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The Importance of Dosimetry to the Medical Management of Persons
Accidentally Exposed to High Levels of Radiation*

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In view of the many persons who have worked among the hazards of the atomic energy industry since 1940, surprisingly small numbers have been killed or seriously injured in radiation accidents. The accidents that have occurred have received a great deal of publicity and study. Perhaps this attention is partly due to general apprehensiveness about radiation effects and the widespread concern that has been expressed about low-dose occupational and environmental exposures. In the radiation accidents, the effects of exposure are clearly demonstrable and no statistician is needed to determine that injury has been sustained. Those of us who are greatly interested in radiation effects are pleased that there is this strong support for the study of radiation accidents. If the effort seems out of proportion to the seriousness of the problem, it can be

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justified on the basis of the increasing use of nuclear energy with attendant possibilities for accidents and on the basis of the wide usefulness of the biologic information derived, for radiation injury involves phenomena applicable to other biologic problems.

For the purposes of this discussion we shall concentrate on acute penetrating total body irradiation received from an external source. The responses to this type of exposure can be taken as the prototype for most types of acute radiation effect, including those caused by internal radioisotopes of short effective half-life. External exposures to radiations of very low penetrating ability present special problems with skin effects out of proportion to hematopoietic or gastrointestinal damage. Similarly, uneven exposures of various parts of the body to penetrating radiations may alter the response and make dosage determination difficult if not impossible. A certain amount of non-uniformity is the rule and the degree of non-uniformity at which the reliability of the dosimetry or specific biological response must be partially discounted will be a matter of subjective judgement for the clinician. Accidental exposure to internal radioisotopes may be of several different types, involving inhalation, ingestion, injection, or wound contamination; here the dosimetry problems include identification of the radioisotope and determination of the amount and distribution in the body. For gamma emitting isotopes, whole-body counters are extremely useful; for those without gamma emissions, determinations of body burdens may depend largely on levels in the urine or expired air, and their estimation may be extremely difficult and unsatisfactory. The problem of plutonium in wounds is an especially knotty one and will be discussed in a later paper in this program. Other specific forms of radiation hazard present their

own peculiar dosimetry problems and several of these will be discussed by later speakers.

Experience at the 1958 Oak Ridge Accident

In June 1958 there was a serious radiation accident in Oak Ridge. It may be informative to consider this accident, particularly in the light of dosimetric considerations as they relate to clinical management. In 1958 there had not been recent serious accidents and our most vivid memory was of the fatal Los Alamos accident of 1946.

In the Oak Ridge accident, some enriched uranium was inadvertently allowed to flow into a large container and criticality occurred. Five men received high doses of gamma and neutron radiation, and three others received lower doses. The accident occurred at 2 o'clock in the afternoon. There was no surface contamination. As a dosimeter, each man was wearing only a small piece of indium foil. All five of the men who received high doses experienced nausea and four vomited. Blood was obtained for ^{24}Na assay and an attempt was made to assay the men in a whole-body counter, but there was so much induced radioactivity that the electronics were overloaded and the counts obtained were not satisfactory. The men were admitted to our hospital at 11:00 p.m. The clinical staff had not been informed of the accident until shortly before the patients arrived at the hospital.

The information available on dosage measurements for the five most heavily exposed is summarized in Table 1. This illustrates the early uncertainty about doses; however, it should be pointed out that as compared with other accidents, the early estimates were much more accurate than are usually made.

The patients had a favorable clinical course after nausea and vomiting ceased. On June 19, the third day after the accident, we felt that a crucial decision had to be made about whether or not to use bone-marrow grafts. Table 2 shows the status of our information at that time. The two sets of doses given came from two separate groups of health physicists working on the problem; one chose to report in rads and one in rems, but the difference in units is not the only basis for the differences in the two sets of figures. In deciding about the use of bone-marrow grafts we also put considerable weight on the clinical and hematologic values. Our estimate then was that without marrow grafts patients B, C, and D had an excellent chance for survival, and patients A and E had at least a 50% chance. We considered giving grafts to all the patients, giving them only to patients A and E, or giving them to none. A decision was made to give no marrow. We had considerable confidence in the physical dose values available at that time and they were one basis for the decision. At that time we were under the impression - with which we would not now agree - that the marrow would have to be given very early to be of any possible value.

