Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Military Medicine

Guidelines for medical management of nuclear/radiation emergencies

Lt Gen Velu Nair, PVSM, AVSM, VSM** (Retd)^{a,1,2,3,*}, Brig D.N. Karan^b,
Lt Col C.S. Makhani^c

^a Former Director General Medical Services (Army), Integrated Headquarters, Ministry of Defence, New Delhi 110001

^b Deputy Director General Medical Services (Information Technology), O/o Directorate General of Medical Services (Army), Integrated Headquarters, Ministry of Defence, New Delhi, India

^c Officer In Charge, Army Medical Research Cell, O/o Directorate General of Medical Services (Army), Integrated Headquarters, Ministry of Defence, New Delhi, India

ARTICLE INFO

Article history:

Received 21 September 2017

Accepted 26 September 2017

Available online 15 November 2017

Keywords:

Nuclear accident

Radiation accident

Acute Radiation Syndrome

Colony Stimulating Factors

Dosimetry

Haematopoietic stem cell transplant

ABSTRACT

Management of victim of radiation injury poses a wide spectrum of challenges to the health care provider starting with the evaluation of the damage, the kind of hospitalization and treatment and the regular monitoring of the patient. Undesirable clinical outcomes are probable if prodromal stage evolves rapidly and is severe.

Critical systems like neurovascular, gastrointestinal, haematopoietic and cutaneous are afflicted in Acute Radiation Syndrome. Three main elements which are essential for assessment of prognosis and selection of treatment are vomiting onset time, kinetics of depletion of lymphocyte, and chromosome abnormalities. Larger incidents warrant, a well-structured national response system. Health care institutions must develop protocols to respond to radiation exposure related emergencies in tandem with the local response teams. Multidisciplinary approach between clinical specialists, nursing staff and psychological experts is of critical significance. External decontamination, estimation of dose and fluid and electrolyte replacements form part of support therapy. Reverse isolation, antacids, H₂ blockers, use of reverse barrier nursing and prophylactic antimicrobials are part of the treatment plan. Patients with severe bone marrow damage will require blood products support. Increased recovery of neutrophils in radiation accident victims is the rationale for the use of Colony Stimulating Factors.

New directions are under evaluation which includes novel cytokine therapies like interleukin-7, keratinocyte growth factor, and thrombopoietin or its analogues. The final decision regarding allogenic haematopoietic stem cell transplant should be considered after

* Corresponding author.

E-mail address: nairvelu2000@yahoo.com (V. Nair).

¹ The author is a member of drafting committee for guidelines for medical management of nuclear/radiation emergencies for Asia-Pacific Blood and Marrow Transplantation (APBMT).

² The author successfully led the group of doctors from the Army Hospital Research and Referral who managed the Mayapuri victims on radiation exposure in 2010, admitted to Army Hospital Research and Referral, Delhi Cantt.

³ Present address 632, C-1, Ansals Palam Vihar, Carterpuri, Gurgaon 122017, Haryana, India

<http://dx.doi.org/10.1016/j.mjafi.2017.09.015>

0377-1237/© 2017 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

considering the irradiation source, particularity of the situations or circumstances, associated injuries and disease.

© 2017 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

Introduction

Since the time nuclear energy has been harnessed and was put to use in industry, medicine, scientific research, military and numerous other fields, undesirable radiation incidents or accidents of variable scales have time and again overshadowed the benefits reaped from it by the mankind.¹ Human exposure to nuclear radiations due to accidents, sabotage and terrorism are a reality and leave in their wake perplexing challenges to competent but relatively unprepared healthcare providers.^{2,3}

The primary principles and objectives of response to nuclear/radiological emergencies includes mitigation of accidents at the site of occurrence and of individual health hazards, rendering primary first aid and imparting injury treatment, reduction of chances of delayed outcomes in the general population, protection of environment and addressing to their psychological impact. On the basis of severity of the nuclear/radiological events and their effects, necessary response should be mobilized without any delay through a trained and equipped team.⁴

Each radiation accident may lead to an acute emergency. Assessment for ionizing radiation exposure and the extent to which the patient is afflicted with radiation induced damage is to be done immediately. This is important to arrive at the provisional diagnosis, and to decide the requirement of hospitalization, type of hospital facility and super-specialty care imperative in the case. The following primary aspects are required to be deliberated for patient care in accidents due to radiation:

