GUIDELINES FOR MEDICAL MANAGEMENT OF NUCLEAR/RADIATION EMERGENCIES

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On behalf of the APBMT NAM Committee

PREFACE

Nuclear energy is a boon which has revolutionized and impacted multiple facets of human life on and beyond this planet. Be it fulfilling the ever-increasing requirement of electrical energy for domestic to industrial use, to research, large scale irradiation, space exploration etc, nuclear power has been a never depleting, efficient, clean source of energy.

However, the technology has had its share of limitations, which have marred its illustrious history and left in its wake a deluge of destruction and mayhem. Though concerted efforts at national and international level are being undertaken to mitigate any ill effects as a result of Nuclear / Radiation accidents, still there is a long way to go.

Nuclear Accident Management (NAM) Committee, of Asia Pacific Blood and Marrow Transplantation (APBMT) Group is in the forefront with other international agencies in providing the desirable expertise and technical inputs suitable to various echelons of medical care and expertise i.e. from the grassroot level to the tertiary care referral health care institutions.

The present guidelines are in continuation with the relentless efforts of NAM in providing the much-needed inputs to the first responders, the Emergency Medical Personnel and Hospital staff who will be required to respond to a nuclear/ radiation emergency situation.

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INTRODUCTION

1. Use of radioactive material has various industrial, medical, military and miscellaneous applications. Possibility of exposure due to accident, act of terrorism cannot be negated. Potential situations in which a radiation emergency can take place are due to exposure to (a) Radiological Exposure Device, (b) Radiological Dispersal Device (Dirty bomb), (c) Food chain contamination, (d) Subversive activity on Nuclear plant or transportation and (e) Improvised Nuclear Device. The detailed tabulation of common radiation sources and their exposure outcomes is given at ***Table 1***.

Group	Facility/source	Potential external exposure	Potential contamination (internal/external)	Both conditions (external exposure and contamination
I	Critical Assembly	Yes	Yes	Yes
	Reactor	Yes	Yes	Yes
	Fuel element manufacture	Yes	Yes	Yes
	Radiopharmaceutical manufacture	Yes	Yes	Yes
	Fuel reprocessing plant	Yes	Yes	Yes
II	Radiation device			
	Particle accelerator	Yes		
	X-ray generator	Yes	No	No
III	Sealed Source (Intact)	Yes	No	No
	Sealed Source (Leaking)	Yes	Yes	Yes
IV	Nuclear medicine laboratory	Yes	Yes	Yes
	In vitro assay laboratory	Yes	Yes	Yes
V	Source transportation	Yes	Yes	Yes
VI	Radioactive waste	Yes	Yes	Yes

Table 1. Exposure Outcomes of Common Radiation Sources.
(Reprinted from: International Atomic Energy Agency, Vienna. Medical Management of Radiation Injuries. International Atomic Energy Agency (IAEA), Vienna; 2020. Safety Reports Series No. 101. https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1891_web.pdf. Accessed 31 Oct 2020.)

2. The primary principles and objectives of response to nuclear/radiological emergencies includes mitigation of accidents at the site of occurrence, prevention of

health effects in individuals, rendering first aid and treatment of injuries, reduction of chances of stochastic effects in the general population, addressing the psychological impact and protection of the environment and property, within the constraints of available resources. Depending on the severity of the nuclear/radiological emergencies and their consequences, the required response should be mobilised without any delay through a well-informed, trained, and well-equipped force as per the International Nuclear Event Scale (INES) evolved by IAEA.

3. Radioactive exposure causes external and internal irradiation along with conventional injuries or comorbidities in general populace. It is known that some tissues and organs in the body such as bone marrow and gonads are more radiation sensitive and susceptible to radiation injury. The skin and gastrointestinal (GI) tract are more likely to be affected from external and internal contamination respectively. Young adults and children have a higher risk of developing radiation induced cancer following exposure. Those exposed to sudden high radiation levels may develop Acute Radiation Sickness (ARS).

