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The Diagnosis and Management of Accidental Radiation Injury

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ALTHOUGH the nuclear age had its birth almost 20 years ago, widespread utilization of nuclear reactors and of large quantities of radioactive materials beyond the confines of governmental facilities has undergone great acceleration only within the past five years. The liberalized Atomic Energy Act of 1954, with its emphasis on peacetime uses of atomic energy, helped to stimulate this development. Thus, the population potentially exposed to peacetime accidental radiation injury has also been expanded to include not only Atomic Energy Commission contractors' employees but also workers in private industry, as well as the general population in their vicinity. This, in turn, means that not only the AEC's industrial physicians, but physicians in general must anticipate the possibility of being obligated to deal with the clinical aspects of radiation injury with very small, but, nevertheless, gradually increasing frequency as the nuclear age advances. And in the disastrous event that the world's peacemakers fail in their tasks, the frequency of such injury may well mount uncontrollably. It is therefore of immediate importance that all physicians be familiar with the diagnosis and management of clinical radiation injury.

Present knowledge of the effects of known doses of various radiations on normal humans is mainly indirect. It comes from controlled experiments with mice, rats, rabbits, and monkeys in the radiobiological laboratory, from analyses of findings in therapeutically irradiated sick humans, and from retrospective studies of accidental human radiation exposures.

Several drawbacks are evident in these data. Because of the variations in radiosensitivity of different tissues in different species, the controlled laboratory studies are not readily extrapolated to man. The biological responses of recipients of therapeutic irradiation are not necessarily those of normal humans. In accidental exposures of normal humans, detailed precise measurements of dose and uniform selection of test parameters and procedures have not always been possible. Because of these drawbacks, it is deemed essential that certain medical guidelines be established for the management of cases of radiation overexposure, not only to facilitate the management of accidental clinical radiation injury in the individual patient, but also to expedite the accumulation of more useful data concerning such injury, as a basis for further improvement in its diagnosis and therapy.

To make maximum use of past experiences with radiation accidents in developing the guidelines for their future clinical management, all presently available data concerning human exposure from criticality accidents have been reviewed. Only normal case material in which the radiation exposure was acute, external, penetrating, and generalized has been con-

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sidered. The clinical syndromes resulting from various protracted, internal, superficial, and localized exposures are too varied for the present purposes.

The sequence of events and resulting personnel exposures of each accident are reviewed and discussed in Part I, "Analysis of Past Accidents—Physical Aspects." Following a discussion of the clinical manifestations of radiation injury, the symptomatology and laboratory findings of the victims of these accidents are reviewed and analyzed in Part II, "Analysis of Past Accidents—Clinical Aspects."

Certain recommendations for diagnosis and management, based on the material reviewed, are made in Part III, "Recommended Medical Procedures." Despite their somewhat empirical and arbitrary nature, it is felt that their incorporation among the procedures used in dealing with these accidents will help to accomplish two vital objectives. These are, first, good immediate care of the patient at hand and, second, more effective therapy for future patients as a result of the improved compilation of usable long-term data concerning the deleterious effects of radiation in man.

Part I. Analysis of Past Accidents —Physical Aspects

Since the onset of widespread research and production activities in nuclear technology dating back to the inception of the Manhattan Project, there have been seven major criticality accidents involving significant overexposures of personnel to ionizing radiation (Table I).

In order to provide a better understanding of the nature and magnitude of these accidents, to demonstrate the problems of patient care, and to emphasize the need for the accumulation of long-term data of a standardized nature, each of these accidents is reviewed in chronologic order.

In addition to accident reports, a number of authors have summarized accidents and incidents involving radiation in nuclear technology activities, either as summary reports or as background or information material in the consideration of general or specific human radiation effects. Hayes[1] summarized accidents and incidents from June, 1945, through December, 1955, and extended the period to December, 1956, in a supplementary report.[2] Gerstner[3] included a summary of accidents up to 1955 as a part of his very comprehensive analysis and discussion of the acute radiation syndrome in man. Similar reports of other authors appear in the literature.[4-9]

TABLE I—CHRONOLOGY OF RADIATION ACCIDENTS

Accident	Date	Type
Los Alamos I	Aug. 21, 1945	Criticality (experimental assembly)
Los Alamos II	May 21, 1946	Criticality (experimental assembly)
Argonne	June 2, 1952	Criticality (reactor)
U.S.S.R.	1953-1954?	Criticality (reactor)
Oak Ridge	June 16, 1958	Criticality (processing)
Yugoslavia	Oct. 15, 1958	Criticality (reactor)
Los Alamos III	Dec. 30, 1958	Criticality (processing)

Accident Dosimetry

The characteristics of fissionable material vary with the mass and shape of the material. It is said to be "critical" when it is of such configuration that a nuclear reaction can be sustained at a fixed level of intensity. If the critical dimensions are exceeded, an exponentially increasing chain reaction will occur. Accidental excursions of this type produce variable intensities of fast neutrons and gamma rays. Accidents of this nature are referred to as criticality accidents. It is noted in Table I that all of these accidents were of this type.

Since the time of the first of these accidents (14 years ago), there has been a continuous evolution and improvement in the techniques and concepts of radiation dosimetry. For example, dose units such as the gram-roentgen are no longer believed to be significant indices of radiation exposure, and time has served to accentuate the complexity of the RBE concept. In a previous report,[10] an effort was made to reevaluate the dose assigned to certain individuals involved in nuclear accidents, using modern techniques of radiation dosimetry.

To put the physical dosimetry of past accidents on a common objective basis, the dose to a given individual is specified in terms of the absorbed dose (in rad), which would have been received by a small mass of tissue located at the position of the individual. This dose will be referred to as the first collision dose. It is realized that correlations of biological data with a single dose reading will be far from perfect unless other physical conditions of exposure are specified. Thus, as much information as is available on parameters such as radiation energy and angular distribution was considered in the previous report.[10]

The use of the rem dose unit is avoided entirely in this report, except as it appears in Table II under reported dose. First collision doses will be given in terms of rads to soft tissue for neutrons and gamma rays separately. This procedure is consistent with the desirability of establishing RBE factors for acute irradiation of man from accident data.

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The method which has been found most reliable for evaluating the neutron dose to persons exposed in mixed radiation fields is the measurement of the amount of radioactive sodium (Na^{24}) which is produced when the neutrons interact with normal sodium (Na^{23}) in the body. It has been found that the neutron dose to the body may be related in a simple way to the spectrum of incident neutrons as determined from threshold detector measurements. This method of dose measurement might be termed "spectral" dosimetry and is described in detail in the previously mentioned report.[10] Likewise, the Na^{24} activation engendered in the body is very simply related to threshold detector measurements of the neutron spectrum. Hence, if one can estimate or measure the neutron spectrum escaping from a critical assembly, the Na^{24} activation in a man may be interpreted in terms of the first collision dose at his position. This method has been used below, whenever data on spectral distribution of neutrons are available. Estimates of the gamma-to-neutron dose ratio are used to allow one to assign both gamma and neutron doses on the basis of Na^{24} activation in the body.

TABLE II—SUMMARY OF EXPOSURE DATA

Accident	No. of Patients	Pt. Code* R	Pt. Code* L	Reported Total Body Dose Neutron	Reported Total Body Dose Gamma	Reported Total Body Dose Total	Calculated Total Body Dose Neutron	Calculated Total Body Dose Gamma	Calculated Total Body Dose Total
LASL-I	2	LA1	1	480 (rem)‡	110 (rem)	590 (rem)	297 (rad)	?	297+ (rad)
		LA2	2	31	0.14	31	18.2	2	20.2
LASL-II	8§	LA3	3	1930 (rem)‡	114 (rem)	2044 (rem)	1230	120	1350
		LA4	4	390	26.4	416	220	22	242
		LA6	6	186	10.7	196	120	12	142
		LA7	7	140	8.7	148	50	5	55
		LA8	8	55	4.37	59	33	3	36
		LA9	9	42	2.72	44	25	2.5?	27.5?
		LA10	10	33	2.41	35	20	2	22
Argonne	4	A1	1	14.2 (rep)	145 (rep)	189 (rem)¶	14.2	145	159
		A2	2	9.6	116	146	9.6	116	126
		A3	3	5.5	55	71	5.5	55	60.5
		A4	4	0.8	10	12	0.8	10	10.8
U.S.S.R.	2	R1	Kh	?	?	450 (r)	?	?	450‖
		R2	M	?	?	300	?	?	300
Oak Ridge	8	OR1	A	96 (rad)	269 (rad)	365 (rad)	96	269	365
		OR2	C	89	250	339	89	250	339
		OR3	D	86	241	327	86	241	327
		OR4	B	71	199	270	71	199	270
		OR5	E	62	174	236	62	174	236
		OR6	F	18	50.5	68.5	18	50.5	68.5
		OR7	G	18	50.5	68.5	18	50.5	68.5
		OR8	H	6	16.8	22.8	6	16.8	22.8
Yugoslavia	6	Y1	V	210 (rem)	630 (rem)	840 (rem)	320	320	640
		Y2	D	256	768	1024	250	250	500**
		Y3	M	214	642	856	290	290	580
		Y4	G	230	690	920	300	300	600
		Y5	H	174	522	696	210	210	420
		Y6	B	102	306	408	175	175	350
LASL-III	2	LA11				12,000 (rem)‡	2300	6900	9200
		LA12				135			

* First column (R) designates code used in this report. Second column (L) designates patient code that appears in the literature.

† Recalculation based on serum Na^{24} data, except Argonne and Oak Ridge cases.[13, 14, 16]

‡ The rem value expressed in the LA I and II cases are based on an assumed RBE value of 5 for fast neutrons with an approximate depth dose penetration equivalent to that of 80KV unfiltered X-rays.

§ Data on patient LA5 not available.

¶ Based on an assumed RBE value of 3 for fast neutrons.

‖ Expressed in original report[15] in r only with no mention of neutron or gamma components. Total rad doses are assumptions only.

** Female patient whose weight is not available in the literature and might be considerably less than 70 Kg standard man, the value used in calculating this dose.

‡ Estimate ± 50%.

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Dose estimates are made only for cases which satisfy the radiation exposure criteria established for this sudy, i. e., acute, external, penetrating, and generalized. Doses due to alpha and beta radiation, either internal or external to the body, are thought to be relatively unimportant, and are not considered.

Los Alamos Accident, LASL I

The first nuclear accident occurred at the Los Alamos Scientific Laboratory, Los Alamos, N. Mex., on Aug. 21, 1945. The clinical, laboratory, and dosimetry aspects of this accident were reported in detail by Hempelmann, Lisco, and Hoffman.[11] In a criticality experiment involving a metal system, a nuclear excursion occurred and two persons were exposed to the mixed radiation field from this assembly. One of them (Case LA1), who died after the accident, was touching the assembly when the chain reaction occurred and so received a very high dose to his hands and a smaller dose to the bulk of his torso. He was exposed to considerable gamma radiation from fission products after the reaction took place, while dismantling the experiment, and would possibly have survived had he left the room immediately instead. His actions during this period are not well known, and the total dose received is correspondingly uncertain. Neither he nor the other person exposed were wearing film badges at the time of the accident. Since the number of fissions which occurred in the assembly is not known accurately, the best index of his neutron exposure is the Na^{24} activity level in his blood. The neutron dose calculated from these data is 297 rad. The gamma first collision dose is impossible to ascertain owing to the uncertainty of his whereabouts in the immediate postcriticality period. Therefore his dose is given simply as 297 + rad in Table II.

Case LA2 was exposed at a greater distance from the reactor than was case LA1 and did not remain in the vicinity after the excursion. From measurements of the ratio of gamma dose to neutron dose leaking from the Godiva reactor[12] designed to reproduce as closely as possible the conditions of their accidents, it is estimated that the gamma-neutron dose ratio was approximately 1:10 in the LASL I accident, independent of distance from the reactor in this range of distances. The resulting estimate of his dose is 18.2 rad of neutrons and 2 rad of gamma.

Los Alamos Accident, LASL II

The circumstances surrounding the second major radiation accident at Los Alamos, on May 21, 1946, were quite similar to those in the first accident. Personal film badge data were not available, and data from badges located on the walls of the room were not very helpful. Eight persons were exposed to significant doses in this incident. It is felt that none of these victims received uniform total body exposures because of various amounts of partial body shielding. One fatality occurred.

The neutron doses to the exposed persons have been estimated as in the case of the LASL I accident, i.e., by using neutron spectral data obtained from the Godiva reactor, together with Na^{24} activation data from the blood of the patients. Table II shows the doses derived on this basis. It has been assumed that the gamma-to-neutron dose ratio was 1:10 for all those exposed. This is probably a good assumption, except for case LA9, who returned to the scene of the accident twice after his initial exposure. The previously mentioned report by Hempelmann et al.[11] also includes this second Los Alamos accident.

Argonne Accident

A reactor criticality accident occurred at the Argonne National Laboratory, near Chicago, on June 2, 1952. Four persons were exposed to a mixed field of radiation in which the gamma-neutron dose ratio was about 10:1. The pertinent clinical and dosimetric aspects of this accident were reported by Hasterlik and Marinelli.[13] There were no fatalities.

Patients 1, 2, and 3 were wearing film badges which were so blackened that it was necessary to evaluate the doses in terms of the reduced silver left after the development of the film. The gamma dose to Patient 4 was evaluated from a knowledge of his position and times of exposure to prompt and delayed fission gamma rays.

The gamma dose is given by the ANL group[14] in terms of first collision dose, i.e., the correction for the effect of the body on the dose received by it has been made. The doses were found to be fairly constant over the bodies of those exposed and can be considered as uniform whole body irradiation.