- (a) Assessment of damage and its extent
- (b) Choosing the type of healthcare facility
- (c) Providing suitable medical care
- (d) Prognosis assessment

Clinical manifestation of Acute Radiation Syndrome

Prodromal signs and symptoms develop within 1–72 hrs of an individual exposed to a dose of 10–20 Gy or more, which include fever, loss of appetite, nausea and vomiting, loose motions, fluid and electrolyte derangement. These may gradually lead to hypotension, loss of consciousness, damage to other organ systems and finally result in death within a few days. A severe and rapid prodromal phase predicts a poor clinical prognosis. It is difficult to ascertain the prognosis from prodromal response if the exposure is less than 2–10 Gy. Subsequent to the prodromal phase occurs the illness targeting various organ systems. The critically important organ systems primarily

affected in Acute Radiation Syndrome are hematopoietic, cutaneous, gastrointestinal and the neurovascular.

Neurovascular Syndrome

Focal transient aberration of the nervous system results from low dose exposure to radiation. Impairment of capillary circulation, acute inflammation, interstitial edema, petechial hemorrhages and meningitis are some of the transient changes. EEGs may show paroxysmal spike and wave discharges and CT scans head and MRIs may show the presence of edema.⁵

Gastrointestinal Syndrome

Doses between 05 and 12 Gy may lead to mild gastrointestinal symptoms like mild diarrhea, abdominal pain and electrolyte imbalance. However, the recovery is almost certain. Extensive damage to the gastrointestinal tract may lead to ulceration and necrosis of the bowel and severe complications like stenosis, ileus, and perforation.

Cutaneous Syndrome

Moist desquamation and erythema of the skin may occur within 1–2 days after early exposure, however the complete manifestations may take years. Such lesions can present simultaneously in various parts of the body, subject to the extent of exposure. The commonly seen signs and symptoms are pruritus, blisters, and bullae, ulceration of skin, subcutaneous tissue, muscle or bone. Blister and bullae associated with or without necrosis generally appear 1–3 weeks after exposure of more than 3 Gy.

It is imperative to grade the severity of involvement of various systems at the earliest after exposure to significant radiation for planning future management strategies. A comprehensive grading system incorporating all above mentioned syndromes has been summarized in Table 1 for the treating teams.⁶

Haematopoietic Syndrome

Clinical manifestations of Haematopoietic Syndrome (HS) may be seen primarily in patients having significant radiation exposure (more than 2 Gy) due to radiation induced damage of the haematopoietic tissue of the bone marrow. Significant radiation exposure leads to aplasia or hypoplasia which may lead to peripheral blood cytopenias. Mild cytopenias without significant bone marrow damage are induced at lower doses of less than 2 Gy radiations, while complete myeloablation without any chance of autologous recovery results from very high dose of more than 10 Gy. The severity of hematotoxicity can be graded from degree 1 to degree 4 based on the

Table 1 – Grading system to guide evaluation of Neurovascular, Gastrointestinal and cutaneous systems.⁶