The patients were treated with very little medication. No blood transfusions were given. Two of them showed a rather alarming degree of hematologic depression in the fifth week after exposure, but all recovered spontaneously.

Clinical Manifestations of Radiation Injury

The effects depend very largely on dose. Although much emphasis has been placed on variations in sensitivity from person to person, there is no reason to believe that this individual variation is greater for radiation than it is for other types of injury, and, in fact, one is impressed by the relative uniformity of response.

Figure 1 illustrates the types of response expected at the different dose levels. Although this information is largely extrapolated from work on experimental animals and may not be correct for the human being, it is helpful in illustrating some very general opinions. Depending on the radiation dose received, the exposed person may show the major injury expressed in the nervous system, the gastrointestinal tract, or in the hematopoietic tissues.

Very high doses, manifested mainly by neurological damage, have not been experienced by human beings under conditions that would allow clear interpretation. The Los Alamos accident in 1958 and the recent Rhode Island accident in 1964 involved doses at these levels and there was believed to be clinical evidence of neurologic damage, but this was complicated by direct damage to the heart and cardiovascular failure in both patients, and damage to nervous tissue was not confirmed at autopsy.

Similarly, a typical picture of gastrointestinal damage has not been seen in the human being; one of the early Los Alamos patients approximated it. The picture is characterized by severe and persistent nausea and vomiting associated with death of the cells lining the intestinal tract, leading to severe loss of body fluids and infection along the intestinal tract. Experience in clinical total-body irradiation for purposes of marrow grafts suggests that the human being may have a high threshold for gastrointestinal damage.

The clinical situation produced by dose levels that damage primarily the hematopoietic system are of much greater importance because experience has shown that many more persons are injured at these dose levels. Furthermore, effective treatment is available, while for neurological and gastrointestinal damage no known treatment

can prevent death. Figures 2, 3, 4, and 5 portray typical hematologic responses to different doses. That there is so long an interval between exposure and the occurrence of maximal hematopoietic depression is particularly interesting.

Treatment

Effective therapy is available for management of patients exposed in the LD₅₀ range, but little can be done for those who have received doses in the supralethal range. For neurologic manifestations there are only purely symptomatic measures - the use of drugs for sedation and control of convulsions. For the severe gastrointestinal syndrome, fluid and electrolytes lost should be replaced, and efforts can be made to control invasion by enteric bacteria; but if the damage to the mucosa of the intestine is severe, these measures will be of no avail.

It is at the lower doses, 200 to 1000 rads, that more is known of therapeutic management. Measures and the indications for them can be outlined as follows:

Rest - Unusual exertion is believed to enhance the damaging effects of radiation.

Sedation - This may be needed to control apprehension and vomiting. However, the early use of sedatives may suppress vomiting, and thus obscure a valuable biologic dosimeter.

Maintenance of fluid and nutritional requirements - This is self-evident.

Prevention of infection - An attempt should be made to place the patient in an environment as near infection-free as possible. Base-line cultures of nose, throat, stool, and urine for pathogenic organisms should be obtained. Judicious attempts are needed to clear up existing sites of infection before severe leukopenia is reached. Prophylactic use of

antibacterial agents is probably not indicated simply on the basis of leukopenia. However, in the presence of severe leukopenia, prophylactic use of nystatin to prevent Candida infections is probably well worth while. Therapy of infection - Once the presence of infection is known or strongly suspected on the basis of fever, thorough efforts should be made to identify the organism. However, it may be necessary to start antibiotic therapy before cultures are reported if the clinical course is unfavorable; the choice of drugs can later be altered on the basis of cultured reports and sensitivity findings. Gamma globulin may be of value in combating infections.