Threshold detector measurements of the neutron spectrum escaping from this assembly are not available. However, Hasterlik and Marinelli quote accurate neutron dose values determined with proportional counter dosimeters. These were obtained by measuring the ratio of fast neutron dose to gamma dose during the experimental run of the reconstructed reactor and applying this ratio to the film badge readings.

The resulting dose determinations, ranging from 159 to 10.8 total rad, are given in Table II.

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Russian Accident

At some undisclosed time, presumably prior to 1954, a reactor accident occurred in the U.S.S.R., resulting in the "short general external" exposure of two persons to neutrons and gamma rays. The clinical course of the patients is detailed by Guskova and Baisogolov.[15] They assign doses of 300 r and 450 r to them but do not give the gamma-neutron ratio in the radiation field. No information is available concerning the structure and composition of the reactor, and so it is not possible to estimate this ratio. In addition, the methods of dosimetry used are not described. The dose assignments must therefore be regarded as ambiguous.

Oak Ridge Accident

A criticality accident occurred on June 16, 1958, in the Y-12 Plant at Oak Ridge, Tenn. Criticality was reached when an aqueous solution of an enriched uranium compound was drained inadvertently into a waste drum having dimensions such that a chain reaction resulted.[16] Eight persons received general whole body doses from the radiations emanating from the critical system, five of these receiving total doses in excess of 200 rad. The technical aspects of this accident are covered in several reports. Brucer[17] and Andrews[18] have presented the clinical and laboratory findings in these cases.

Film badges were not worn by any of those exposed to the radiation field. Blood sodium activity was chosen as the most reliable measure of neutron and gamma doses in this accident. The neutron dose to a man at a given distance from the assembly was deduced from the Na^{24} concentration in his body by employing a phantom (in this case a burro). The phantom was exposed to the neutron field escaping from a "mock-up" reactor of dimensions and composition closely similar to those of the accident assembly. The blood serum Na^{24} level of the phantom resulting from irradiation by a measured first collision neutron dose was determined and was used to convert blood activity data to first collision neutron dose, assuming that the neutron spectrum did not vary with distance from the reactor. During another run of the same "mock-up" reactor, a measurement of the gamma-neutron dose ratio was made and was used to obtain the gamma doses. Table II shows the doses for the persons exposed. No deaths resulted from this exposure.

Yugoslavia Accident

In an accidental supercritical excursion of a zero-power reactor on Oct. 15, 1958, at the Boris Kidrich Institute of Nuclear Sciences at Vinca, near Belgrade, Yugoslavia, eight individuals were irradiated. Six of them received significant doses of neutrons and gamma rays.[19-21] One man died as a result of the irradiation. Clinical studies of the six acutely irradiated patients are reported by Jammet et al.[19] and hematological findings by Mathé et al.[22]

Although only incomplete information is available concerning the neutron and gamma leakage spectrum from the reactor and the disposition of people and apparatus at the time of the accident, it is possible to make estimates of the doses from Na^{24} activation data for the six patients treated at the Curie Foundation in Paris. These dose estimates, ranging from 640 to 350 rad, are presented in Table II.

Los Alamos Accident, LASL III

The most recent radiation accident occurred on Dec. 30, 1958, at the Los Alamos Scientific Laboratory.[23-25] In the course of a routine plutonium salvage operation, the material attained a critical state. A man (Case LA11) who was standing in close proximity to the critical system received a lethal dose.[23, 24]

The dose to the middle of his body is thought to be distinctly higher than that to other portions of his body. The Na^{24} activity found in his body may be used to obtain a whole-body average dose from previously described calculations. The fast neutron dose was estimated to be 2,200 rad and the gamma ray dose to be 6,600 rad.

Part II. Analysis of Past Accidents —Clinical Aspects

The Clinical Manifestations of the Radiation Syndrome

The clinical characteristics of the acute radiation syndrome in man have been learned from radiation accident cases, radiation therapy patients, and the casualties of atomic bombing. Although variations in types of radiation given, in the health of the recipients, and in the feasibility of valid, controlled clinical observations all serve to confuse the outlines of a clear-cut symptom complex, certain landmarks emerge. These have been compiled and reviewed by many authors, including a recent summary by Gerstner.[26]

The general concensus is that when man is exposed to a single whole-body dose of ionizing radiation, he exhibits certain clinical signs, symptoms, and laboratory findings which are collectively termed the radiation syndrome. The frequency and severity of occurrence of these manifestations are roughly related to the dose received and the sensitivity of the indi-

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vidual patient. Exposures to less than 100 rad rarely result in clinical symptomatology; hence for our present purposes the radiation syndrome may be thought of as those clinical findings associated with total-body doses of radiation of over 100 rad.

The typical chronologic sequence of events following a large whole-body radiation exposure can be divided into four clinical stages: the initial or prodromal stage, the latent stage, the manifest illness stage, and the recovery stage. The prodromal clinical findings include anorexia, nausea, vomiting, extreme sweating, fatigue, and prostration. These changes remit in the latent period, which begins about two days later. After about two to three weeks of well-being a number of developments begin within a short time of one another. These may include fever, overt or occult infections, scalp hyperesthesia and epilation, purpura and hemorrhage, diarrhea, ileus, cardiovascular collapse, severe lethargy, and changes in sensorium. By about the end of the sixth week after exposure the situation has usually been resolved and clinical improvement of the surviving patients is rapid, although fatigue may continue for some time.

DOSE-RESPONSE RELATIONSHIPS—About 15% of patients exposed to a dose of 100 rad may be expected to show some of the signs and symptoms of the syndrome. The frequency increases sharply up to the level of approximately 200 rad, at which level most of those exposed would be expected to exhibit some clinical symptomatology.

The occurrence of fatalities has been considered generally to begin at about 200 rad, increasing to 50% at about 450 to 500 rad. The findings of this survey of radiation accidents do not substantiate these estimates, probably as a result of therapeutic intervention. Death did not occur in any of these treated patients with known exposure to less than 500 rad. The LD_{50} is impossible to estimate on the basis of the small amount of such data accumulated thus far. A fatal outcome is probably inevitable at about the 800 rad dose level.

RADIATION INJURY GROUPS—In spite of the implication in the foregoing paragraph, and in the radiobiological literature, that there is a useful relationship between magnitude of exposure dose and severity of clinical sequelae, it is considered essential to approach the problem of individual patient management from a somewhat different standpoint. This is necessitated in part by the difficulty in obtaining quick and accurate dose estimates in accident situations which are usually very complicated. In addition, even if complete dosimetric information were available, the biological response of one individual to a known exposure would still differ from that of his confrère exposed under identical physical circumstances. We have, therefore, deemed it useful in the management of radiation accidents arbitrarily to divide patients showing various symptoms and signs of the acute radiation syndrome into five different "radiation injury" groups.

The five radiation injury groups are defined in terms of our present recognition and understanding of certain definitive clinical occurrences which have appeared in normal persons accidentally exposed to external, penetrating, whole body radiation overdosage. Briefly the pertinent characteristics of each group may be summarized as follows:

Group I: Most of these patients are asymptomatic; a few may have minimal prodromal symptoms.

Group II: These patients develop this acute radiation syndrome in a mild form. After transient prodromal nausea and vomiting, laboratory and mild clinical evidence of hematopoietic derangement dominates the picture.

Group III: A serious course occurs in these patients. Complications of hematological malfunction are severe and, in the upper part of the group, some evidence of gastrointestinal damage may also be present.

Group IV: An accelerated version of the acute radiation syndrome occurs. Complications of gastrointestinal injury dominate the clinical picture. The severity of hematopoietic disturbances are related to the length of survival time following exposure.

Group V: A fulminating course with marked central nervous system impairment occurs in this group.

The radiation injury group classifications of the accident cases mentioned in the preceding section are indicated in Table III.

HYPOTHETICAL CLINICAL CASE ILLUSTRATIONS—In order to establish basic points of reference and to provide a better appreciation of the relevant clinical characteristics and laboratory findings, we shall present herein a hypothetical case report containing the expected findings of a patient in each injury group. For the purpose of illustrating all of the possible characteristic phenomena, each case will be portrayed as having experienced all or most of these findings. It must be borne in mind, however, that the radiation syndrome is similar to any other clinical entity in that it is unusual for any individual case to show all of the "textbook" findings.

Group I: Hypothetical Patient 1, a 27-year-old male technician, was exposed to a total body dose

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TABLE III—PATIENTS CLASSIFIED BY CLINICAL RADIATION INJURY GROUPS

Group	No. of Patients	Patients by Code			
I	14	LA2	A1	OR6	
		LA6	A2	OR7	
		LA7	A3	OR8	
		LA8	A4		
		LA9			
		LA10			
		LA12*			
II	8	LA4	R2	OR1	Y6
				OR2	
				OR3	
				OR4	
				OR5	
III	6	LA1	R1*		Y2
					Y3
					Y4
					Y5
IV	2	LA3			Y1
V	1	LA11			
Total patients	31				

* Insufficient data for complete profiles; not included in averages.

of 14 rad of fast neutrons and 39 rad of prompt gamma radiation. This exposure was experienced as the result of not employing certain safety features while performing an experiment with a low-power reactor.

When first seen by the facility physician in the dispensary, 10 minutes after the accident, the patient exhibited no clinical symptoms other than a moderate tachycardia and moist palms. Blood was immediately drawn for base-line blood counts and for Na^{24} activation measurements. Bed rest in the dispensary was advised, pending the report of the first estimations of the magnitude of the exposure. The patient became increasingly restless and apprehensive over the next two hours; and, since no reasonably accurate dose estimates were at that time available, it was thought advisable to hospitalize the patient.

The initial blood data, which included hematocrit, total leukocyte, total lymphocyte, total neutrophile, and platelet counts, and differential formula, were normal. One hour later, blood specimens were obtained for repeat counts, as well as base-line blood chemistry determinations. The latter were all within the normal range, and there was essentially no change in the counts. The patient's apprehension continued until four hours after hospitalization, at which time it had been definitely determined that his exposure was to less than 100 rad. The patient was informed of this estimate and appraised of the favorable clinical prognosis. His restlessness, tachycardia, and vasomotor symptoms disappeared almost immediately, and he was discharged from the hospital the next day.

He was observed in the outpatient department for the next month, during which time he was completely asymptomatic and showed no alterations in his laboratory findings. He then returned to work in a nonexposure area. Thereafter, he was observed at increasing intervals. At no time were there any clinical or laboratory manifestations that could be attributed to his radiation exposure. No abnormalities were noted in the bone marrow studies.

Group II: Hypothetical Patient 2, a 46-year-old male laborer, was exposed to 90 rad of fast neutrons and 240 rad of gamma rays in a criticality type of accident at a production facility. He was hospitalized almost immediately but at the time of admission felt perfectly well. The admission physical examination and laboratory findings were all within normal limits. About two hours later, he began to experience rather persistent nausea and vomited five times within the next 24 hours.

During the next four and one-half days, he exhibited no abnormal symptoms other than weakness and fatigue. His appetite remained hearty, and there were no gastrointestinal symptoms. An uneventful clinical course, except for persistence of the weakness and fatigue, was observed until Day 16, when the patient stated that his scalp was tender to the touch, especially over the occipital and right parietal regions. These were the areas most frequently in contact with his pillow. Very little further attention was given to this symptom until Day 18 when it was noted that frank epilation was beginning over these areas. The epilation continued, involving not only patchy areas of the scalp, but the hair on the chest, thighs, and legs as well. His epilation stopped on Day 29.

On Day 18 the patient complained of a severe sore throat. He had a temperature of 100.2° F. accompanied by a proportionate tachycardia. Physical examination revealed an acute follicular tonsillitis with accompanying cervical adenopathy. It should be noted from Figure 1 that there was no leukocyte response to this infection. The erythrocyte sedimentation rate increased to 32 mm. This rise preceded the clinical infection by 24 hours. Throat cultures were made and the patient was immediately started on crystalline procaine penicillin in 600,000 unit doses, intramuscularly, every six hours. There was a temperature spike in the afternoon to 104.6° F. This was preceded by a rigorous chill lasting approximately 20 minutes. The patient's throat became so sore that he was unable to swallow even sips of water. His fever was reduced with sponge baths and large doses of acetylsalicylic acid (aspirin) per rectum. Two liters of 5% dextrose in saline were administered intravenously through the afternoon and evening. There were two more episodes of chills and hyperpyrexia during the next 12 hours. It then became evident that the patient had an early peritonsillar abcess.

The growth from the throat culture was identified as an alpha-hemolytic Streptococcus, and tube sensitivity studies revealed a high sensitivity of the organism to tetracycline and a relative resistance to penicillin. He was then started on a continuous slow intravenous infusion of 1 gm of tetracycline in saline, over a 24-hour period. The

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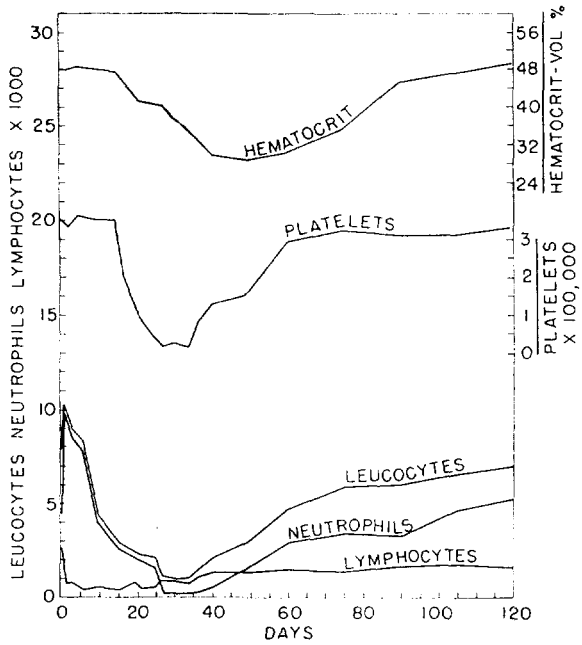

Fig. 1—Blood counts, hypothetical patient 2.

tetracycline was then continued by intramuscular injections of 100 mg every six hours. During the night of the 20th day, the abscess drained spontaneously and the patient was afebrile on the following morning. He tolerated a liquid diet in sufficient amounts to maintain a satisfactory intake without the use of parenteral fluids. By Day 23, there was complete clinical recovery and the antibiotic therapy was discontinued.

