A SIMPLE PLAN FOR DIAGNOSIS AND THERAPY OF THE ACUTE RADIATION SYNDROME

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This presentation summarizes the current status of diagnosis and therapy of the acute radiation syndrome under two circumstances, 1) that in which there are minimal or no facilities for care and 2) that in which some facilities are available both for diagnosis and treatment. Finally a few suggestions for additional research will be proferred.

1. Acute Radiation Injury Under Medically Austere Conditions

The concepts presented here are taken from a committee report chaired by M. Ingram which although done for civil defense purposes gives useful information for other purposes. (1).

The degree of radiation injury would have to be estimated on the basis of clinical observations even though some radiation detection devices might be available. The amount of shielding at the time of a detonation would have to be obtained by individual patient history as would subsequent exposure to fallout. Concurrent injury and disease would also be significant factors when present.

Radiation injury is classified by five injury groups as shown in Table 1 slightly modified from (2). It is divided into four stages as shown in Table 2 (3).

Under these conditions the salient characteristics of clinical manifestations and leukocyte picture following various degrees of injury are summarized in Table 3 (1). For this situation Patient Group V is omitted from consideration since such individuals could not be offered any therapy.

The observations of Table 3 are those following a single short term exposure. Factors which can modify the individual response and which can be elicited by history and physical examination are given in Table 4.

Recording of symptoms and signs in a standardized way simplifies the grouping of each individual particularly if the time of each observation is recorded. The relevant symptoms and signs for the prodromal and manifest illness stages are given in Tables 5 and 6,(3). It is essential to record the length of the latent period. The rapidity at which these occur and their severity will serve as a guide to the severity of radiation injury (4).

Combined injury may possibly occur under conditions of actual warfare although the importance of these kinds of injuries is minimized by some acknowledged experts on this subject. If such situations should occur clinical description of degrees of radiation injury may become misleading.

There is likely to be an unduly high index of suspicion with respect to radiation injury as a cause of any gastrointestinal symptoms, malaise and fever. It is particularly important to reserve judgment about the degree of radiation injury in acutely ill patients who have sustained severe burns, fractures and the like. Severely burned patients will probably become nauseated and vomit; so may patients with fractures. Shock may obscure the symptoms and clinical signs of radiation injury in the severely traumatized patient. Little information about acute radiation injury in infants and children is available, hence a high degree of caution in accepting nausea, vomiting and diarrhea as infallible signs of severe radiation injury is indicated when evaluating pediatric patients. An objective attitude about the relative importance of radiation as a cause of observed symptoms would help allay patients' anxiety when it stems from fear of radiation injury. Nevertheless in our studies (5) we have not observed vomiting from sham irradiation. In recent severe combat experience vomiting was not associated prominently with psychic stress.

Where radiation contributes significantly to injury, triage based on the above findings becomes the most important task of the medical officer in the first days and weeks especially if there are no medical facilities. His responsibility is to preserve the health of Group I and II patients so that they may survive and return to their duties. They are the ones for whom food, fluids and best sanitation efforts need be directed. The limited emergency supplies could in no way affect the levels of morbidity or mortality of Group III-V individuals in this situation. Particular care need be directed towards limiting care of other injuries in these latter categories.

If any simple laboratory test were available the most desirable would be simple white cell counts and absolute lymphocyte counts. The typical findings of the white cell count for various dose levels are shown in Figure 1 (4). The use of the absolute lymphocyte count in the first 48 hours is of particular value and the findings are illustrated in Figure 2 (6).

Treatment is limited to rest, adequate fluids and foods and maintenance of personal hygiene to the degree possible. Tranquilizers, medicines for other complaints and antibiotics are highly desirable if available.

2. Diagnosis and Treatment where Facilities are More Adequate

With somewhat more elaborate facilities - field or stationary hospitals and some available medical and paramedical personnel, both diagnosis, triage and therapy can be improved. In this circumstance five injury groups may be considered. Until recently Group V was considered to be due to central nervous system changes. Recently Fanger and Lushbaugh (7) have described two cases of death following high radiation doses with a mechanism of cardiovascular shock as well as clinical CNS changes. Pathological changes of the central nervous system were minimal, however.

With adequate hematological service a somewhat more predictive method of evaluation can be utilized (Figure 3) (8). If a large number of patients are to be managed, the relevant examinations should be carried out as shown in Table 7 (3).