Symptom	1st Degree	2nd Degree	3rd Degree	4th Degree
Neurovascular system				
Nausea	Mild	Moderate	Severe	Extremely severe
Vomiting	1/day, occasional	2–5/day, intermittent	6–10/day, persistent	More than 10/day, refractory
Anorexia	Able to eat	Decreased intake	Intake minimal	Require parenteral nutrition
Fatigue	Nil	Work impaired	Needs assistance for ADLs	Nil ADLs ^a
Fever	Less than 38 °C	38–40 °C	More than 40 °C and less than 24 h	More than 40 °C and more than 24 h
Headache	Mild	Moderate	Intense	Extremely severe
Hypotension	HR more than 100/BP more than 100/170 mm Hg	BP less than 100/70 mm Hg	BP less than 90/60 mm Hg and transient	BP less than 80/? Mm Hg and persistent
Neurological deficits	Difficult to detect	Detected easily	Neurological impairment prominent	Life threatening deficit
Cognitive deficits	Mild loss	Moderate loss	Severe impairment	Impairment complete
Gastrointestinal system				
Diarrhea				
Frequency	2–3 stools/day	4–6 stools/day	7–9 stools/day	More than 10 stools/day
Consistency	Bulky	Loose	Persistent	Watery
Bleeding	Occult	Intermittent	Loose	Persistent with large amount
Abdominal pain	Mild	Moderate	Intense	Severe
Cutaneous system				
Erythema	Mild and transient	Moderate, less than 10% of BSA ^b	Marked; 10–40% of BSA ^b	Severe; more than 40% of BSA ^b
Sensation/itching	Pruritus	Slight with intermittent pain	Moderate with continuous pain	Severe with continuous pain
Swelling/edema	Present but asymptomatic	Symptomatic	Mild dysfunction	Total dysfunction
Blistering	Rare	Rare	Bullae with sterile fluid	Bullae with hemorrhage
Desquamation	Absent	Dry and patchy	Moist patchy	Moist and confluent
Ulcer/necrosis	Epidermal are only	Dermal	Subcutaneous	Muscle or/and bone involvement
Hair loss	Thinning	Visible and patchy	Complete but reversible	Complete but irreversible
Onycholysis	Nil	Mild	Mild	Complete

Note: Adapted from: Flidner T.M., Friesecke I., Beyrer K., British Institute of Radiology, editors. Medical management of radiation accident—manual on the Acute Radiation Syndrome (METREPOL European Commission concerted action) British Institute of Radiology; Oxford: 2001. p. 1–66; compendium p. C1–C21. Table no. Nil, Neurovascular system; p C3; Table No. Nil, Haematopoietic system; P C4; Table No. Nil, Cutaneous system; p C4; Gastrointestinal system; p C5.

^a ADLs: activities of daily living.

^b BSA: body surface area.

Table 2 – Severity of hematotoxicity following radiation exposure according to blood counts.⁶

Blood counts/symptoms	Degree 1	Degree 2	Degree 3	Degree 4
ALC ^a	More than or equal to $1.5 \times 10^9/L$	$1-1.5 \times 10^9/L$	$0.5-1 \times 10^9/L$	Less than $0.5 \times 10^9/L$
ANC ^b	More than or equal to $2.0 \times 10^9/L$	$1-2.0 \times 10^9/L$	$0.5-1 \times 10^9/L$	Less than $0.5 \times 10^9/L$
Platelet counts	More than or equal to $100 \times 10^9/L$	$50-100 \times 10^9/L$	$20-50 \times 10^9/L$	Less than $20 \times 10^9/L$
Hb ^c	Normal Hb	Less than 10% decrease in Hb	10–20% decrease in Hb	More than 20% decrease in Hb
Infection	Localized and no requirement of antibiotics	Localized and requirement of only local antibiotics	Systemic and requirement of oral antibiotics only	Sepsis may set in and requirement of IV ^d antibiotics

^a ALC absolute lymphocyte count.

^b ANC absolute neutrophil count.

^c Hb Hemoglobin.

^d IV Intravenous.

Note: Adapted from: Flidner T.M., Friesecke I., Beyrer K., British Institute of Radiology, editors. Medical management of radiation accident—manual on the Acute Radiation Syndrome (METREPOL European Commission concerted action) British Institute of Radiology; Oxford: 2001. p. 1–66; compendium p. C1–C21. Table No. Nil, Haematopoietic system; P C4.

Table 3 – Overall prognosis of the Haematopoietic syndrome on the basis of the degree of severity.⁶

Grading	Degree of damage	Extent of involvement	Prognosis
H1	1st Degree	Mild damage	Autologous recovery without critical phase
H2	2nd Degree	Moderate damage	Autologous recovery with low risk critical phase
H3	3rd Degree	Severe damage	Autologous recovery with high risk critical phase
H4	4th Degree	Damage fatal	Autologous recovery unlikely

Adapted from: Flidner T.M., Friessecke I., Beyrer K., British Institute of Radiology, editors. Medical management of radiation accident—manual on the Acute Radiation Syndrome (METREPOL European Commission concerted action) British Institute of Radiology; Oxford: 2001. p. 1–66. Table No. 6, Overall prognostic aspects of the HS on the basis of the clinical grading (critical phase = duration with constant cell counts below the normal range, resulting in high or low risk groups for developing clinical symptoms such as bleeding and infectious diseases owing to differences in the absolute cell counts); p 21.