On Day 22, the platelet count began a progressive fall to a level of only 20,000 on Day 26. It remained at essentially that level until Day 30, on which a stepwise recovery began and was complete by Day 27. Paralleling the thrombocytopenia, but delayed by three days in its onset, there was a progressive fall in the leukocyte count, reaching a level of 850 on Day 32. The absolute lymphocyte count decreased from Day 27 to a level of 275 on Day 30. A slight reduction in the hematocrit also paralleled the other cytopenias. Purpura appeared first on the lower extremities on Day 25 and became generalized by Day 30. On Days 27 and 28, the patient noted that his gums bled when he brushed his teeth. Microscopic hematuria was also noted on Day 28. There was no other evidence of hemorrhage. During this period there was marked hypocellularity of the bone marrow. Hematological findings are presented graphically in Figure 1.

During the first 45 days, the patient lost 14 pounds. The clinical course from then on was uneventful. There was complete clearing of his purpura and a stepwise return to normal levels of all of the components of his hemogram by Day 60. It is interesting to note, however, that his sedimentation rate remained elevated for eight months. There was complete restoration of hair growth by the end of the third postexposure month. The patient's weakness and fatigue gradually diminished and he returned to light work in a nonradiation area five months after the accident. Periodic follow-up over the next three years failed to reveal any significant clinical or laboratory abnormalities, except for the persistent elevation of the sedimentation rate for eight months.

Group III: Hypothetical Patient 3, a 37-year-old male worker, received an estimated total body dose of 182 rad of fast neutrons and 536 rad of prompt gamma radiation in a criticality type of reactor accident.

He experienced no immediate reactions to this exposure; however, within a few minutes after his arrival at the hospital admitting room, approximately 45 minutes after the accident, he became nauseated and experienced violent retching and vomiting, perspired profusely, and felt extremely weak. Initial physical examination failed to reveal any significant abnormalities other than a moderate tachycardia, sweating, and a slightly increased respiratory rate. The rectal temperature was normal, as was the blood pressure. Blood and urine samples were obtained immediately for complete blood counts and base-line biochemical values, urinalysis, and Na^{24} measurement. The initial blood counts and urinalysis were within normal limits.

During the next 12 hours of his hospitalization, the patient continued to have nausea and vomiting. The sweating subsided, but the weakness persisted. A second blood count, made on the 12th hour, revealed a normal hematocrit and a normal platelet count. The total leukocyte count was elevated to approximately 13,000, almost all of which were neutrophils. The lymphocyte count had fallen to 800. A temperature elevation to 100° F. was noted.

A mild generalized erythema was noted toward the end of Day 1. The patient also complained of vague sensations of numbness of the upper extremities. The initial symptoms of anorexia, nausea, vomiting, weakness, erythema, and low-grade fever persisted.

There was a somewhat abrupt remission of these initial symptoms toward the end of Day 4. His appetite returned and he was essentially asymptomatic for the next nine days. The weakness, low-grade fever, and excessive sweating, however, persisted throughout this period. On Day 14, there was a sudden temperature elevation to 103° F. Physical examination revealed an acute pharyngitis accompanied by a diffuse hyperemia of the gums and buccal mucosa. Anorexia returned with the onset of this infection. A throat culture was made and antibiotic therapy was immediately initiated. He was given intramuscular doses of 600,000 units of penicillin, and 0.5 gm of steptomycin every six hours. There was a progressive temperature rise over the next 18 hours, reaching a level of 104.5° F. Early ulceration was noted in the pharynx. The hyperemia of the gums became marked. There was slight loosening of the teeth. Tube antibiotic sensitivity studies of the throat culture material revealed the pathogen to be most

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sensitive to tetracycline, which was immediately administered by continuous intravenous drip. A total of 1 gm was given by this method over the next 24 hours. The penicillin and streptomycin were also continued. The temperature dropped precipitously to its previous level of approximately 100° F. on Day 17. The tetracycline was then administered orally in 250 mg doses every 6 hours. Elevation of the sedimentation rate, first noted on Day 12, decreased slightly at this time.

At the same time, Day 17, beginning epilation of the scalp was noted. The patient experienced pain and bleeding of the gums when brushing his teeth. From this time on, until death on Day 29, all stool examinations revealed occult blood. Purpura of the oral mucosa and skin of the trunk was first noted on Day 19. This became generalized, and during the terminal stages of the illness multiple large ecchymotic areas of the skin were present.

Bone marrow biopsy revealed almost complete acellularity, which was reflected in the peripheral counts by a profound pancytopenia. Figure 2 provides a graphic illustration of all blood counts. By Day 23, the patient's general condition had progressively deteriorated to the point that he was prostrate with profound weakness, lethargy, and intermittent disorientation. The total urinary output was reduced to less than 400 cc per 24 hours. This oliguria persisted until death. Fresh whole blood and platelet transfusions were administered over the next four days.

Diarrhea, accompanied by abdominal pain and cramps, began on Day 25 and increased in severity until Day 28, at which time massive hemorrhage from the lower gastrointestinal tract ensued. There were also continuous oozing of blood from the gums and one episode of hematemesis. Microscopic hematuria was also observed.

There was almost complete epilation of all of the hair of the body by this time. Early on Day 29, further severe bleeding from the lower gastrointestinal tract began. The patient went into profound shock, became comatose, and, in spite of vigorous transfusion therapy, died during the latter part of Day 29.

Group IV: Hypothetical Patient 4 was a 31-year-old male scientist who received a total body exposure to fast neutrons and gamma rays in a criticality reactor accident. It was estimated that his exposure resulted in a dose of 124 rad of fast neutrons and 830 rad of gamma rays. He immediately ran from the reactor building and was taken to the laboratory dispensary. He experienced nausea, vomiting, and retching 30 minutes after the exposure. He was hospitalized immediately. The nausea and vomiting increased in severity and frequency during the next four hours. During the third hour, he experienced severe intermittent abdominal cramps followed by two watery bowel movements within a period of 20 minutes. He was weak and prostrate, but there was progressive improvement, and by the 16th hour he had entered the latent phase of relative clinical well-being. He had a low-grade fever during the first 24 hours. On Day 1, there was an

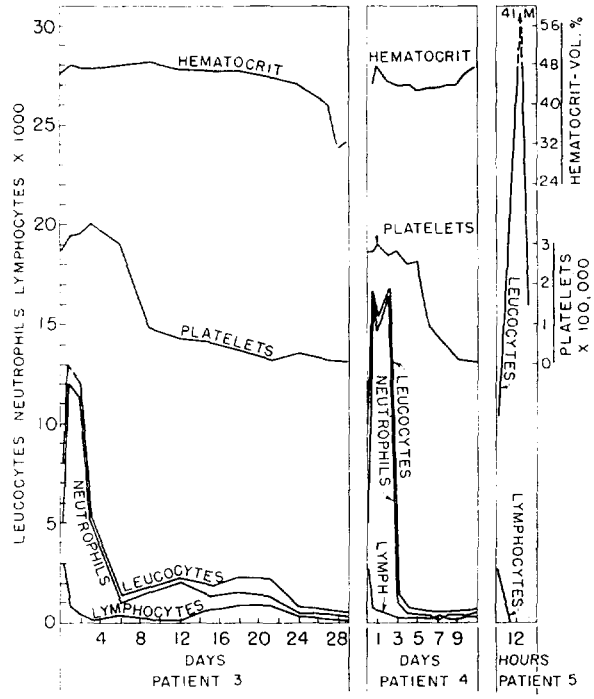

Fig. 2—**Blood counts, hypothetical patients 3, 4, and 5.**

initial leukocytosis, almost all of which was due to an increase in neutrophils as his absolute lymphocyte count fell to 600. His leukocytosis persisted. The lymphopenia was progressive, reaching a level of 250 on Day 3. Throughout the remainder of his illness, the absolute lymphocyte count never rose above this level.

Except for a continuation of his fatigue and a temperature elevation to 100.5° F. on Day 2, he was asymptomatic for the next five days. The low-grade fever persisted until Day 7.

About noon of Day 7, there was a recurrence of his nausea, vomiting, and watery diarrhea. This was accompanied by a rise in temperature to 103.2° F. and a corresponding elevation in the pulse rate. Almost simultaneous with the onset of these clinical symptoms, there was a precipitous fall in the cellular elements of his peripheral blood. The total leukocyte count decreased to 1,200, with a corresponding fall in the neutrophils. The platelet count decreased from its previous normal levels to 120,000. Hematologic results are shown in Figure 2.

The nausea and vomiting became increasingly severer, and early on Day 8 nasal gastric suction was established. There was also an increase in the severity of the diarrhea. Parenteral administration of fluids and electrolytes as well as whole blood was started, and he was placed on intramuscular penicillin and streptomycin. His temperature reached a high of 103.8°F. and the blood count showed 300 leukocytes and 80,000 platelets. There was hypocellularity of the bone marrow. On Day 9, his condition was essentially unchanged.

On the 10th day, the frequency of the diarrhea increased and the watery stools became bloody.

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His temperature rose to 104° F. and his pulse was rapid and weak. Extreme prostration ensued; he was cyanotic, and his respirations were shallow and rapid. Tetracycline was given intravenously, and he was placed in an oxygen tent. In spite of whole blood transfusions, the shock became more profound. For a few hours, the circulatory collapse was successfully overcome with intervenous methoxamine HCl (Vasoxyl); however, early on Day 11, the temperature rose to 105.8° F., the shock again became profound, and he died.

Group V: Patient 5, a 37-year-old production specialist, received an estimated total body exposure to 2,000 rad of fast neutrons and 5,000 rad

TABLE IV—TIME OF ONSET AND DURATION OF

Group	I																
	LA2	LA6	LA7	LA8	LA9	LA10	LA12	A1	A2	A3	A4	OR6	OR7	OR8	LA4	R2	OR1
Anorexia	....	....	....	....	*6*a(<1)	....	....	*6(1)*	....	3(1)	....	....	....	....	*6(12)*	*1*(4)	*2*(5)
Nausea	....	....	....	....	*6*a(<1)	....	....	*6(1)*	....	3(1)	....	....	....	*2*(1i)	*6(12)*	*1*(4)	*2*(5)
Vomiting	....	....	....	....	....	....	....	*6(1)*	....	3(1)	....	....	....	....	*6(1)*	*1(4)*	*2*(2)
Diarrhea	....	....	....	....	....	....	....	....	....	3(1)	....	....	....	....	....	....	....
Abdominal pain	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Conjunctivitis	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Erythema	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Fever	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Sweating	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Oliguria	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Weakness*	....	....	....	....	....	....	....	....	....	....	....	....	....	*2*(1)	1(70)	*1*(4)	....
Prostration	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1(10)	*1*(4)	....
Hyperesthesia	....	1(<1)	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Paresthesia	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Ataxia	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Disorientation	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Shock	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Coma	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Death	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....

Arabic number indicates postirradiation day of onset.

Arabic number *in italics* indicates postirradiation hour of onset.

Number in (parentheses) indicates duration.

* Includes fatigue.

† Limited to burned areas of upper extremities.

a Approximate time.

i Intermittent.

TABLE V—TIME OF ONSET AND DURATION OF CLINICAL

Group	I																
	LA2	LA6	LA7	LA8	LA9	LA10	LA12	A1	A2	A3	A4	OR6	OR7	OR8	LA4	R2	OR1
Anorexia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	6(5)	24(20)	..
Nausea	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Vomiting	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Diarrhea	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Abdominal pain	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Adbominal distention	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Conjunctivitis	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Erythema	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Jaundice	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Fever	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5(6)	24(9)	31(3)
Infection	..	..	..	..	..	..	..	..	..	..	..	..	..	6(2a)	..	..	31(3)
Purpura	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	24(20a)	25(4)
Hemorrhage	..	..	..	..	..	..	..	..	..	..	15(<30)	..	..	..	..	24(20a)	25(2)
Scalp pain	..	..	..	..	..	..	..	..	..	..	..	..	..	..	17(>2)	13a(—)	16(4a)
Epilation	..	..	..	..	..	..	..	..	..	..	..	..	..	..	18(<30)	13(—)	17(27)
Sweating	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Oliguria															..	..	..
Weakness*	3(60)	..	..	..	..	..	..	..	..	17(16)	..	..	..	..	1(70)	24(20)	30a(56a)
Prostration															..	..	..
Weight loss	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1p(20)	NA	1p(6)
Hyperesthesia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Paresthesia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	15(10)	..	..
Ataxia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Disorientation	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Shock	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Coma	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Death	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Cataract left	..	..	..	..	..	..	..	..	..	..	..	..	..	..	32 mo.	..	..
Cataract right	..	..	..	..	..	..	..	..	..	..	..	..	..	..	58 mo.	..	..

Arabic number indicates post irradiation day of onset.
Arabic number *in italics* indicates post irradiation hour of onset.
Number in (parentheses) indicates duration.
* Includes fatigue.
† Patient had history of intermittent abdominal discomfort for several years.
‡ Epistaxis also occurred on day 14.
§ Epistaxis also occurred on day 12.
¶ Episode of supraventricular tachycardia. (History of previous episode.)
a Approximate time.
i Intermittent.
m Minutes.
p Presumed.