Whole blood and platelet transfusions - These are mainly needed for bleeding. Unless there is significant anemia, requiring whole blood replacement, concentrated fresh platelets are often desirable, and using very large quantities may be necessary. The need for platelets is ~~gauged on the presence of clinical hemorrhagic phenomena~~, and to some extent on the patient's platelet count.

Bone-marrow grafts - These are advisable in situations in which recovery is unlikely without them. Probably some patients can be saved by a temporary marrow graft. The marrow should probably be given some time later than the first two or three days after exposure, but before two weeks have elapsed. The decision to give the graft is based on biologic and dosimetric evidence that the exposure has been so high that recovery without this therapy is unlikely. Perhaps in the future large volumes of normal donor white cells will be advisable, and these may be an adequate or preferable substitute for bone marrow.

Early Management of an Accident

Certain points appear important to clinicians who have had experience with radiation accidents. In retrospect it is obvious that in all accidents important information has been lost in the excitement of the situation. It is desirable for someone to keep a very careful record of all pertinent events and the exact time that they occur. If there is associated trauma or if radiation contamination is present on the external surface of the body, these are probably more in need of immediate attention than are the effects of the absorbed radiation dose. Clothing, including the fasteners, contents of pockets, etc, should be saved and carefully labeled to be studied for contamination and induced radioactivity. If the patient's body has external contamination, prompt efforts should be made to remove it; this may require shaving off contaminated hair. A whole-body counter is a valuable instrument in this situation for showing induced or surface activity, or both, and the spectrum may help to make the differentiation. However, in all accidents in which neutron exposures are significant, or in which there is sufficient contamination to represent a hazard, the activity will be sufficient to overload the sensitive electronics of low level whole-body counters. Therefore, it is wise to plan simple alterations, generally the installation of small crystals, which will make possible early post-exposure evaluations.

There is need to obtain early and repeated blood samples for hematologic tests, for measurements of induced radioactivity, and for special biochemical tests. To use ^{24}Na as an index of induced radioactivity, a sample of serum or plasma should be counted in a calibrated instrument, and at the same time a sample of serum should be measured for stable sodium. All urine excreted by the patient should be refrigerated and saved for biochemical tests. Samples of hair and nails, carefully

identified as to location on the body, are also of value for determinations of induced radioactivity; these measurements may serve as the basis for neutron dosimetry and may be especially helpful in showing uneven doses to different parts of the body.

Biologic Dosimetry

The history of radiation accidents has shown that the physician has been justified in putting great reliance on biologic manifestations as early indices of dose. The presence of nausea and vomiting during the first few hours after exposure suggests that the dose has probably been more than 200 rads. Incidental or emotionally induced vomiting is always mentioned as a possibility, but in most radiation accidents it has not been a major cause of confusion. The absence of vomiting is strong evidence that the dose of radiation is less than a lethal one and throws serious doubt on the validity of dose estimates placed in the lethal range. Early diarrhea is an ominous sign and suggests a lethal dose, as does the persistence of vomiting after the first 48 hours. Figure 6 shows correlation between dose and incidence of anoxia, nausea, and vomiting in a series of patients exposed accidentally and therapeutically in Oak Ridge. The presence of erythema of large portions of the skin is a very ominous sign, although perhaps less so if the radiation is known to include a large low-energy component. Early neurologic signs and hypotension are, of course, indicative of a very high dose. Among laboratory tests, the absolute lymphocyte count appears to be of greatest value. Figures 7 and 8 give data on this. Increased amounts of beta-aminoisobutyric acid, taurine, and possibly creatine in the urine appear to be related to the dose, but these biochemical assays are not established for clinical purposes as yet.