4. Radiation accident may lead to an acute emergency necessitating initiation of a specific sequence of steps. It is important to assess quickly for exposure to ionising radiation and the extent of radiation related damage in the patient. This is necessary to arrive at the first provisional diagnosis, and to decide whether hospitalization is required or not and the type of health care facility and super-specialty care which will be necessary. Accordingly, for management of a patient in a radiation accident, four cardinal issues are required to be considered: -

(a) Assessment of the severity of damage
(b) Decision on the kind of hospitalization
(c) Provision of appropriate therapeutic interventions
(d) Evaluation of the patient’s prognosis

5. Nuclear/Radiological incidences, accidental or deliberate can result in detrimental effect on the human body due to blast wave injuries, thermal pulse, ophthalmic injuries, radiation injuries and fallout effects. In nuclear detonation the effects will be variable depending upon the zone where the victim is present, be it the Light Damage (LD) zone, Moderate Damage (MD) zone and Severe Damage (SD) zone. It is essential for medical personnel to understand the spectrum of radiation exposure for effective management of a casualty who has radiation-related injuries. This can be broadly classified into irradiation and contamination (***Table 2.***). Contamination in turn can be further categorized into internal and external. Radiation exposure of a casualty can occur from either of the following.

(a) Direct exposure to source or radioactive substance released thereof
(b) Airborne material (volatiles, aerosols, particulates) inhalation
(c) Radiation from ground or surface deposition
(d) Skin and clothing contamination

Area of Application	Source, radionuclide	Potential exposure during radiation accident	Example
Industry			
(a) Sterilization	Co-60, Cs- 137	Whole body or Local Exposure	Nesvish, Belarus (1991)
(b) Radiography	Ir-192, Cs-137	Whole body or Local Exposure	Yanango, Peru (1999)
Medicine			
(a) Diagnostics	X-ray generators	Local Exposure	Los Angeles, USA (2008-09)
(b) Therapy	Co-60, Cs-137 and accelerators	Whole body or Local Exposure	San Jose, Costa Rica (1996)
Research	Broad spectrum of sources, including reactors	Whole body or Local Exposure	Sarov, Russian Federation (1997)
Orphan sources	Co-60, Cs-137 and others	Whole body or Local Exposure, Internal and external contamination (if unsealed)	Goiania, Brazil (1987)
Nuclear reactors	Cs-137, Sr-90, I-131	Whole body, Internal and external contamination	Chernobyl (1986)

Table 2. Radiological and Nuclear Accidents Resulting in Radiation Injury.
(Reprinted from: International Atomic Energy Agency, Vienna. Medical Management of Radiation Injuries. International Atomic Energy Agency (IAEA), Vienna; 2020. Safety Reports Series No. 101. https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1891_web.pdf. Accessed 31 Oct 2020.)

6. A casualty can have a combination of the above and in addition also have traumatic injury and burn related injuries. The prognosis for patients with mixed injuries is worse compared to casualties who have only radiation-related injuries. It is imperative that treatment of life-threatening concomitant medical condition must be addressed prior to assessment and management of radiation exposure. The priority of management of casualties would be resuscitation followed by external decontamination and then specific management of irradiation and internal contamination. A flow chart showing the different phases (triage, diagnosis and therapy) in the management of radiation accident victims is depicted in ***Figure 1.***