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of gamma rays. By a complex series of technical errors, a large volume of enriched uranium in a liquid form was allowed to become supercritical.

The patient stated that he immediately felt a burning sensation over his entire body. He was able to stagger out of the building and attempted to reach a vehicle parked on the road. A maintenance man working across the road stated that he staggered aimlessly about like a drunken man for a minute or so and then collapsed on the ground. He began to retch violently within eight minutes after the exposure. He attempted to walk to the ambulance but was markedly ataxic and confused.

Clinical Signs and Symptoms—Initial Stage

II					III						IV		V
OR2	OR3	OR4	OR5	Y6	LA1	R1	Y2	Y3	Y4	Y5	LA3	Y1	LA11
2(1)	2(4)	4(3)	2(2)	1(1)	1(2)	1(3)	1(2a)	1(2a)	1(2a)	1(2a)	1(<1)	1(2a)	15m(35)
2(<1)	2(4)	4(3)	2(2)	1(1)	1(2)	1(3)	1(2a)	1(2a)	1(2a)	1(2a)	1(<1)	1(2a)	15m(35i)
....	2(4)	4(2)	2(6)	....	1(1)	1(3)	1(2a)	1(2a)	1(2a)	1(2a)	1(<1)	1(2a)	15m(35i)
....	....	....	....	....	....	....	....	....	....	....	4(1)	4(—)	45m(35i)
....	....	....	....	....	....	....	....	....	....	....	....	....	30m(1)
....	....	....	....	1(—)	....	....	1(—)	1(—)	1(—)	1(—)	—(—)	1(—)	30m(35)
....	....	....	....	....	....	....	1(14)	1(14)	1(14)	1(14)	1(9)	1(14)	30m(35)
....	....	....	....	....	1(24)	....	....	....	....	....	1(9)	....	30m(12)
....	....	....	....	1(>90)	....	....	1(>90)	1(>90)	1(>90)	1(>90)	....	1(31)	30(5)
....	....	....	....	....	....	....	....	....	....	....	1(2)	....	<1a(35)
....	....	....	....	1(>120)	1(24)	1(4)	1(>120)	1(>120)	1(>120)	1(>120)	1(1)	1(31)	5m(35)
....	....	....	....	....	1(1)	1(4)	....	....	....	....	1(1)	....	5m(35)
1(<1)	....	....	....	....	1(24†)	....	....	....	....	....	1(9†)	....	1m(35)
....	....	....	....	1(2a)	1(1†)	....	1(2a)	1(2a)	1(2a)	1(2a)	1(—†)	1(2a)	....
....	....	....	....	....	....	....	....	....	....	....	....	....	1m(35p)
....	....	....	....	....	....	....	....	....	....	....	....	....	1m(35p)
....	....	....	....	....	....	....	....	....	....	....	....	....	30ma(35p)
....	....	....	....	....	....	....	....	....	....	....	....	....	33(2)
....	....	....	....	....	....	....	....	....	....	....	....	....	35

m Minutes.
p Presumed.
t Includes terminal recurrence.
— Known to have occurred, but time unknown.
> More than, or later than.
< Less than, or earlier than.
NA Specific information about occurrence not available.
Leaders (....) indicate nonoccurrence.

Signs and Symptoms—Manifest Illness Stage

II					III						IV		V
OR2	OR3	OR4	OR5	Y6	LA1	R1	Y2	Y3	Y4	Y5	LA3	Y1	LA11
..	..	..	..	..	10(9t)	19(17)	30(6)	24(6)	30(6)	32(7)	6(4)	22(11)	15m(35)
..	..	..	..	..	10(9t)	..	30(6)	24(6)	30(6)	32(7)	6(4)	22(11)	15m(35)
..	..	..	..	..	17(1)	..	..	..	..	..	6(4i)	..	15m(35)
..	..	..	..	..	12(15)	..	..	..	..	..	7(3i)	..	45m(35)
..	24(1)†	..	..	21a(—)	10(4a)	..	31(6a)	29(6a)	29(6a)	29(6a)	6(4i)	22(9i)	..
..	..	..	.	..	10(4a)	..	..	..	..	29(6p)	6(4i)	22(9i)	..
..	..	..	..	..	14(4a)	..	..	..	..	..	..	..	<0.5(35)
..	..	..	..	..	3(23)	..	..	..	..	..	1(9)	..	<0.5(35)
..	..	..	..	..	25a(1p)	..	..	..	..	39(1a)	9(1t)	24(9a)	..
..	..	13(1)	..	..	1(25)	19(17)	21a(14ai)	21a(14ai)	21a(14ai)	21a(14ai)	1(9)	4(10it)	<0.5(35)
10(10)	..	10(34a)	3(10)	..	10a(13t)	19(17a)	31(—)	29(—)	29(—)	29(—)	..	NA	..
25(5)	..	..	..	..	..	19(22)	..	..	..	26(14)	..	..	..
..	..	..	26(2)	—(—)	..	19(22)	26(18)	26a(20a)	26a(20a)	26a(20a)	..	27(6‡)	..
..	16(4a)	..	16(4a)	..	..	..	..	..	..	..	..	..	..
17(14)	17(>27)	17(10)	17(14)	20(<90)	17(10)	NA	14(<90)	16(<90)	18(<90)	17(<90)	..	14(18)	..
..	..	..	..	1(>90)	..	19a(>22)	1(>90)	1(>90)	1(>90)	1(>90)	..	1(32)	30(5)
..	..	..	..	..	..	..	30(6a)	24(7a)	30(6a)	32(7a)	8(2)	24(9a)	<1a(35)
30a(56a)	44a(42a)	44a(42a)	44a(24a)	1(>120)	1(25)	19(22a)	1(>120)	1(>120)	1(>120)	1(>120)	1(9)	1(>120)	5m(35)
..	..	..	..	..	6(21)	19(22)	30(6)	24(7)	30(6)	32(7)	6(4)	24(9)	5m(35)
..	1p(4)	1p(5)	..	>10(>120)	1p(25)	NA	1(<120)	1(>118)	1(>118)	1(<106)	1(9)	1(32)	1p(35p)
..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	1m(35)
..	..	..	..	..	21a(4a)	..	..	..	..	..	7(3)	..	1m(35)
..	..	..	..	..	15(1)	..	..	..	..	..	8(2)	NA	<0.5(35)
..	..	..	..	..	25(1)	..	..	..	..	..	8(2a)	NA	33(2)
..	..	..	..	..	25	..	..	..	..	..	9	32	35
..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..

t Includes terminal recurrence.
— Known to have occurred but time unknown.
> More than, or later than.
< Less than, or earlier than.
NA Specific information about occurrence not available.
Leader (..) indicates nonoccurrence.

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On admission to the hospital, 20 minutes after exposure, the patient was vomiting and had an explosive involuntary watery bowel movement. He was cyanotic and in acute respiratory distress. A generalized erythema was noted, and he was in clinical shock as evidenced by a blood pressure of 70/50. Vigorous therapy with whole blood transfusions was employed but failed to combat the clinical shock. Intravenous methoxamine HCl (Vasoxyl) was begun during the fourth hour. The response to this therapy was insufficient to raise the patient's blood pressure out of the range of clinical shock. The vomiting and confusion persisted. The sensorium remained clouded. On the 10th hour, 90 cc. of urine was obtained by catheterization, indicating that there was an almost complete anuria from the onset. By the 16th hour, prostration was marked. The patient became progressively more disoriented, and twitching of various muscles was noted. He became comatose in the 21st hour, convulsed, and died a few minutes later.

The blood counts made during the first hour were normal in every respect. Blood taken hourly for counts revealed a progressive increase in the leukocyte count to a level of 41,000 in the 16th hour followed by a steady decrease to the level of 16,000 just prior to death. By the third hour, the lymphocyte count had decreased to 950, and by the seventh hour there was a complete disappearance of lymphocytes from the peripheral blood. The findings of the bone marrow biopsy made during the early hours were not remarkable. Hematological data are presented graphically in Figure 2.

Only 180 cc. of urine was obtained from the time of the initial catheterization until death. Consistent with this oliguria, there was a steady rise in the NPN and BUN levels reaching 82 and 19 mg % respectively.

Analysis of Accident Cases

The hypothetical cases just presented were developed from the data contained in reports of the accident cases reviewed in this section. In Table III the actual cases are classified by radiation injury groups. We shall now consider the clinical data in these cases.

CLINICAL SIGNS AND SYMPTOMS — The time of onset and of duration of clinical signs and symptoms in the early postirradiation period are given in Table IV. A similar compilation in Table V presents the clinical phenomena of the stage of manifest radiation illness. Where an early finding disappeared and then recurred after the latent period, it has been handled as a newly occurring finding. If, on the other hand, it persisted from the start, it has been recorded identically on both tables. Great variations in the observations made, the clarity with which they were reported, the many forms of therapy employed, and the small number of cases involved make these data a somewhat imprecise basis from which to reach firm diagnostic and prognostic conclusions. Nevertheless, certain generalizations appear warranted.

Initial Stage—The classic prodromal gastrointestinal symptoms of the acute radiation syndrome, i.e., anorexia, nausea, and vomiting, were present in all patients in Group III and above, within an hour after exposure. They generally continued for about two days. In Group III, the triad was somewhat slower in appearing, beginning within six hours, but continuing intermittently for about the same duration. Two of the eight patients did not vomit at all. Only 4 of the 14 Group I patients had anorexia or nausea, and only 2 of them vomited. In one of these, the symptoms occurred on the third day and were considered by the physician in charge as "a manifestation of anxiety and tension rather than radiation sickness."

The occurrence of diarrhea in this stage seemed to be of serious prognostic importance. Other than in the previously mentioned patient in Group I who had the anxiety reaction, this symptom occurred only in the Group IV and V cases, all three of which were fatal. It appeared on Day 4 in both Group IV patients. In the Group V patient it started in 45 minutes, shortly after the onset of abdominal pain.

Weakness and fatigue were found in occasional Group I and II cases but were present and prolonged in *all* cases above that level of injury. Early prostration was also sometimes noted for a short time in Group II and above.

Other symptoms which were frequent almost exclusively in Group III and above included conjunctivitis, erythema, sweating, and paresthesias. Oliguria was seen in only one Group IV case and the Group V case.

Immediate central nervous system symptomatology, including ataxia, disorientation, and cardiovascular collapse, were seen only in the latter patient. He later became comatose and died about 36 hours after radiation exposure with no evident latent period after the start of his illness. All other patients did have a variably long period of remission of early symptoms before the manifest illness stage began.

Manifest Illness Stage—Patients in Group I showed no clinical evidence of illness of any kind after the initial stage subsided, except for one upper respiratory infection, one small retinal hemorrhage, and two complaints of weakness.

The most frequent finding above Group I was weakness and fatigue. This occurred in all cases. Onset in Group II was most often in the fifth or sixth week. In Group III and above it appeared almost immediately. Duration was variable, but generally the symptom lasted for several months.

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TABLE VI—PROFILE VALUES ASSIGNED FOR VARIOUS RANGES OF ABNORMALITY
HEMATOLOGY—PERIPHERAL COUNTS

Test	Units	Normal*	Profile Value							
			1	2	3	4	1	2	3	4
			(For increase above:)				(For decrease below:)			
Hemoglobin	Gm.%	M-15.8	18	19	20	21	14	12	10	8
		F-13.9	16	17	18	19	11.5	10	8.5	7
Erythrocytes	Mill/mm³	M-5.4	6.0	7.0	8.0	9.0	4.5	3.5	2.5	1.5
		F-4.8	5.5	6.5	7.5	8.5	4.0	3.0	2.0	1.0
Hematocrit	Vol.%	M-47	54	56	58	60	40	35	30	25
		F-42	47	49	51	53	37	32	27	22
Leucocytes	1000/mm³	7.4	12	18	24	30	4.0	3.0	2.0	1.0
Neutrophils	1000/mm³	4.4	7.7	14	21	28.0	1.8	1.3	0.9	0.5
Lymphocytes	1000/mm³	2.5	4.8	7.0	10	12.0	1.0	0.75	0.5	0.3
Platelets	1000/mm³									
Rees-Ecker		405	545	700	850	1000	273	200	100	30
Brecher-Cronkite		257	440	600	750	900	140	100	50	30
Fonio		234	350	500	650	800	130	100	50	30
Dameshek		716	900	1000	1500	2000	500	350	100	30
Reticulocytes	%RBC	1.5	4	8	15	25	.5	0		
Erythrocyte Sedimentation Rate	mm/hr.	M-5	10	20	30	40				
		F-10	20	30	40	50				

* Expressed as "universal mean" value—taken from Albritton.[25]

Another common finding in all groups above the first one was epilation. Time of onset ranged from 13 to 20 days, with 10 of 14 patients beginning to lose hair between the 16th and 18th days. Two other patients, dying in one and one-half and in nine days, did not epilate. No data are given in the remaining case. No clear relationship of time of onset or of duration to injury group is evident.

Scalp hyperesthesia or pain occurred in most Group II patients one or two days before epilation. No similar finding was noted in the higher groups.

Sporadic episodes of fever were observed in half of the patients in Group II and in all of those above that group. These were of short duration in Group II, but lasted one or more weeks in most of the more injured patients.

Clinical evidence of infection was seen between the second and fourth weeks in half of Group II, including two of the four febrile patients. In Group III all cases showed such indications. Definite clinical infection was not noted in Groups IV and V.

Hemorrhagic phenomena, such as gingival bleeding, epistaxis, petechiae, and purpura, were observed in most cases of Group II and above who survived beyond the third week. Serious hemorrhage was limited to two patients in the fourth postexposure week. One, in Group III, had menorrhagia and another in Group IV died with uncontrollable hematemeses and, finally, hemoptyses.