Therapeutic considerations should be directed toward problems associated with neutropenia whenever possible. Under conditions of grave emergency, possible isolation, careful skin care, systemtic antibiotic therapy, triple antibiotic therapy to injection site and nares, and bowel and staphyloccal prophylaxis can be considered to some degree. Disruption of the intact skin and mucous membrane should be avoided. Rectal temperature and gastric intubation should be avoided.

Bowel sterilization can be done as follows:
- Neomycin 1 gram P.O. q.6.hr.
- Oxacillin 500 mg. P.O. q.6.hr.
- Nystatin 500,000 units P.O. q.6.hr.

Staphyloccal Prophylaxis
- Bacitracin to nares
- Oxacillin 500 mg. q.6.hr.

If elaborate facilities become available for selected patients the following measures should be considered on admission: reverse isolation, screening blood tests and cultures, monitoring for radioactivity, daily hemogram, daily bath, stool softener, daily vitamins especially Vitamin C, daily weight, no aspirin.

During the critical stages the reverse isolation is strict with no visitors. Additional measures include canned food, bedrest to avoid trauma, tests for blood in feces and urine, oral antibiotics as needed, adequate fluids, recording of urinary output, avoidance of bed sores. Bone marrow transfusion at present seems of practical value only in identical twins.

A few recommendations concerning future research are made:

1. Dose rate studies - Information is lacking as to whether very high dose rates would produce a more severe clinical episode than would low dose rates. An allusion to this problem occurs in connection with Table 3.

2. Influence of diet - In spite of many studies on the intestinal flora and their relation to many manifestations of acute radiation injury, we lack information as to whether to provide human beings with high or low residue diets or with changes in balance between fat, carbohydrate or protein.

3. Immune systems - Further implications of work with immunosuppressive agents should be analyzed with a view towards relating these methods to allografts of bone marrow. Studies of lymphocytes and stem cells to develop transplantable cultures with specific immune capabilities would be a consideration.

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REFERENCES

1. Treatment of Acute Radiation Injury Under Medically Austere Conditions, OCD Subtask 2431F, TRC-67-21, p. 9, Table VII, April 1967.

2. Exposure to Radiation in an Emergency, Report No. 29, p. 60-62, National Committee on Radiation Protection and Measurements, January 1962.

3. Medical Aspects of Radiation Accidents, ed. Eugene L. Saenger, published by the U.S. Atomic Energy Commission, available from U.S. Government Printing Office, Washington, D.C. (pages 42, 44, 65).

4. Radiobiological Factors in Manned Space Flight. ed. W.H. Langham, National Academy of Sciences, National Research Council, Washington, D.C. (p.94) 1967.

5. Metabolic Changes in Humans Following Total-Body Irradiation (DASA 1844 and 2179). DASA Contract No. DA49-146-XZ-315, Defense Atomic Support Agency, Washington, D.C. (Available from Defense Documentation Center, Alexandria, Virginia).

6. Personnel Dosimetry for Radiation Accidents. International Atomic Energy Agency, Vienna, p. 13, 1965.

7. Radiation Death from Cardiovascular Shock Following a Criticality Accident. H. Fanger and C.C. Lushbaugh, Arch. Path. Vol 83, p.446-460, May 1967.

8. The Diagnosis and Management of Accidental Radiation Injury. G.E. Thoma, Jr. and N. Wald. J. Occup. Med. 1:421-447, 1959.

TABLE 1

RADIATION INJURY GROUPS

Group I: Less than half this group vomit within 24 hours after the onset of exposure. There are either no subsequent symptoms or, at most, weakness and easy fatigue. There is a decrease in the white blood cell count (which is most marked in the case of lymphocytes) and in the platelet count. Less than 5 per cent (1 out of 20) require medical care. All others can perform their customary tasks. Any deaths that occur are caused by complications. Sickness of this type has been seen seen after brief, whole-body doses of gamma and X-radiation in the range of 50-200 R. An ERD of external gamma radiation of 50-200 R may have a similar effect.

Group II: More than half this group vomit soon after the onset of exposure and are sick for a few days. This is followed by a period of 1-3 weeks when there are few or no symptoms. During the latent period, typical changes occur in the blood count and can be used for diagnosis. At the end of the latent period, epilation (loss of hair) is seen in more than half, and this is followed by a moderately severe illness due primarily to the damage to the blood-forming organs. Most of the people in this group require medical care. More than half will survive, with the chances of survival being better for those who received the smaller doses. Sickness of this type has been seen after brief, whole-body doses of gamma or X-radiation on the order of 200-450 R. An ERD of external gamma radiation of the same size will probably cause a similar illness.