Table 4 – Selected methods for estimating radiation dose.⁷

Dosimetry	Method	Utility
Biological	Whole-body counting Chromosomal aberrations (dicentric, ring forms) Lymphocyte depletion kinetics	Generally not available The “gold standard.” Requires 4–5 days of processing time. Not expensive but requires 2–4 days for decline at doses of 4–6 Gy and 4–6 days at 2–4 Gy Under development
Clinical	Interphase aberrations Symptoms and signs	Practical but sensitivity is lost at low doses.

Adapted from: Dainiak N, Waselenko JK, Armitage JO, MacVittie TJ, Farese AM. The Hematologist and Radiation Casualties. Hematology 2003 2003;473–496; doi:10.1182/asheducation-2003.1.473. available from <http://asheducationbook.hematologylibrary.org/content/2003/1/473.full.pdf+html>. Table No. 3. Selected methods for estimating radiation dose. p 478.

polymorphonuclear leucocytosis level, lymphocytic, platelet count, and the associated blood loss or infection as elaborated in Table 2.⁶ The management depends on severity of involvement of hematological toxicity.

Based on above mentioned severity of hematotoxicity grading of HS can be done from H1 to H4 for initial risk stratification and prognostication as shown in Table 3.⁶

Laboratory evaluation

A fall in absolute lymphocyte count is a practical and reliable approach for early assessment based on the radiation exposure dose. Three main elements which are essential for assessment of prognosis and selection of treatment are time required for onset of vomiting, depletion of lymphocytes and its kinetics, and chromosomal changes. Few approved methods for estimating radiation exposure have been summarized in Table 4.⁶

Triage

Majority of casualties may not require immediate medical attention and the “well and worried” might form a large number. The concerned department shall be made responsible for limiting further damage, decontamination, protection of general public, and disposal of radioactive material. In addition to a hematologist, a trauma specialist, burns specialist, neurologist and dermatologist may be made available. Detailed clinical assessment should be done at the earliest on receiving the patient. Health care institutions should develop protocols which are in tandem with the local resources and health care teams.⁶ Bigger incidents warrant a national response system to be in place.

Emergency medical teams: role and responsibility

Subsequent to triage, victims of radiation exposure should be immediately moved to the nearest appropriate health care facility where a preliminary evaluation and treatment can be started.

Overlapping roles of various specialists will be instrumental in management of each patient. A well-structured and coordinated care by various specialties supported by good nursing care for inpatients, especially those admitted in ICU will be the bedrock for successful outcomes. To overcome the detrimental effects on the psychology of the patients and their relatives, the role of Psychiatrists and Social workers cannot be negated.⁶

The European protocol METREPOL (Medical Treatment Protocols for radiation accident victims) assigns clinical and routine laboratory finding based scoring, as given in Table 5.⁵

Based on the signs and symptoms severity each patient is given a “response category”.

Supportive therapy

The following are the indispensable components of the support therapy:

- Dose estimation
- Psychological support
- Fluid and electrolyte estimation

If a patient has had a complete body dose of more than 2–3 Gy, reverse isolation, antacids and H2 blockers are given. If

Table 5 – Primary scoring based on METREPOL during first 48 h.⁸

	Score 1	Score 2	Score 3
Average delay before symptoms appear	Less than 12 h	Less than 5 h	Less than 30 min
Cutaneous erythema	Nil	+/-	+++ before 3 h
Asthenia	+	++	+++
Nausea	+	+++	++++
Vomiting per 24 h	Maximum 1	1–10	Above 10; and intractable
Diarrhea/number of stools per 24 h	Maximum 2–3; bulky	2–9; soft	Above 10; watery
Abdominal pain	Minimal	Intense	Excruciating
Headache	Nil	++	Excruciating; signs of raised Intracranial Pressure
Temperature	Below 38 °C	38–40 °C	Above 40 °C
Blood pressure	Normal	Normal; possible temporary decrease	Systolic below 80
Temporary loss of consciousness	Nil	Nil	+/coma
Depletion of blood lymphocytes			
At 24 h	Above 1500/mcl	Below 1500/mcl	Below 500/mcl
At 48 h	Above 1500/mcl	Below 1500/mcl	Below 100/mcl
	Outpatient monitoring	Hospitalization for curative treatment	Hospitalization multi-organ