In Group III and above a number of symptoms including recurrent anorexia and nausea, abdominal discomfort, prostration, and oliguria appeared at the peak of manifest illness. These findings occurred earlier in the more acutely ill patients, who also had the additional symptoms of vomiting, diarrhea, and abdominal distention. Disorientation, shock, coma, and death followed in several instances.

Jaundice was noted in mild transient form at the end of this period in two individuals in Group III and in more marked form terminally in the two Group IV patients.

Weight loss was mild and not of long duration in Group II. In higher groups it appears to have been severer but details are somewhat scant.

Subsequent cataracts have been observed in one member of Group II. No other long-term effects have been reported.

LABORATORY FINDINGS — A large number of laboratory examinations of many varieties were performed in the radiation accident patients discussed in this report. In order to consider and compare the laboratory observations, it was clearly necessary to develop a procedure for their analysis which would allow broad conclusions to be drawn despite differences in details of methodology employed in the diverse study centers.

The accepted normal range of results of each test procedure which was widely used among the cases under study, or which is recommended for such future use, was determined. A scoring system was then devised which assigned values from 1 to 4 to ranges of increasing deviation from the normal range. Using the resultant values, "profiles of injury" could be scored for the individual patients whose laboratory findings were so analyzed. These have been called "profile scores." The values assigned to

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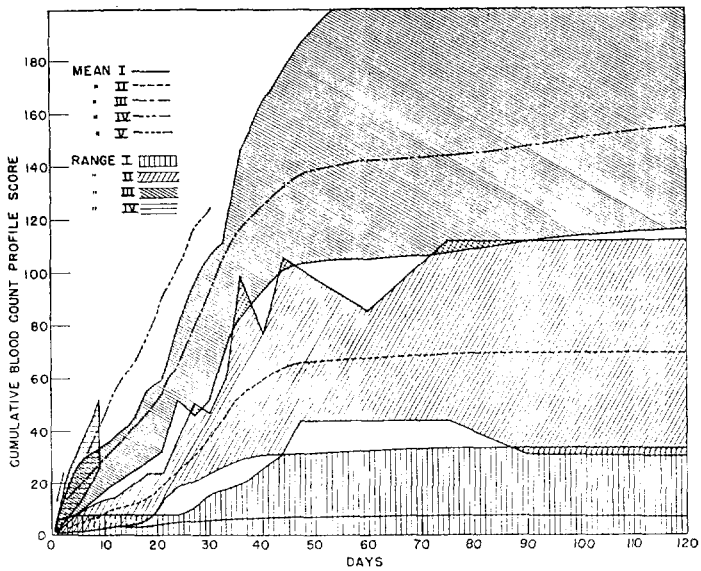

Figure 3

the various deviations of laboratory tests from the normal range have therefore been designated "profile values." The profile values for hematological tests are given in Table VI. Profile values for coagulation tests and for biochemical tests of urine and blood are published elsewhere.[29] Profile values were not assigned to tests which are not suited to this type of analysis.

Profile scores were determined for all possible tests in each individual case. These were analyzed individually and also cumulatively over the postexposure time period. Then, to facilitate intragroup comparisons, an attempt was made to determine the mean profile score for each radiation injury group on each type of test procedure at various convenient postexposure time intervals.

Unfortunately, it was found that only in the category of hematological tests were there a sufficient number of observations performed in uniform enough time periods in a large enough number of the accident patients to permit determination of mean profile scores for each clinical radiation injury group. It is possible, however, that profile scores for other tests might also be useful in the future, provided that they are performed at relatively frequent and consistent intervals. For this reason, suggested profile values for ranges of abnormalities of standard blood clotting, blood chemistry, and urine chemistry tests are given in another report.[29]

Peripheral Blood Counts—Previous reports have indicated the utility of one or another of the components of the peripheral blood count as an indicator of radiation injury.[11, 18, 30] Granulocytes, lymphocytes, monocytes, platelets, and reticulocytes have all been shown to contribute helpful information. We have reviewed the hematological data with two main questions in mind. One is how much they aid in the assignment of an unknown case to a specific injury group, with all the therapeutic and prognostic implications appertaining thereto. The other is how well they help to detect complications or therapeutic responses to the subsequent course.

Total blood count profile score is made up of scores for counts of erythrocytes or hematocrit, leucocytes, granulocytes, lymphocytes, and platelets. Other elements were omitted on the previously discussed grounds of infrequency and irregularity of tests.

When the means of such integral scores were cumulated by groups and graphed (Fig. 3) variations in the rate of accumulation of injury over time, and its maximum magnitude, were evidently closely related to the signs of clinical injury upon which injury group selection was based. It was possible to separate the mean score of cases falling into Group I and II from those of the sicker ones after 48 hours or less. Group V was also quite distinguishable from the outset. By the sixth day, Group I was distinct from II, and III from IV.

Examination of the ranges of the cumulative group mean scores portrayed in Figure 3 shows the value of the blood count in indicating radiation injury. It also makes clear the difficulty of relying solely on this measure in the initial stage of radiation illness when there is considerable overlapping of group mean profile score ranges.

If one wishes to refine the estimation of injury group assignment further, certain individual tests which go into the previous total scores may be considered individually. It must be realized, however, that the more data that can be compared with the mean scores herein, the greater the confidence that can be placed in the resultant prognostic conclusions.

The lymphocyte scores appeared to be the best prompt laboratory indicators of radiation injury. In 48 hours Groups II, III, IV, and V were well separated in mean score. However, a few of the Group II cases showed little early lymphocyte fall and the opposite occurred in Group I, so that there remained some overlapping of the two lower groups. If one considered the presence or absence of prodromal (nausea and/or vomiting) symptoms in addition to the

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lymphocyte score in assigning patients to these two groups, the likelihood of correct decision was further enhanced.

The neutrophil score did not facilitate differentiation of Groups I and II. Nevertheless, it was useful supportive evidence in separating the two lower groups from the three higher ones by Day 3. Also Groups III and IV were becoming distinct on Day 3 by this means. However, Groups I and II were not separable for the first month.

The leukocyte score gave rather similar information but not as distinctly as did the neutrophil score. This was, of course, a reflection of the fact that neutrophil variations account for most of the white count changes, but lymphocyte shifts are also involved. Thus the distinction between Groups I and II was present earlier here than in the neutrophil score.

The platelet score was not very useful in the early days after exposure. However, the differentiation of Group IV from Group III was apparent by this test as early as Day 6. After the third week, sharp changes separated Groups II and III from the unaltered Group I.

Erythrocyte scoring was least helpful early. There was a reversal of Groups III and IV. However, a difference between Groups II and III was discernable after the first month. Therapeutic efforts, such as transfusion, and some preexposure abnormalities confused the data from this test.

Regarding the value of hematological profile scores as an indicator of complications no clear findings emerge. Neither infections nor bleeding began *only* when neutrophil or platelet levels were lowest, although this was generally so. Distinct deviations of an individual case from the group pattern during the course might indicate complications. However, more data are needed to define the ranges of the group patterns before this procedure can be evaluated adequately.

Reflections of therapy, other than that of transfusions already mentioned in the previous discussion of erythrocytes, may have occurred in the Yugoslavian cases. The Group IV data are based on Y6 alone after the death of LA3 on Day 9. The near normal neutrophil integral scores on Days 15 and 18 follow embryonal myeloid tissue transfusion, and the one on Day 30 follows adult marrow transfusion. The integral platelet score on Day 30 also is normal. Similar effects of marrow transplantation in cases Y2, Y3, Y4, and Y5, all in Group III, may be responsible for the improvement of that group's neutrophil and platelet scores somewhat earlier than those of Group II.

Other Hematological Tests—Bone Marrow: Examinations were made at various times in many of the cases. However, quantitation or codification of results is not possible; so no profile could be devised. Detailed discussions of bone marrow findings are given in several reports.[11, 15, 17, 18]

In general, relation of appearance of an aspirated sample of marrow to amount of injury or prognosis is not sufficiently obvious to use in making injury group assignments. There is a hypocellularity from the early period after exposure, with depression of the granulycytic series in particular. Mononuclear cells of the reticulum and plasma cell varieties remain, with variable concentrations of erythroid precursors. Megakaryocytic diminution and deterioration is present later. Regeneration of erythroid and myeloid precursors may develop in the face of falling peripheral counts and a subsequent fatal outcome.

Reticulocytes: Data were insufficient for profiling. Depression of levels was generally prompt, but depth was not clearly related to injury level. Recovery was indicated by reticulocytosis, with possible direct relationship of its height to the level of previous injury.[18]

Erythrocyte Sedimentation Rate: The results of this test were available serially only in the Oak Ridge cases. Here a close relationship of elevation to the early stages of infection seems to have been present. However, the abnormality persists far beyond the infection which it heralded. Further data would be useful in evaluating the apparent usefulness of this test as a warning of infection at a time when the usual signs, such as fever or leucocytosis, may not be of service.

Blood Coagulation Tests: The coagulation time was the test most consistently performed. Patients LA3, LA4, and LA6 showed significant prolongations. The maximum deviation of the latter two occurred on Day 6. In the case of LA3, a Group IV patient, there was a progressive prolongation of the clotting time. Just prior to death on Day 9, the blood was uncoagulable. An increase in clotting time was noted on many occasions in various patients from the Yugoslavian accident.

A variety of tests to measure components of the prothrombin complex were carried out in some of the cases. In general, there was no evidence of derangement, except in a few of the patients severely injured. The plasma prothrombin time was moderately increased in LA3. A decrease in Ac globulin and proconvertin was noted in Y2. The tourniquet test was positive on many determinations made on the Yugoslavian patients, especially patients

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Y4, Y5, and Y6. Of the five Oak Ridge patients in Injury Group II, four had elevated levels of Ac globulin; all had distinctly elevated levels of antihemophilic globulin at the peak of their thrombocytopenia. These abnormalities of the plasma clotting factors are believed to be related, at least in part, to the thrombocytopenia.

Blood Chemistry—The blood electrolytes were measured in practically all of the patients, and failed to reveal any significant abnormalities, other than those associated with prolonged vomiting or diarrhea. Nitrogen retention was noted in all patients exhibiting oliguria. Calcium and phosphorus metabolism appeared to be unaltered, except in the case of LA3, in which there was a decrease in blood calcium, which would have been expected in a patient with severe nitrogen retention.

Total protein measurements and electrophoretic fractionation were carried out on practically all Group II, III, and IV patients. The results of these determinations were extremely variable and completely inconsistent. There was evidence of hyperbilirubinemia in patients LA3, LA1, and Y1, either terminally or at postmortem examination. A number of other biochemical procedures were carried out, none of which revealed any significant abnormalities.

Urine Chemistry — Urinary output was recorded for all patients except R1 and R2. In all Group III cases and above, except LA1, a decrease to oliguric levels was noted during the critical period of the manifest illness stage.

There were no significant effects in either total nitrogen, amino nitrogen, or uric acid excretion in the Group II Oak Ridge patients.

Quantitative determinations of urinary amino acids were made in most of the cases in all groups. Increased excretion of a variety of these was noted as early as 12 hours after irradiation, but there was no quantitative dose correlation. A newly discovered urinary amino acid, beta-aminoisobutyric acid (BAIBA), was excreted in increased amounts by the Oak Ridge patients in Group II.[17] Excretion was maximum during the first few days after exposure and returned to normal by Day 10. The magnitude of the increase in excretion of BAIBA in these cases appears to be related to dose.

Significant increases in bile pigment excretion was noted in LA3, LA4, and occasionally in some of the Yugoslavians. There was presumptive evidence of an increase in LA1. The increase in coproporphyrin excretion in LA4, a Group II patient, first occurred and was at the highest level on Day 2. It recurred intermittently through Day 13. An increase in urobilinogen was noted on Day 6 only.

Miscellaneous Observations — Bacteriology procedures carried out on a number of patients in all groups were not particularly helpful. Occult blood was found in the stools of several patients in Groups II and above at the time of other hemorrhagic manifestations.

Seminal fluid examinations made on the male Argonne patients showed an aspermia by the 10th month in A1, the patient who received the highest dose. In all of the surviving male Yugoslavian patients there were marked quantitative and morphologic changes in the sperm. At autopsy of Y1, a total depopulation of the seminiferous tubules was found. Similar findings were noted in LA1, and LA3 at autopsy. LA4 had aspermia at the seventh month which persisted for 17 months. Testicular biopsy in this patient revealed marked atrophy at the 10th month. Biopsy at 50 months after irradiation again revealed atrophy but there was evidence of partial regeneration.

Slit lamp examinations of the lens were made in most of the nonfatal cases. Only one, LA4, developed lens opacities. The first was noted in the left eye at 32 months after exposure, and by 58 months an incipient cataract in the lens of his right eye had developed.

Part III. Recommended Medical Procedures

The selection and time of performance of appropriate diagnostic and clinical procedures will be strongly influenced by three kinds of knowledge. The first is the clinical acumen and judgment which would be brought to bear on the medical management of any patient. The second is an awareness of the underlying pathophysiology of the acute radiation syndrome in man. The third is a general idea of the magnitude and type of radiation to which the patient has been exposed. Discussion of the first of these is beyond the scope of this paper. The next two have already been mentioned, but their application in the individual accidental exposure case warrants some further consideration.