Group III: This is a more serious version of the sickness described as Group II. The initial period of illness is longer, the latent period is shorter, and the main episode of illness is characterized by extensive hemorrhages and complicating infections. People in this group need medical care and hospitalization. Less than half will survive, with the chances of survival being poorest for those who received the largest doses. Sickness of this type has been seen after brief whole-body gamma radiation with doses in excess of 450 R. It is possible that an ERD of external gamma radiation of the same size will have a similar effect.

TABLE 1
(continued)

Group IV: This is an accelerated version of the sickness described as Group III. All in this group begin to vomit soon after the onset of exposure, and this continues for several days or until death. Damage to the gastrointestinal tract predominates, manifested by intractable diarrhea, which soon becomes bloody. Changes in the blood count occur early, and within a few days the total white cell count may be less than 500 per mm. Death occurs before the end of the second week, and usually before the appearance of hemmorrhages or epilation. All in this group need care, and it is unlikely that many will survive. Sickness of this type has been seen after brief, whole-body exposure to gamma radiation in excess of 600 R. During protracted exposure to external gamma radiation, it is not probable that an illness of this type would be the first evidence of injury.

Group V: This is an extremely severe illness in which damage to the brain and nervous system predominates. Symptoms, signs, and rapid prostration come on almost as soon as the dose has been received. Death occurs within a few hours or a few days. Sickness of this type has been seen after a brief whole-body exposure to gamma rays in excess of several thousand R and to equivalent doses from neutrons. Cardiac failure may well play a role in the changes observed in this category.

TABLE 2

CLINICAL STAGES OF THE ACUTE RADIATION SYNDROME

	approximate duration
1. Initial or prodromal stage	0 to 48 hours.
2. Latent stage	2 to 3 weeks.
3. Manifest illness stage	2d or 3d to 6th week.
4. Recovery stage	8 to 15 weeks.

TABLE 3

LABORATORY AND CLINICAL OBSERVATIONS

(Single Short-Term Exposure)

Degree of Injury	Nausea	Vomiting	Diarrhea	Fever	Lymphocytes (per mm^3 at 48 hrs. or later)	Total Leukocytes (per mm^3)
Patient Group I	±	±	0	0	not lower than 800	minimal change
Patient Group II	++	++	±	±	not lower than 400	Neutrophils variable on days 1 and 2; decreased to ~ 3000 by days 5-10.
Patient Group III	+++	+++	± to +	+	not lower than 200	Transient rise in neutrophils and total WBC count within few hrs followed by precipitous drop to ~ $1000/mm^3$ at 10 days.
Patient Group IV*	++++	++++	++++	++++	< 200	Greater neutrophil and WBC increase, then a fall to $<1000/mm^3$ in less than 1 week.

*The severaly injured patients in Patient Group IV would have an extremely poor prognosis and therapy other than that for relief of symptoms would not be indicated.

TABLE 4

FACTORS MODIFYING RESPONSE TO RADIATION

1. Location of subject, degree of shielding, exposure, kind of shielding, immediate subsequent action.
2. Evidence of other injury.
3. Prior or concurrent disease.
4. Prior and subsequent physical activity.

TABLE 5

SYMPTOMS AND SIGNS FOUND IN PRODROMAL STAGE

OF ACUTE RADIATION SYNDROME

Anorexia	Prostration
Nausea	Diarrhea
Vomiting	Abdominal pain
Weakness & fatigue	
Conjunctivitis	Sweating
Erythema	Oliguria
Fever	
Hyperesthesia	Paresthesia
Ataxia	Coma
Disorientation	Death
Shock	

TABLE 6

SYMPTOMS AND SIGNS FOUND IN MANIFEST ILLNESS

STAGE OF ACUTE RADIATION SYNDROME

Anorexia	Sweating
Nausea	Oliguria
Vomiting	Weakness & fatigue
Diarrhea	Prostration
Abdominal pain	Weight loss
Abdominal distention	Hyperesthesia
Conjunctivitis	Paresthesia
Erythema	Ataxia
Jaundice	Disorientation
Fever	Shock
Infection	Epilation
Purpura	Coma
Hemorrhage	Death
Scalp pain	