Adapted from: Akashi et al. Therapeutical management according to the European consensus conference. European approach for the medical management of mass radiation exposure. Available from <https://sremc.files.wordpress.com/2012/11/ebmt-nac-pocket-guide2.pdf>.

severe Granulocytopenia is observed, reverse barrier nursing, prophylactic antimicrobials should be given. Blood component products are introduced if patient has severe bone marrow damage.⁶

Specific therapeutic approaches

Colony Stimulating Factor (CSF)

Haematopoietic CSFs like Granulocyte Colony Stimulating Factor (G-CSF), Pegylated Granulocyte Colony Stimulating Factor (PEG-G-CSF or Pegfilgrastim), Recombinant Granulocyte Macrophage Colony Stimulating Factor (GM-CSF), Erythropoietin (EPO), Thrombopoietin analogs and Thrombopoietin receptor agonists like Eltrombopag are available.

CSFs facilitate neutrophil recovery in radiation induced bone-marrow suppression as they promote multiplication and differentiation of granulocyte progenitors for generation of neutrophils. Newer modalities being evaluated are novel cytokine therapies like interleukin-7 and keratinocyte growth factor.⁶

Allogenic haematopoietic stem cell transplant (HSCT)

For patients with severe bone marrow aplasia HSCT is lifesaving, however the approach is complicated by concomitant burns and traumatic injuries. Generally, the approach should be that a sample for HLA typing is taken initially, followed by a potential donor search, however transplant is undertaken not before the minimal observation period of 14–21 days is elapsed. HSCT is undertaken only after considering the factors like irradiation source, patient specific issues, any additional injuries and previous diseases.⁶

Conclusion

Nuclear and radiation accidents are a reality in the present world. Multi organ system pathology is generally the outcome of radiation exposure. The management of victims of these accidents is challenging and needs to be undertaken with meticulous assessment of the various factors. Awareness of these medical challenges is the need of the hour and a structured organizational approach will deliver desirable outcomes.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Coeytaux K, Bey E, Christensen D, Glassman ES, Murdock B, Doucet C. Reported radiation overexposure accidents worldwide, 1980–2013: a systematic review. Carpenter DO, ed. PLOS ONE. 2015;10(3):e0118709. <http://dx.doi.org/10.1371/journal.pone.0118709>.
2. Bagla P. Radiation accident a 'wake-up call' for India's scientific community. *Science*. 2010;328(5979):679.
3. LiVolsi V, Abrosimov A, Bogdanova T. The Chernobyl thyroid cancer experience: pathology. *Clin Oncol*. 2011;23:261–267.
4. National Disaster Management Guidelines—Management of Nuclear and Radiological Emergencies. New Delhi: National Disaster Management Authority (IN); February; 2009. 170 pp. Available from <http://nidm.gov.in/pdf/guidelines/new/managementofnuclearradiologicalemergencies.pdf>.

5. Gorin NC, Fliedner TM, Gourmelon P, et al. Consensus conference on European preparedness for haematological and other medical management of mass radiation accidents. *Ann Hematol.* 2006;85:671–679.
6. Fliedner TM, Friesecke I, Beyrer K, British Institute of Radiology, eds. *Medical Management of Radiation Accident—Manual on the Acute Radiation Syndrome (METREPOL European Commission concerted action)*. Oxford: British Institute of Radiology; 2001:1–66. compendium p. C1–C21.
7. Dainiak N, Waselenko JK, Armitage JO, MacVittie TJ, Farese AM. The hematologist and radiation casualties. *Hematology.* 2003;2003(1):473–496.
8. Akshi M, Allenet-Le Page B, Blaise D, et al. *Therapeutical Management According to the European Consensus Conference. European Approach for the Medical Management of Mass Radiation Exposure.* 2007. Available from <https://sremc.files.wordpress.com/2012/11/ebmt-nac-pocket-guide2.pdf>.