In a given accident, the exposure dose would seem to be the logical piece of information which upon clinical management can be planned. As has already been indicated, however, it is not necessarily helpful in the individual case for two reasons: First, the dose, if it can be determined, is not usually available as soon as needed. Second, no given individual will necessarily respond exactly as his confreres in a given dose category. Therefore, the highest priority diagnostic recommendations in the early postexposure period are planned for the

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accumulation of sufficient information to establish the response "profile" of the individual under study in comparison with those of others who were studied in a similar manner after whatever dose of radiation. When this information is available, a reasonably accurate prognosis can be made and planning of clinical management can proceed even in the absence of dosimetry information. It is highly desirable, of course, to obtain physical dosimetry data as soon as possible to supplement the clinical estimate of injury.

Subsequent tests will be recommended to serve four purposes: to validate the original diagnostic and prognostic conclusions in the patient; to detect promptly the development of clinical complications in the patient's course; to provide more data for improved profile scoring of future cases; and to supply more information about radiation pathophysiology.

Diagnostic Procedures

Given one or more individuals who have accidentally received, in all probability, a significant acute injurious radiation overexposure of neutron and/or gamma ray type, how should the attending physician proceed? It is rather obvious that in our present state of knowledge of human radiation injury there really is no procedure which might not be productive of some new information of immediate or eventual applicability. However, it is also obvious that diagnostic tests must include those that are most essential and none that are detrimental to the individuals involved. The resultant limitation in number and frequency makes a well-informed selection all the more important.

In the course of this analysis of all available criticality accidents, certain diagnostic hints have emerged which may aid in dealing with similar situations in the future. Further experience may alter these recommendations completely, but at this time the procedures listed in Table XII seem to be the most likely to facilitate preliminary clinical evaluation and subsequent management.

The diagnostic tests have been outlined in tabular form for convenience of the reader. Frequency and duration of test performances are given. Suggestions based on the analysis of previous studies are made for each of the five clinical injury groups. In line with the objectives of these diagnostic recommendations, test procedures have been categorized as Type A, B, or C. Type A procedures are of particular applicability in the early diagnostic and prognostic appraisal of clinical radiation injury. Type B procedures are of more help in confirming the earlier estimations of injury

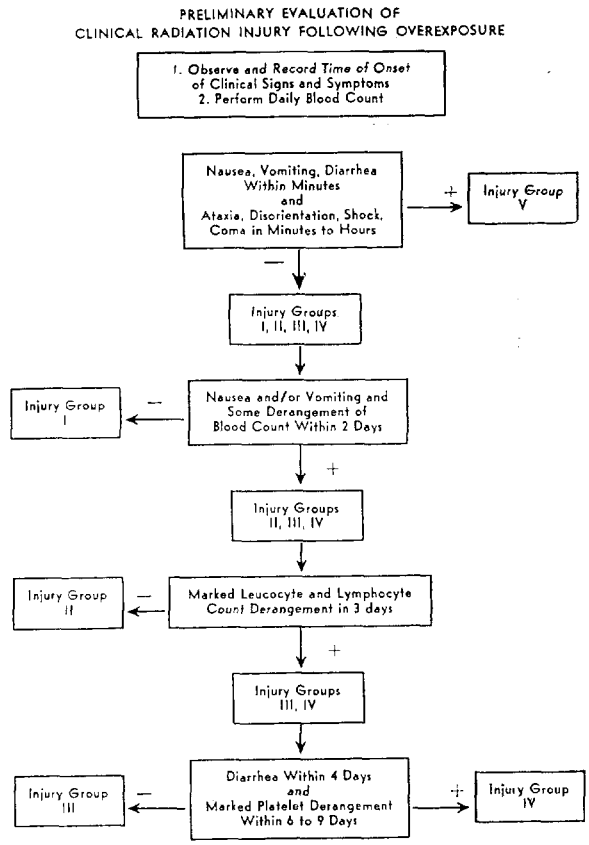

Figure 4

and in recognizing and managing the development of complications. Type C procedures are of possible but not yet verified value for future use in either of the two previous categories. In order to determine their suitability, they should be utilized when feasible.

While this procedural outline is thus segmented, somewhat arbitrarily, for the sake of clarity of presentation, it should be clearly understood that each individual case must be viewed and studied in its own right as the particular symptomatology and course require. It should also be recognized that it is beyond the purpose of this listing to include specific recommendations for future scientific lines of investigation of the acute radiation syndrome. Such radiobiological studies, while assuredly desirable, must emanate from the interest and availability of appropriate research personnel in each particular instance. For the purposes which have stimulated the preparation of this report it should suffice to point out that the accumulation of good basic clinical and laboratory data in a consistent and logical form from these unfortunate episodes will itself be a distinct contribution to radiobiological knowledge as well as a means of facilitating clinical patient management.

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TABLE VII—BLOOD COUNTS AND PROFILE SCORING—HYPOTHETICAL CASE 3

Day	Hematocrit			Leucocytes			Neutrophils			Lymphocytes			Platelets			Total Score	
		Score			Score			Score			Score		Count	Score			
	Vol %	D	C	Count	D	C	Count	D	C	Count	D	C	X 1000	D	C	D	C
1	48	0	0	13,000	1	1	12,100	1	1	800	1	1	320	0	0	3	3
2	47	0	0	12,100	1	2	11,200	1	2	290	4	5	330	0	0	6	9
3	47	0	0	5,300	0	2	5,000	0	2	100	4	9	350	0	0	4	13
4	47			3,900			3,700			150							
5				2,900			2,550			280							
6	48	0	0	1,400	3	5	1,060	2	4	260	4	13	300	0	0	9	22
7				1,550			1,300			200							
8				1,600			1,350			180							
9	48	0	0	1,700	3	8	1,500	1	5	150	4	17	90	2	2	10	32
10				2,000			1,800			100							
11				2,050			1,950			90							
12	47	0	0	2,100	2	10	2,000	0	5	90	4	21	60	2	4	8	40
13				2,050			1,700			300							
14				1,950			1,500			400							
15	47	0	0	1,950	3	13	1,250	2	7	650	3	24	50	2	6	10	50
16				2,050			1,280			760							
17				2,150			1,300			820							
18	47	0	0	2,250	2	15	1,350	2	9	880	1	25	40	3	9	8	58
19				2,250			1,300			900			30				
20				2,150			1,200			920			20				
21	45	0	0	2,100	2	17	1,150	2	11	950	1	26	10	4	13	9	67
22				1,750			1,000			750			20				
23				1,300			700			600			30				
24	44	0	0	900	4	21	550	3	14	300	3	29	50	4	17	14	81
25				850			500			250			30				
26				800			550			200			20				
27	39	1	1	750	4	25	600	3	17	100	4	33	10	4	21	16	97
28	31			600			500			84			10				
29	32	2	3	500	4	29	400	4	21	75	4	37	10	4	25	18	115

D Daily
C Cumulative

TABLE VIII—INTEGRAL AND CUMULATIVE RANGE

Day	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0	0	0	0	0–2	0.54	0–2	0.54	0–2	0.69	0–2	0.69
2	0	0	0	0	0–1	0.23	0–3	0.77	0–1	0.23	0–3	0.92
3	0	0	0	0	0–1	0.23	0–3	1.00	0–1	0.23	0–3	1.15
6	0	0	0	0	0–2	0.15	0–3	1.15	0–2	0.15	0–3	1.30
9	0	0	0	0	0	0	0–3	1.15	0	0	0–3	1.30
12	0	0	0	0	0–1	0.08	0–3	1.23	0–1	0.08	0–3	1.38
15	0	0	0	0	0	0	0–3	1.23	0	0	0–3	1.38
18	0–1	0.08	0–1	0.08	0	0	0–3	1.23	0	0	0–3	1.38
21	0–1	0.08	0–2	0.16	0	0	0–3	1.23	0	0	0–3	1.38
24	0–1	0.08	0–3	0.24	0–1	0.08	0–4	1.31	0–1	0.08	0–4	1.46
27	0–1	0.23	0–4	0.47	0–1	0.08	0–5	1.39	0–1	0.08	0–5	1.54
30	0–1	0.23	0–5	0.70	0–1	0.08	0–5	1.47	0	0	0–5	1.54
33	0–1	0.08	0–5	0.78	0–1	0.08	0–5	1.55	0	0	0–5	1.54
36	0–1	0.08	0–5	0.86	0–1	0.08	0–5	1.63	0	0	0–5	1.54
40	0–1	0.08	0–5	0.94	0–2	0.15	0–5	1.78	0–2	0.15	0–5	1.69
44	0–1	0.08	0–6	1.02	0–2	0.15	0–7	1.93	0–1	0.08	0–5	1.77
48	0–1	0.08	0–7	1.10	0	0	0–7	1.93	0	0	0–5	1.77
60	0–1	0.08	0–8	1.18	0	0	0–7	1.93	0	0	0–5	1.77
75	0–1	0.08	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77
90	0	0	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77
105	0	0	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77
120	0	0	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77

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PRELIMINARY EVALUATION OF RADIATION INJURY—An attempt has been made, utilizing the early clinical data recorded in the past accident cases, to identify those findings which have the greatest early prognostic value by indicating the correct injury group assignment and thus subsequent clinical course. On this basis a plan has been drawn up which should aid in planning for subsequent patient care. It is briefly summarized in Figure 4. This evaluation plan rests on the early and accurate performance of two familiar diagnostic procedures called for in Table XII — continuous detailed clinical observations and blood counts. The necessary clinical observations include a complete history of the immediate episode as well as of previous and preexisting abnormalities in health. A complete physical examination is indicated both to find any abnormalities present and to serve as a base-line observation for subsequent changes. Items of particular interest are the exact time of onset and duration of symptoms and signs listed in Table IV. Central nervous system and gastrointestinal findings are of greatest importance in the preliminary evaluation process.

The blood counts should include erythrocyte count and/or hematocrit, leukocyte count, differential count, calculated total lymphocytes and neutrophils, and platelet count. They should be performed at least once daily for the first three days. To evaluate the results, the blood count profile scoring method is recommended.

DIAGNOSTIC USE OF PROFILE SCORING METHOD —To demonstrate the use of the scoring method, the hematological findings of Hypothetical Case 3 are presented in Table VII. The leukocyte count on Day 1 is 13,000. On Day 2, a count of 12,100 scores 1 again. Thus the integral score again is 1, but the cumulative leukocyte score is now 2. These steps are carried out for all components of the blood count.

The integral and cumulative scores of individual counts and total counts are then compared with those presented as group mean scores and their ranges on Tables VIII, IX, X, and XI. The total cumulative scores of Hypothetical Case 3 for Days 1, 2, and 3 are 3, 9, and 13. Since the mean scores of Group III are 1.6, 7.6, and 14.0 while those of Group II are 1.4, 2.4, and 3.3, it appears that Hypothetical Case 3 is most likely to present a rather severe version of the clinical course of Group III. Referring to Figure 4, one also can narrow down this patient's injury pattern to that of Group III or IV. Further clinical and blood count data are needed to make a more definite distinction between Group III and IV. The amount of platelet derangement mentioned in Figure 4 can be determined by looking at the appropriate space in Table X.

It should be pointed out that when more frequent counts are performed than the recom-

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP I

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–1	0.23	0–1	0.23	0	0	0	0	0–4	1.46	0–6	1.46
0–1	0.15	0–2	0.38	0	0	0	0	0–2	0.61	0–6	2.07
0–1	0.08	0–2	0.46	0	0	0	0	0–3	0.54	0–7	2.61
0–1	0.23	0–2	0.69	0	0	0	0	0–4	0.53	0–8	3.14
0–1	0.15	0–3	0.84	0	0	0	0	0–1	0.15	0–8	3.29
0–1	0.08	0–3	0.92	0	0	0	0	0–2	0.24	0–8	3.53
0–1	0.15	0–4	1.07	0	0	0	0	0–1	0.15	0–8	3.68
0–1	0.15	0–5	1.22	0	0	0	0	0–1	0.23	0–8	3.91
0–1	0.15	0–6	1.37	0	0	0	0	0–1	0.23	0–8	4.14
0–1	0.15	0–7	1.52	0	0	0	0	0–2	0.39	0–8	4.53
0–1	0.08	0–8	1.60	0–2	0.23	0–2	0.23	0–4	0.70	0–11	5.23
0	0	0–8	1.60	0–3	0.23	0–5	0.46	0–5	0.54	0–16	5.77
0	0	0–8	1.60	0	0	0–5	0.46	0–2	0.16	0–18	5.93
0	0	0–8	1.60	0	0	0–5	0.46	0–2	0.16	0–20	6.09
0–1	0.08	0–9	1.68	0	0	0–5	0.46	0–6	0.46	0–26	6.55
0–1	0.08	0–10	1.76	0	0	0–5	0.46	0–5	0.39	0–31	6.94
0	0	0–10	1.76	0	0	0–5	0.46	0–1	0.08	0–32	7.02
0–1	0.08	0–10	1.84	0	0	0–5	0.46	0–1	0.16	0–33	7.18
0–1	0.08	0–10	1.92	0	0	0–5	0.46	0–1	0.16	0–34	7.34
0	0	0–10	1.92	0	0	0–5	0.46	0	0	0–34	7.34
0	0	0–10	1.92	0	0	0–5	0.46	0	0	0–34	7.34
0	0	0–10	1.92	0	0	0–5	0.46	0	0	0–34	7.34

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mendations call for, the most abnormal one in the particular time period is used for scoring.

RADIOASSAY PROCEDURES—Although the radioassay tests, such as determination of Na^{24} activation in urine, blood, and whole body following neutron exposure, are dosimetry tests performed by the health physicist rather than clinical laboratory procedures, they are mentioned in Table XII, since they require the cooperation and judgment of the physician. If at all possible, the accomplishment of these procedures should be facilitated since knowledge of the physical exposure dose is a most valuable supplement to the clinical injury estimate. It may allow for early identification of the hyperresponsive patient and make clinical management easier thereby. Details of the dosimetry techniques are in a recent report[10] concerning radiation accident dosimetry.

