level doubled on fifth day postirradiation. See text for possible meaning of these abnormalities.



sure revealed a low concentration of sperm (2.3 million per milliliter) with only slight morphological abnormality. Sperm examination repeated 14 months after radiation exposure showed normal sperm count (77 million per milliliter) with no morphological abnormality.

Comment

When this patient arrived at the hospital, there was serious doubt about whether he had experienced an accidental exposure, because no one

knew for sure whether the source had been on when he entered the radiation facility. His radiation monitoring badge would not be reported for many hours. When the patient began to vomit, this appeared to us to be strong evidence that he had been seriously exposed. We were not inclined to give much weight to the possibility that the vomiting could be psychogenic in origin. We believe emotionally induced vomiting is very unlikely in association with stress in unexposed

persons who have been frightened by the possibility of exposure. "Psychogenic vomiting," referred to in discussion of radiation accidents, is, in this context, something of a myth. Our opinion was further strengthened by the nature of the bouts of vomiting, which came on suddenly, even interrupting unexpectedly the patient's conversation. Further confirmation of the exposure came a few hours later when a sharp decrease in blood lymphocytes was noted.

The patient's general hematological response to irradiation of this magnitude was typical of that seen in other radiation accidents.¹⁰ One detail in which his response was somewhat unusual, however, was in the pattern of later leukocyte changes. Instead of a distinct nadir at about 30 days, there was an unusually prolonged valley in the WBC curve, with a rather delayed and slow recovery. At the time of lowest leukocyte values, a mouth infection occurred, possibly causing greater utilization of granulocytes that could not fully be compensated for by the recovering marrow.

The pattern of the thrombocyte curve, on the other hand, was exactly as expected. After day 15 the platelet values followed an arithmetic rate of decline, a type of loss seen with death from senescence in the absence of replacement. The time from beginning of fall to nadir, representing the life-span of the platelets, was in his case approximately 12 days, a value consistent with published data.

Unless bleeding due to thrombocytopenia or damage to the gastrointestinal tract occurs after irradiation, red blood cell (RBC) changes are not as dramatically manifest as are the leukocyte and platelet fall. However, early maturation arrest of erythroid precursors in the marrow, decreased utilization of iron by these precursors, and reciprocal increase in serum iron level are evidence of damage to the production of RBCs.

The overall hematological response seemed a little greater than might be expected from the estimated size of the absorbed radiation dose, possibly because of the rapidity with which the irradiation was delivered. Few ra-

diation accidents have involved such a high-dose rate, estimated as 157 rads/min to the marrow.

One might wonder what effect the unevenness of the dose would have on either the severity or time course of the response, especially the hematological effects. Could the marrow in the posterior portion of the torso, having received less exposure than the other areas of cellular marrow, serve to provide stem cells for early recovery, or minimize the overall effect? It is well known that, in other mammals, shielding part of the marrow will enhance survival after high-dose irradiation.¹¹ In this clinical experience no clear evidence of any features that can be related to the unevenness of the dose was noted. There was no early recovery, but a rather delayed regeneration of granulocytes, and the overall response was possibly somewhat greater than expected.

Although there was slightly delayed recovery of blood granulocyte levels, marrow repair was evident early. Severe chromosome damage in marrow obtained from the sternum 29 hours postirradiation had disappeared by day 19. However, elimination or reduction in number of damaged chromosomes cannot be equated with recovery of marrow function. It is clear that evidence of recovery of marrow production of cellular elements must precede their appearance in the circulation by an interval sufficient to allow for their maturation.

Because of the known proximity of the patient's hands to the cobalt 60 source, it was likely that significant tissue damage had occurred; lack of epilation led us to believe in retrospect that the radiation dose had been below 1,200 rads. The patient's descriptions of the deep, dull pain in his right hand suggested intermittent ischemia; thrombosis or spasm of the smaller blood vessels could have occurred without producing objective changes. The faint white lines seen in the nails of the right hand were similar to Beau lines, which occur after injury to the nail bed or after severe illness. Pigmented lines, probably with similar significance, were seen

in the natives of the Marshall Islands accidentally exposed to fallout in 1954.¹² The fact that our patient had them on only the right hand would suggest that they were due to local radiation rather than systemic effect.

Fatigue, a symptom difficult to assess, has been a subjective complaint of radiation accident victims, including the present one. One may conjecture that the rise in CPK levels observed in this patient was due to muscle damage by irradiation with release of enzyme after the added stress of exercise; this finding may have some bearing on the excessive fatigue reported after irradiation with high doses. Additional evidence of tissue damage and increased cell destruction is supplied by the data on the urinary excretion of purines and pyrimidines. The initial elevated levels of the four components quantified (Table 2) are consistent with rapid breakdown of cells.

As soon as enough information was available to assess the degree of injury, it appeared to us that this patient had received a serious but almost certainly sublethal dose of irradiation, and our opinion did not change. Therefore, conservative therapy was employed, and we withheld other therapeutic measures that might have been needed for more severe damage. Our views on treatment for more pronounced degrees of radiation injury have been published elsewhere.¹³

A single, nonfatal, fairly uniform exposure to total-body irradiation does not generally produce permanent or chronic somatic damage that is clinically obvious. Nonuniform acute exposure can produce chronic lesions in local areas, but such doses would be fatal if given to the whole body. The prevalence of the erroneous belief that high-dose radiation always produces obvious irreversible damage may be based on experience with chronic or repeated exposure.

In certain instances the exposure, whether local or general, chronic or acute, can contribute to the development of late effects—that is, the possible induction of leukemia or cancer. The statistical likelihood of these se-

quelae will remain low.

Perhaps the most encouraging aspect in the treatment of acute total-body exposure is the knowledge that if the patient can be supported through the period of maximum marrow depression, chances for survival and full clinical recovery are excellent in most cases.

Kathryn Lore and Shirley Colyer performed the hematology determinations; R. Ricks, PhD, the physiological studies; L. Gayle Littlefield, PhD, the cytogenetic studies; Allen Webb the chemistry determinations; J. E. Mroczek, PhD, and C. D. Scott, PhD, the high-resolution liquid chromatographic studies of the urine; J. MacLeod, PhD, the microscopic examination of the spleen morphology; and W. L. Beck, MS, the phantom radiation dosimetry studies.

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