The Role of Dosage Measurements

At the same time that the clinician is trying to assess the degree of injury to his patient by watching the clinical responses and laboratory tests, he is anxiously awaiting the results of the measurements reported by the health physicist. If preplanned dosimetry systems are in operation this information may be quickly available; if not, many hours or even several days may be needed to derive information by indirect means. In either situation it is now apparent that the most sensitive and reliable "detectors" are sodium and sulfur activation in the blood and hair respectively. Alone, these detectors serve largely as indicators of neutron exposure, rather than as dosimetric tools. However, in conjunction with other data, including the results of calculation of neutron and gamma-ray leakage spectra from similar assemblies, good approximation of dose can be made quickly. Of course, where such devices are used, information on dose in radiation accidents can be derived from film badges, area monitoring systems, and from studies of induced radioactivity. It is reasonable to assume that at large nuclear installations, such as the Oak Ridge National Laboratory, at which both personnel and nuclear accident monitoring systems are utilized, estimates of the first collision absorbed dose could be made with a precision of $\pm 25\%$ within one to three hours postexposure, unless the exposure is grossly non-uniform. Sometimes a simulated repetition of the accident is required to establish certain facts needed for dose determination.

Although information on dose is needed as soon as it can possibly be obtained, an early grossly erroneous estimate (e. g. error greater than a factor of 2) is worse than none. Total dosage is not enough; such an estimate should include, as far as possible, information on the quality and depth-dose distribution of the radiation. Several papers to be presented here deal with devices for measuring some characteristics

of the radiation field from nuclear accidents. It is reasonable to assume that, if used, any or all would yield important data for computing "doses." However, we must keep in mind that the system used is no better than the men who use it and that having any system is no guarantee, a priori, that good estimates will be obtained from the system. Consequently, all sources of information available at the time of an accident should be used.

There are three main clinical uses for information on dose:

(1) After the initial needs of the postaccident situation have been met, dosage figures give some help in appraising the magnitude of the clinical problem, what special hospital, consultant, and supportive facilities may be needed, and how the outlook can best be described to those concerned.

(2) During the later, most important period of clinical management of irradiated patients, while the clinician will wish to rely mainly on detectable biologic responses of patients to determine therapy, he will also be assisted by physical dose data, especially in a typical or borderline clinical situations.

The physical dosimetry is an important indicator for assisting in the clinical prognosis; the scientific basis for this is constantly improving. The clinician can thus make prognoses with greater accuracy than he can on the basis of day-to-day clinical manifestations. For example, when the dosimetry for the Y-12 accident in Oak Ridge was established, the relatively reassuring values were a major factor in the decision not to give marrow infusions.

(3) More information on radiation effects in man is greatly needed. Clinical total-body irradiation therapy may have excellent dosimetry,

but the results are biased by the underlying disease being treated. Radiation accidents, unfortunate as they are, are the best source of information on radiation responses of the normal person. If the patient recovers, extensive clinical and laboratory observations will be available. If the patient dies, autopsy will allow many observations on radiation effects that can be correlated with clinical and laboratory findings. However, none of this information will be of much value in improving our knowledge of the radiosensitivity of man without accurate radiation dosimetry.

Table 1

Dose Estimate Range as a Function
of Time After the Accident

Time after accident	Dose estimates
13 hours	320 to 706 rems "Probably not less than half these figures; possibly higher."
3 days	163 to 276 rads *201 to 320 rems
Weeks later	236 to 365 rads

*The Day-3 estimates were made by two separate groups
of health physicists.

Table 2

The Final Dose Estimates for the Five
Most Highly Irradiated Persons

Patient	Dose Estimates				Hematologic Changes Rank Order*	Clinical Course Rank Order*
	Group 1		Group 2			
	rads	Rank Order*	rems	Rank Order*		
A	276	1	320	1	1	1
B	188	4	256	4	3	3
C	230	3	292	2	4	5
D	239	2	272	3	5	4
E	163	5	201	5	2	2

*Rank Order: 1 - most severe; 5 - least severe