SUBSEQUENT DIAGNOSTIC PROCEDURES—When

TABLE IX—INTEGRAL AND CUMULATIVE RANGE

	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Day	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0	0	0	0	0–1	0.25	0–1	0.25	0–1	0.25	0–1	0.25
2	0	0	0	0	0	0	0–1	0.25	0	0	0–1	0.25
3	0	0	0	0	0	0	0–1	0.25	0	0	0–1	0.25
6	0	0	0	0	0–2	0.50	0–2	0.75	0	0	0–1	0.25
9	0–1	0.13	0–1	0.13	0–2	0.75	0–3	1.50	0–1	0.13	0–1	0.38
12	0	0	0–1	0.13	0–2	1.00	0–5	2.50	0–1	0.13	0–2	0.51
15	0	0	0–1	0.13	0–2	0.75	1–6	3.25	0	0	0–2	0.51
18	0–1	0.13	0–1	0.26	0–1	0.50	2–7	3.75	0	0	0–2	0.51
21	0–1	0.50	0–3	0.76	0–2	0.88	2–8	4.63	0	0	0–2	0.51
24	0–1	0.50	0–4	1.26	0–2	1.13	3–10	5.76	0–2	0.38	0–2	0.89
27	0–2	0.25	0–6	1.51	0–3	1.63	3–13	7.39	0–4	1.13	0–6	2.02
30	0–1	0.25	0–6	1.76	1–4	2.25	4–17	9.64	0–4	1.63	0–10	3.65
33	0–3	0.88	0–9	2.64	1–3	2.38	6–20	12.02	0–4	2.13	1–13	5.78
36	0–3	0.88	0–12	3.52	1–3	2.38	8–23	14.40	0–4	2.25	1–16	8.03
40	0–3	1.00	0–15	4.52	1–3	1.88	9–25	16.28	0–3	1.50	1–19	9.53
44	0–3	1.13	0–18	5.65	0–2	1.25	9–27	17.53	0–2	0.75	1–20	10.28
48	0–2	0.75	0–20	6.40	0–2	0.63	9–27	18.16	0–2	0.50	1–20	10.78
60	0–2	0.63	0–21	7.03	0–1	0.13	9–27	18.29	0	0	1–20	10.78
75	0–2	0.63	0–22	7.66	0	0	9–27	18.29	0	0	1–20	10.78
90	0–2	0.25	0–22	7.91	0	0	9–27	18.29	0	0	1–20	10.78
105	0–1	0.13	0–22	8.04	0	0	9–27	18.29	0	0	1–20	10.78
120	0	0	0–22	8.04	0	0	9–27	18.29	0	0	1–20	10.78

TABLE X—INTEGRAL AND CUMULATIVE RANGE

	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Day	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0–1	0.80	0–1	0.80	0–1	0.20	0–1	0.20	0–2	0.40	0–2	0.40
2	0	0	0–1	0.80	1	1.00	0–2	1.20	2	2.00	0–4	2.40
3	0–1	0.40	0–2	1.20	1–3	2.00	2–3	3.20	0–2	0.60	0–6	3.00
6	0–1	0.40	0–3	1.60	1–3	2.00	3–6	5.20	0–3	0.80	0–9	3.80
9	0–1	0.40	0–4	2.00	0–3	2.00	5–9	7.20	1–2	1.20	1–10	5.00
12	0–1	0.60	0–5	2.60	0–4	2.20	5–13	9.40	0–4	1.20	1–10	6.20
15	0–1	0.60	0–6	3.20	0–3	2.00	5–16	11.40	0–2	0.80	1–11	7.00
18	0-1	0.60	0–7	3.80	0–3	2.00	5–19	13.40	0–3	1.20	1–12	8.20
21	0–1	0.60	0–8	4.40	1–3	2.20	6–22	15.60	0–3	1.00	1–13	9.20
24	0–2	1.00	0–10	5.40	2–4	3.00	10–25	18.60	0–4	2.00	1–17	11.20
27	0–2	1.20	0–12	6.60	2–4	3.40	13–29	22.00	1–4	3.20	2–20	14.40
30	1–2	1.75	4–14	8.35	3–4	3.75	21–33	25.75	0–4	3.00	2–21	17.40
33	1–3	2.00	7–16	10.35	3–4	3.75	25–37	29.50	3–4	3.75	6–25	21.15
36	1–2	1.75	8–18	12.10	2–4	3.00	28–41	32.50	0–4	2.50	10–29	23.65
40	1–2	1.50	10–20	13.60	0–4	2.25	30–45	34.75	0–4	2.00	13–33	25.65
44	1–2	1.75	12–22	15.35	0–4	2.00	30–49	36.75	0–3	1.50	14–36	27.15
48	1–2	1.25	15–24	16.60	0–3	1.25	31–52	38.00	0–2	0.50	14–38	27.65
60	1–2	1.25	16–26	17.85	0–3	0.75	31–55	38.75	0–2	0.50	14–40	28.15
75	1	1.00	17–27	18.85	0–1	0.25	31–56	39.00	0	0	14–40	28.15
90	0–1	0.50	17–28	19.35	0–2	1.50	33–58	40.50	0	0	14–40	28.15
105	0–1	0.50	17–29	19.85	0–2	1.00	35–60	41.50	0	0	14–40	28.15
120	0–1	0.25	17–30	20.10	0–2	1.00	36–62	42.50	0–1	0.25	14–41	28.40

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the preliminary radiation injury group assignment of a given patient has been made, further diagnostic tests are designed to verify the assignment, to identify complications, and to aid in their management. Only a few Type B tests have been mentioned in Table XII. These are not intended to exclude others, but are merely the ones which seemed most useful in past cases and the ones for which early baseline values might be desired.

The few Type C procedures in Table XII are those used in some of the cases reviewed which seemed to be related to the extent of injury. Insufficient frequency of application prevent any definite opinion about their value as yet. Of course, many other procedures may also prove to be applicable to this type of clinical problem.

CLINICAL MANAGEMENT—As in the case of diagnostic procedures, a consideration of the

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP II

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–2	0.88	0–2	0.88	0	0	0	0	0–2	1.38	0–3	1.38
0–2	1.00	0–4	1.88	0	0	0	0	0–2	1.00	1–4	2.38
0–2	0.88	0–6	2.76	0	0	0	0	0–2	0.88	1–6	3.26
0–4	1.88	0–8	4.64	0	0	0	0	0–4	2.38	2–10	5.64
0–3	1.38	1–10	6.02	0	0	0	0	0–5	2.39	3–13	8.03
0–3	1.25	2–12	7.27	0–1	0.25	0–1	0.25	1–4	2.63	4–15	10.66
0–3	0.75	2–15	8.02	0–1	0.13	0–2	0.38	0–4	1.63	10–19	12.29
0–3	0.75	2–18	8.77	0–2	0.88	0–4	1.26	0–5	2.26	11–24	14.55
0–3	1.38	2–21	10.15	1–4	1.88	1–6	3.14	2–7	4.64	15–24	19.19
0–2	1.13	2–21	11.28	1–4	2.50	2–9	5.64	2–9	5.64	19–38	24.83
0–2	0.63	2–23	11.91	2–4	2.63	4–12	8.27	2–13	6.27	21–51	31.10
0–2	0.75	2–25	13.03	1–4	2.50	6–15	10.77	2–14	7.38	24–47	38.48
0–2	1.00	2–27	13.66	1–4	2.50	8–18	13.27	2–13	8.89	27–60	47.37
0–2	0.63	2–29	14.29	1–3	1.88	9–20	15.15	2–13	8.02	29–89	55.39
0–2	0.25	2–31	14.54	0–3	1.13	10–21	16.28	2–11	5.76	31–78	61.15
0–2	0.38	2–33	14.92	0–2	0.25	10–21	16.53	0–8	3.76	31–106	64.91
0–2	0.25	2–35	15.17	0–2	0.25	10–21	16.78	0–8	2.38	44–110	67.29
0–2	0.25	2–35	15.42	0–1	0.13	10–21	16.91	0–2	1.14	44–86	68.43
0	0	2–35	15.42	0	0	10–21	16.91	0–2	0.63	44–112	69.06
0–4	0.50	2–35	15.92	0	0	10–21	16.91	0–4	0.75	31–112	69.81
0–1	0.38	2–35	16.30	0	0	10–21	16.91	0–1	0.51	31–112	70.32
0–2	0.25	2–35	16.55	0	0	10–21	16.91	0–2	0.25	31–112	70.57

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP III

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–1	0.20	0–1	0.20	0	0	0	0	1–4	1.60	1–4	1.60
3	3.00	0–4	3.20	0	0	0	0	6	6.00	1–10	7.60
2–4	3.40	2–8	6.60	0	0	0	0	4–9	6.40	5–17	14.00
3–4	3.40	6–11	10.00	0–2	0.40	0–2	0.40	5–9	7.00	10–25	21.00
2–4	2.80	8–15	12.80	0–2	0.60	0–3	1.00	5–9	7.00	15–32	28.00
1–4	2.00	9–19	14.80	0–2	0.60	0–4	1.60	4–11	6.60	20–38	34.60
1–3	2.00	10–21	16.80	0–2	1.00	0–6	2.60	4–9	6.40	24–43	41.00
1–4	1.80	13–22	18.60	0–2	0.80	0–7	3.40	2–13	6.40	27–56	47.40
1–4	2.00	14–23	20.60	2–3	2.20	2–10	5.60	5–11	8.00	32–60	55.40
2–4	3.00	16–26	23.60	2–4	2.20	4–13	7.80	7–16	11.20	52–79	66.60
0–4	3.00	16–30	26.60	2–4	2.80	7–16	10.60	12–17	13.60	46–96	80.20
1–4	3.00	17–32	29.60	2–3	2.75	10–19	13.35	9–17	14.25	55–113	94.45
0–4	2.25	21–36	31.85	2–3	2.25	12–21	15.60	10–17	14.00	72–130	108.45
0–4	2.00	22–40	33.85	0–2	1.25	13–21	16.85	4–16	10.50	84–146	118.95
0–4	1.25	22–44	35.10	0–2	1.00	14–21	17.85	2–16	8.00	93–162	126.95
0–3	0.75	22–47	35.85	0–2	0.50	14–22	18.35	1–14	6.50	100–176	133.45
0–3	1.25	22–48	37.10	0–1	0.50	14–23	18.85	3–9	4.75	103–185	138.20
1–3	1.75	24–51	38.85	0–1	0.25	14–23	19.10	2–10	4.50	105–195	142.70
0–1	0.50	25–52	39.35	0	0	14–23	19.10	1–3	1.75	106–198	144.45
1–3	2.00	28–54	41.35	0–1	0.50	15–24	19.60	1–6	4.50	112–204	148.95
1–4	2.25	29–58	43.60	0	0	15–24	19.60	1–7	3.75	115–211	152.70
1–3	1.50	30–61	45.10	0–1	0.25	15–25	19.85	1–8	3.25	116–219	155.95

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TABLE XI—INTEGRAL AND CUMULATIVE RANGE

	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Day	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0–1	0.50	0–1	0.50	0–1	0.50	0–1	0.50	0–2	1.00	0–2	1.00
2	0	0	0–1	0.50	1	1.00	0–2	1.50	2	2.00	0–4	3.00
3	0	0	0–1	0.50	1–2	1.50	1–4	3.00	0–4	2.00	0–8	5.00
6	0	0	0–1	0.50	2–4	3.00	3–8	6.00	0–4	2.00	0–12	7.00
9	0	0	0–1	0.50	3–4	3.50	6–12	9.50	3–4	3.50	3–16	10.50
12	0	0	1	0.50	4	4.00	10	13.50	3	3.00	6	13.50
15	0	0	1	0.50	2	2.00	12	15.50	0	0	6	13.50
18	1	1.00	2	1.50	3	3.00	15	18.50	1	1.00	7	14.50
21	1	1.00	3	2.50	4	4.00	19	22.50	4	4.00	11	18.50
24	1	1.00	4	3.50	3	3.00	22	25.50	3	3.00	14	21.50
27	1	1.00	5	4.50	4	4.00	26	29.50	4	4.00	18	25.50
30	1	1.00	6	5.50	1	1.00	27	30.50	0	0	18	25.50

INTEGRAL AND CUMULATIVE RANGE AND

1	2.00	2.00	3.00	3.00	4.00	4.00
2	0	2.00	3.00	6.00	4.00	8.00

choice and results of past methods of therapy helps to shape the present recommendations. The types of agents employed in the accidents reported herein are listed in Table XIII. It will be seen that only in cases which fall into Group II or above has specific treatment appeared necessary. In general, since the means to reverse the basic cellular mechanisms which underlie radiation effect are not yet at hand, the clinical approach has been supportive, with specific therapy being reserved for symptomatic indications.

As has already been indicated, it is desirable for all cases with a probability of significant acute injurious radiation overexposure to be hospitalized for close observation. The accomplishment of the preliminary estimation of clinical radiation injury as described in the preceding section on diagnostic procedures should indicate within 72 hours those cases falling into Group II or above. These should be kept hospitalized. The others can be reassured of their favorable prognosis and released from inpatient care when asymptomatic.

GROUP I—These patients can be followed as outpatients, using the previously suggested tests. There is no specific medical contraindication to a return to work as soon as dosimetry, clinical symptoms and findings, and laboratory data have established the low level of overexposure. Considerations of public opinion, medicolegal sequelae, and the like, doubtless have played a role in the more conservative prescription of a rest period of varying length which has been utilized in several cases within Group I. It is definitely recommended that subsequent work be in a capacity in which further radiation overexposure is unlikely.