Table 7

Recommended Diagnostic Procedures for Clinical Management of Radiation Injury

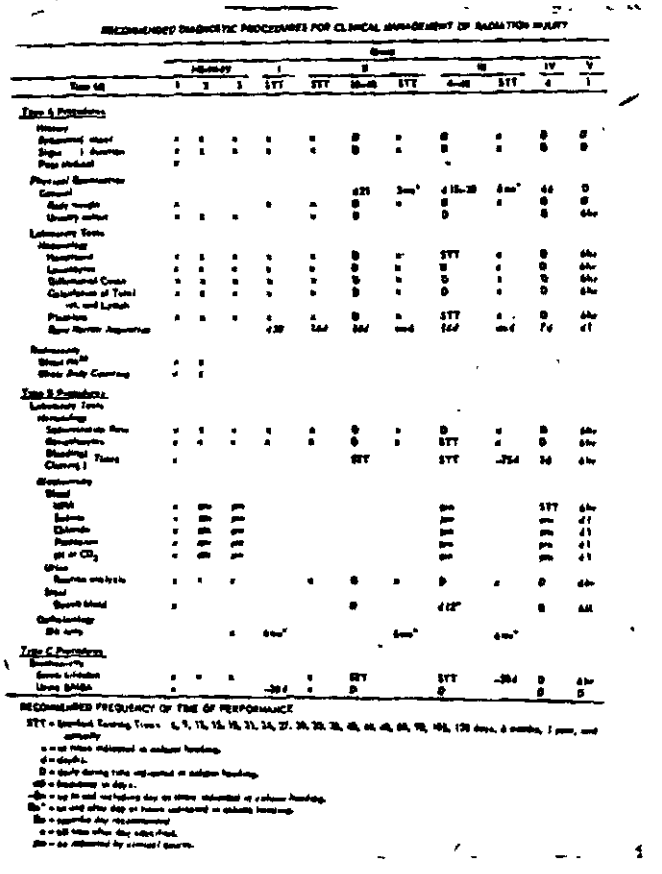

Figure 1 (a) and (b)

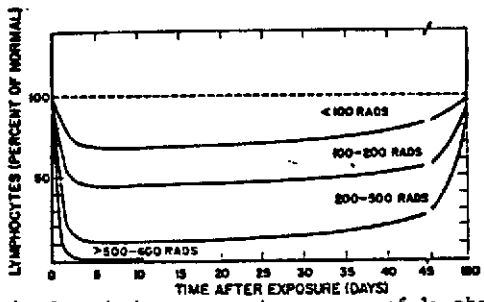

Figure 1(a) Smoothed average time-course of lymphocyte changes in human cases from accidental radiation exposure as a function of dose.

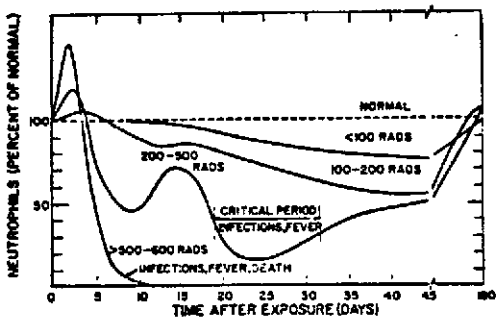

Figure 1(b) Smoothed average time-course of neutrophil changes in human cases from accidental radiation exposure as a function of dose.

Figure 2. Schematic relationships between lymphocyte levels and dose

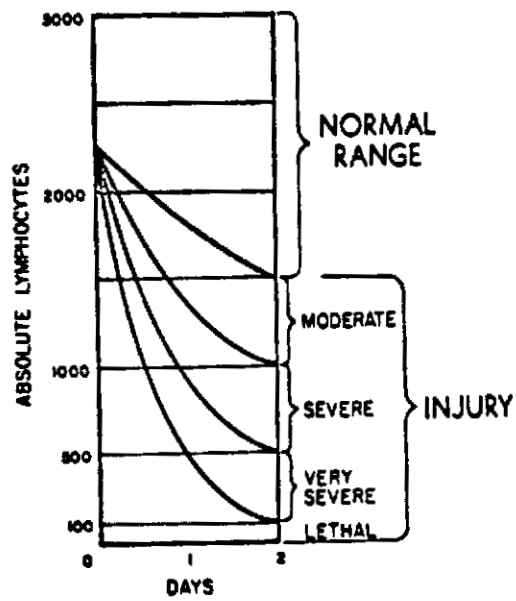

Figure 3. Preliminary Evaluation of Clinical Radiation Injury Following Overexposure.