GROUP II—Patients in this group will exhibit transient nausea and vomiting which will probably not require more than the administration of antiemetic agents, if that. There is no definitive therapeutic procedure for radiation epilation other than reassurance concerning its impermanence in this group.

Complications of the existing bone marrow damage, such as anemia, infection, and evidences of bleeding, have been mild when present at all in Group II. It is therefore considered advisable to adopt a conservative attitude of watchful waiting, with the means for vigorous and definitive treatment available if and when needed. Thus, blood and perhaps platelet transfusions, antibiotics, and the like should be ready in reserve. An attempt to reduce the likelihood of infections by emphasis on personal hygiene and the use of aseptic isolation methods may well be warranted.

The mechanism of the observed weakness and fatigue of these patients is not clear, and therefore no specific therapy can be recommended at this time. Rest is indicated until symptoms and major laboratory abnormalities subside. The opportunity for future occupational radiation exposure should be minimal.

GROUP III—It is the therapeutic management of patients in Group III that presents the most challenging opportunity to alter an otherwise unfavorable prognosis. In this group one can expect to deal with the major complications of serious bone marrow damage, some gastrointestinal injury, and secondary renal and cardiovascular problems.

Prompt bed rest, bland diet, good nursing care, and a realistic but generally reassuring appraisal of the medical situation are indicated

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AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP IV

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–2	1.00	0–2	1.00	0	0	0	0	1–5	3.00	1–5	3.00
4	4.00	0–6	5.00	0	0	0	0	7	7.00	1–12	10.00
4	4.00	4–10	9.00	0	0	0	0	5–10	7.50	6–22	17.50
4	4.00	8–14	13.00	2	2.00	2	2.00	8–14	11.00	14–36	28.50
3–4	3.50	11–18	16.50	2–4	3.00	4–6	5.00	11–16	13.50	25–52	42.00
4	4.00	15	20.50	3	3.00	7	8.00	14	14.00	39	56.00
4	4.00	19	24.50	3	3.00	10	11.00	9	9.00	48	65.00
3	3.00	22	27.50	4	4.00	14	15.00	11	11.00	59	76.00
3	3.00	25	30.50	4	4.00	18	19.00	15	15.00	74	91.00
1	1.00	26	31.50	4	4.00	22	23.00	11	11.00	85	102.00
4	4.00	30	35.50	3	3.00	25	25.00	16	16.00	101	118.00
4	4.00	34	39.50	0	0	25	26.00	6	6.00	107	124.00

MEAN OF BLOOD COUNT PROFILE SCORES—GROUP V

4.00	4.00					13.00	13.00
4.00	8.00					11.00	24.00

as soon as dosimetry, symptomatology and hematological "profile" makes classification in Group III apparent.

Antiemetics are indicated for severe and prolonged nausea and vomiting in the initial phase or later. Intravenous feeding may be necessary as well, to maintain fluid and caloric balance in the early stage or in the later course when gastrointestinal symptoms may recur. The maintenance of acid-base and electrolyte balance should be attempted also, with frequent serum pH, acid-base, and electrolyte studies as a guide.

When increasing evidence of depression of bone marrow function ensues toward the second and third weeks after exposure, certain precautions are indicated. To reduce infections, an effort to minimize bacterial exposure should be attempted, utilizing isolation and aseptic techniques in contacts with the patients. Although prophylactic antibiotics have been employed in many instances, real proof of their value for this purpose is not too clearcut. There are indications that such use may have blunted their effectiveness in subsequent infections during the course. Recently, it has been suggested[27] that penicillin and aureomycin be used orally, starting at five to seven days after exposure in doses of 100,000 units every four hours and 250 mg every six hours respectively. Bacteriocidal antibiotics in parenteral form should be reserved for therapeutic use in high dosage when infections of overt or even occult nature occur. These may be suggested by symptoms, by fever, or simply by a sharp rise in a previously low sedimentation rate, despite the absence of any resultant leucocytosis. Bacterial sensitivity studies should be performed and their results used as a therapeutic guide, if possible.

Hemorrhagic phenomena are difficult to treat by any conventional means. Platelet transfusions have been tried with some possible temporary benefit resulting.[19] Anemia, which develops insidiously, will respond to conventional transfusion therapy. This should be used only when a clinically significant fall in red cell volume has developed.

A new form of therapy may be utilized to treat severe pancytopenia accompanied by distinct clinical sequelae, such as uncontrollable infection or bleeding, with a clearly grave prognosis. This is the performance of bone marrow transplantation using cells from a homologous donor, matching in sex, and in major, and most minor blood subgroups. The time for successful performance of this procedure had previously been considered to be limited to a few days after radiation exposure. Now, the recent, apparently helpful, use of such a transplantation procedure in the Yugoslavian accident patients[22] about a month after exposure suggests that the decision concerning its use can await the unfolding of the clinical course. This delay removes the necessity to base such action on the preliminary physical dosimetry and early, fragmentary data concerning the extent of radiation injury.

Very little is known as yet about the utility or even desirability of bone marrow transplantation in man. In the treated Yugoslavian patients, a prompt rise to a peak occurred in the level of granulocytes, platelets, and reticulocytes before such improvement was found in a lower dose patient recovering spontaneously. Also, the pattern of platelet response was some-

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TABLE XII—RECOMMENDED DIAGNOSTIC PROCEDURES FOR CLINICAL MANAGEMENT OF RADIATION INJURY

Group	I-II-III-IV			I	II			III		IV	V
Procedure / Time (d)	1	2	3	STT	STT	18-48	STT	4-48	STT	4	1
TYPE A											
History											
Symptoms } onset	x	x	x	x	x	D	x	D	x	D	D
Signs } duration	x	x	x	x	x	D	x	D	x	D	D
Past Medical	x										
Physical Examination											
General	x					d21	3 mo+	d15–30	3 mo+	d6	D
Body weight	x			x	x	D	x	D	x	D	D
Urinary output	x	x	x		x	D		D		D	6 hr
Laboratory Tests											
Hematology											
Hematocrit	x	x	x	x	x	D	x	STT	x	D	6 hr
Leukocytes	x	x	x	x	x	D	x	D	x	D	6 hr
Differential Count	x	x	x	x	x	D	x	D	x	D	6 hr
Calculation of Total Neut. and Lymph.	x	x	x	x	x	D	x	D	x	D	6 hr
Platelets	x	x	x	x	x	D	x	STT	x	D	6 hr
Bone Marrow Aspiration				d30	14d	14d	mo6	14d	mo6	7d	d1
Radioassay											
Blood Na^{24}	x	x									
Whole Body Counting	x	x									
TYPE B											
Laboratory Tests											
Hematology											
Sedimentation Rate	x	x	x	x	x	D	x	D	x	D	6 hr
Reticulocytes	x	x	x	x	x	D	x	STT	x	D	6 hr
Bleeding } Times / Clotting }	x					STT		STT	–75d	3d	6 hr
Biochemistry											
Blood											
NPN	x	prn	prn					prn		STT	6 hr
Sodium	x	prn	prn					prn		prn	d1
Chloride	x	prn	prn					prn		prn	d1
Potassium	x	prn	prn					prn		prn	d1
pH or Co_2	x	prn	prn					prn		prn	d1
Urine											
Routine analysis	x	x	x		x	D	x	D	x	D	6 hr
Stool											
Occult blood	x					D		d12+		D	All
Ophthalmology											
Slit lamp			x	6mo+			6mo+		6mo+		
TYPE C											
Biochemistry											
Serum bilirubin	x	x	x		x	STT		STT	–30d	D	6 hr
Urine BAIBA	x			–30d	x	D		D		D	D

STT Standard Testing Times—6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 40, 44, 48, 60, 75, 90, 105, 120 days 6 mo., 1 yr. and annually.

Recommended frequency of time of performance:

x —— at times indicated in column heading
d —— daily during time indicated in column heading
nd —— frequency in days
–dn —— up to and including day at times indicated in column heading
dn+ —— on and after day at times indicated in column heading
dn —— specific day recommended
n —— all time after day specified
prn —— as indicated by clinical course

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TABLE XIII—SUMMARY OF THERAPEUTICS EMPLOYED IN GROUPS II, III, IV, AND V

	Group II								Group III						Group IV		Group V
Therapy	LA4	R1	R2	OR1	OR2	OR3	OR4	OR5	Y6	LA1	Y2	Y3	Y4	Y5	LA3	Y1	LAII
Sedation	....	....	....	....	....	X	....	....	....	....	....	....	....	....	....	....	X
Analgesics	....	X	....	....	....	X	....	....	....	X	....	....	....	....	X	....	X
Antiemetics	....	....	....	X	....	X	X	X	....	....	....	....	....	....	....	....	....
Antispasmodics	....	X	....	....	....	X	....	....	....	....	....	....	....	....	....	....	....
Parenteral fluids	X	....	....	....	....	....	....	....	....	X	....	....	....	....	X	....	X
Electrolytes	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Whole blood	X	X	X	....	....	....	....	....	X	X	X	X	X	X	X	X	....
Plasma	X	....	....	....	....	....	....	....	....	....	....	....	....	....	X	....	X
Platelets	....	....	....	....	....	....	....	....	....	....	X	X	....	....	....	X	....
Bone marrow	....	....	....	....	....	....	....	....	....	....	X	X	X	X	....	X	....
Antibiotics	X	X	X	X	....	....	X	....	X	X	X	X	X	X	X	X	....
Vasoconstrictors	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	X
Vitamins	....	X	X	....	....	....	....	....	X	X	X	X	X	X	....	X	....
Hematinics	....	X	X	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Miscellaneous	....	X	X	....	....	....	....	....	....	X	....	....	....	....	....	X	....

X Therapy used one or more times.

what different. Furthermore, red cell agglutination tests indicated a phase of increase in the number of donor cells during the time when transfused cells would have been decreasing. However, there may be a relative and gradual recession of the hematological picture subsequently at a time when the late "immune disease" which characterizes graft rejection in lower mammals might be expected.

It may prove that the donor marrow served as a temporarily functioning bridge over the hiatus in the patients' blood formation process. What the over-all value of the transplant procedure will be cannot yet be stated. It should be reserved as a desperate measure against overwhelming clinical odds for seriously ill patients in Group III and above until more data become available.

In the more seriously affected patients in Group III, occurrence of rather severe gastrointestinal symptomatology, including partial intestinal obstruction, may take place. A bland diet in the acute illness phase may be helpful in minimizing such difficulties.

GROUP IV—The patients in this range have run a course similar to those in the upper end of Group III but telescoped into a shorter time period, and with a fatal outcome. Gastrointestinal difficulties require the major therapeutic effort before hematological disturbances reach full fruition. Vigorous treatment, including tubal gastrointestinal decompression, fluid replacement with correction of electrolyte and caloric deficits, the use of antiemetics, antihypotensive agents, antibiotics, and bone marrow transplantation, are advocated in this situation.

Secondary cardiovascular and renal failure may further complicate this grave clinical state. Response to hemodialysis in one such instance was poor. Detailed biological data collection is particularly indicated in these difficult cases if present-day therapeutic inadequacy is to be altered in the future.

GROUP V—The one case in this group showed the evidence of the experimentally anticipated central nervous system injury associated with very high radiation dose. Palliation of the accompanying hypotension and gastrointestinal symptoms was carried out. No specific recommendations are yet available for this situation, other than supportive therapy.

LATE SEQUELAE—The only late sequela of radiation overexposure in the accident cases reported herein has been the development of bilateral cataracts. There is no known prophylaxis against this occurrence, but if the usual spontaneous regression of the radiation cataract is inadequate, the ordinary surgical procedure for its removal is satisfactory.

No other long-term effects can be anticipated specifically in any given case, although the general statistical probability of leukemogenesis, carcinogenesis, or genetic mutation may be slightly enhanced. There are no such findings reported in any of these cases.

Conclusions

The general medical findings in the radiation accident patients reviewed in this report are not novel. They correspond with those reported in a number of other situations in which humans have been exposed to significant whole-body radiation overexposure. However, these particular findings stem from the types of accidents which are of special interest to an increasing number of physicians now coming into contact with the fast-growing field of nuclear technology. For this reason, conclusions drawn from this series may be especially useful.

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It is rather reassuring to find that, despite the disturbing physical complexity of nuclear criticality accidents, the key procedures for clinical evaluation of resultant injury are such familiar ones as a detailed medical history, thorough physical examinations, and accurate blood counts. The additional support provided by improvements in radiation dosimetry and modern clinical laboratory procedures is, of course, very helpful as well.

In the therapy of such patients also, good medical management, firmly based on an understanding of the pathophysiology of the acute radiation syndrome, does not really differ from the treatment of less modern maladies. The development of bone marrow transplantation as a possible specific form of treatment for this syndrome does provide, however, a somewhat specialized therapeutic procedure.

Concerning the relative value of physical dose measurements and biological signs of injury as aids in the care of human radiation overexposure, the nature of the exposure incident is most important. What is suited to the triage of victims of a nuclear warfare catastrophe is not necessarily appropriate for the industrial accident victim. The utilization of precise clinical observations and frequent laboratory tests as advocated herein, with calculation of the injury profile score, may not be feasible under other circumstances. However, it is considered to be of particular value, especially when supplemented with good mixed radiation dosimetry, in medical management of the accidents of nuclear technology.

Summary

In order to familiarize the medical profession with current concepts about the diagnosis and management of a rare but increasingly frequent clinical entity, the acute radiation syndrome, all pertinent radiation accident cases have been reviewed. Circumstances; dosimetry; clinical signs, symptoms, and course; laboratory findings; and therapy are considered. On the basis of these data, recommendations for diagnosis and treatment are made to aid in clinical management, to facilitate the development of improved diagnostic procedures, and to increase the fund of biomedical data from which stems our understanding of human radiation injury.

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