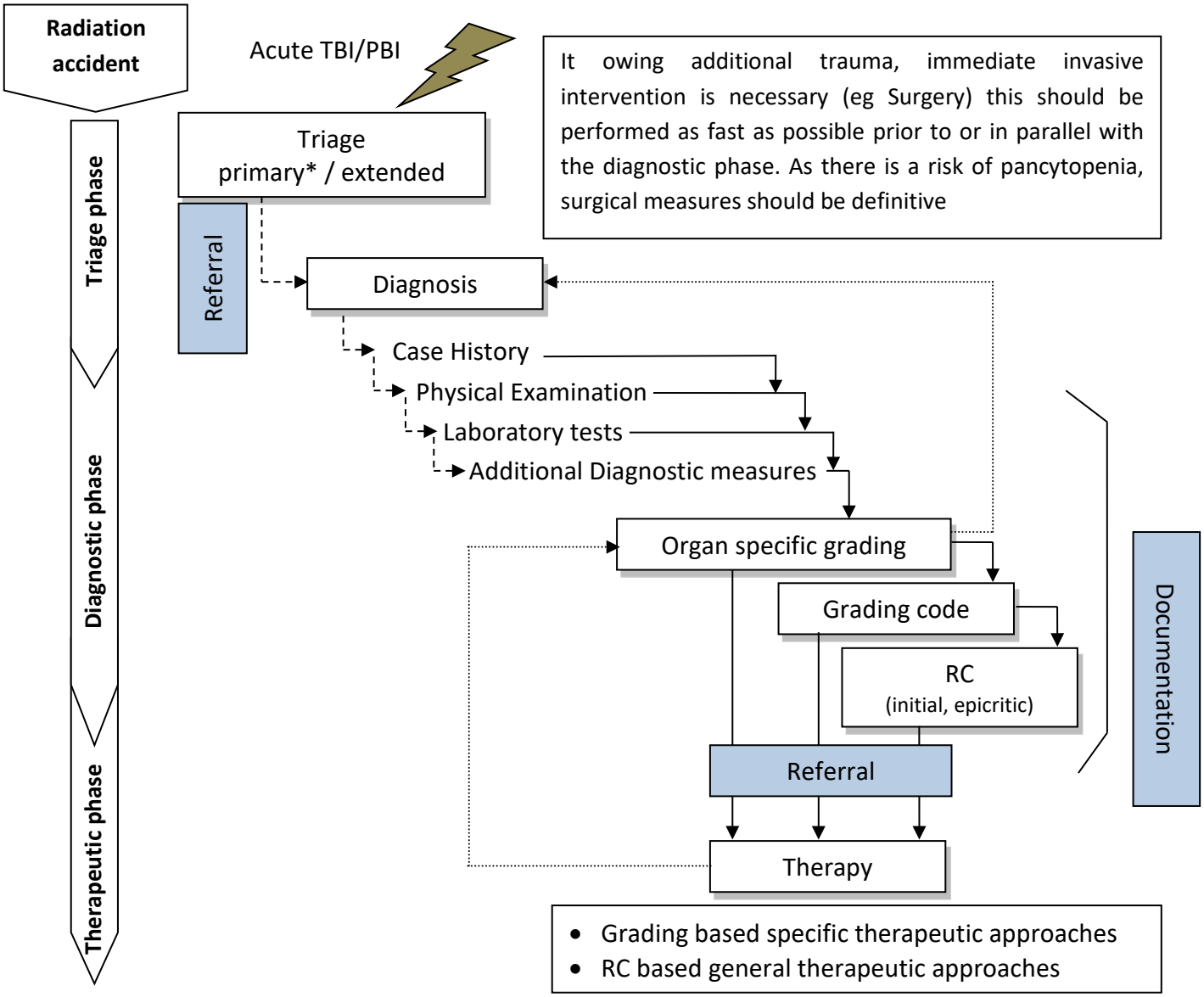

Figure 1. Flow Chart for Medical Management of Radiation Accidents. (Triage, diagnostic and therapeutic phases can be distinguished. These are connected by workflow, information flow and feedback of information). (Source: Medical Management of Radiation Accidents: Management of the Acute Radiation Syndrome – A publication of The British Institute of Radiology- © 2001. Edited by T M Fliedner, I Friesecke and K Beyrer)

CHAPTER 2

History

Chapter- 2

HISTORY

7. Nuclear science has come of age since the time Martin Klaproth discovered Uranium in 1789. Some important milestones in the evolution of nuclear science are as under:

Year	Milestone
1895	Wilhelm Rontgen discovered Ionising Radiation
1896	Henri Becquerel discovered effects of Pitchblende on photographic plate
1896	Pierre and Marie Curie coined the term Radioactivity
1911	Frederick Soddy discovered Isotopes
1932	Cockcroft and Walton discovered Nuclear changes as a result of accelerated protons bombarding atoms
1932	James Chadwick discovered Neutron
1938	Otto Hahn and Fritz Strassmann demonstrated Atomic Fission
1939	Otto Robert Frisch experimentally confirmed energy release of 200 million electron volts during Atomic Fission
1939	Francis Perrin coined the concept of Critical Mass
1939	Joseph Gilbert Hamilton, Mayo Soley and Robley Evans published the first paper on the diagnostic uses of iodine-131 in patients
1941	Saul Hertz and Arthur Roberts used first targeted radionuclide therapy for treatment of hyperthyroidism
1942	Manhattan Project was initiated
1945	Successful testing of the first atomic device in New Mexico
1945	06 Aug 1945, U-235 device dropped in Hiroshima, Japan
1945	09 Aug 1945, Pu-239 device dropped on Nagasaki, Japan
1946	Clinton Laboratories (Oak Ridge National Laboratory) delivered Carbon-14 radioisotope to Barnard Free Skin and Cancer Hospital, St Louis,
1946	Samuel M. Seidlin, Leo D. Marinelli and Eleanor Oshry successfully treated advanced thyroid cancer using I-131
1948	Commercial radioisotope distribution by Abbott Laboratories
1949	First Atomic Clock announced by National Bureau of Standards (NIST)
1950	Heart blood pool imaging using I-131 labelled human serum albumin by Crispell and Storaasli
1951	First Experimental Breeder Reactor (EBR-1) generated electricity at Idaho, USA
1951	US FDA approved first radiopharmceutical Sodium Iodine-131 for use in Thyroid Patients
1952	Nuclear Reactor at Clark River, Ontario had a nuclear accident
1954	Atom Mirny (AM-1) reactor of capacity 30 MWt operational at Obninsk, USSR
1954	*USS Nautilus ,* first Nuclear powered submarine commissioned
1957	IAEA is created
1957	Nuclear accident at Kyshtym, Urals
1958	Scintillation Camera invented by Hal Anger
1960	Yankee Rowe, the first commercial Pressurised Water Reactor operational

1960	Remote weather stations and Sea navigation buoys are powered by small nuclear power generators
1960	Health physicists are certified by the American Board of Health Physics
1961	Nuclear powered submarine USS Thresher (SSN-593) lost at sea with no survivors and submarine was never recovered
1961	First fatal US nuclear accident at SL-1 Stationary Low Power Reactor, Idaho Falls, Idaho.
1962	Emission Reconstruction Tomography later known as SPECT and PET was invented by David Kuhl
1963	Limited test ban treaty signed by USA and USSR prohibiting underwater, atmospheric and outer space nuclear tests
1964	Baltimore Light, Chesapeake Bay, Maryland is the first nuclear powered lighthouse
1965	SNAP-10A becomes the first nuclear reactor in space
1965	A nuclear weapon loaded aircraft with pilot falls off USS Ticonderoga and sinks into the North pacific near Japan never to be found
1968	Grave accident aboard the Soviet Nuclear Submarine K-27
1969	SNAP-27 nuclear generator deployed on lunar surface by Apollo -12
1971	Nuclear Medicine is recognized as a speciality by American Medical Association
1977	FDA approved New England Nuclear to distribute thallium-201 for Myocardial Perfusion and diagnosis and location of Myocardial Infarction
1979	Core meltdown at Three Mile Island Nuclear Power Plant, Harrisburg, Pennsylvania, USA
1982	Potassium Iodide approved by US FDA for thyroid protection against radiation
1984	US vessel USS Kitty Hawk and Soviet submarine carrying nuclear weapons collide
1985	Irradiation of pork to curb Trichinosis approved by FDA
1986	Chernobyl nuclear reactor accident
1990	Irradiation of packed fresh or frozen poultry for microbiological control approved by US FDA
1996	Radiotherapy accident in Costa Rica
1999	Tokaimura nuclear accident
2004	Mihama nuclear power plant accident
2010	Mayapuri radiological accident
2011	Fukushima I nuclear accident
2019	Nyonoksa radiation accident

Table 3. Significant Developments/Incidences in Radiation History.

CHAPTER 3

Important Terms/Definitions

IMPORTANT TERMS/ DEFINITIONS

8. Various Important terms and definitions generally covered in the guidelines and on the subject are given below

(a) **Alpha Particles**: charged particles emitted from heavy nuclei such as U, Pu, or Am. Alpha particles cannot travel far and are shielded by the dead layer of the skin or clothing. They are therefore a negligible external hazard but can be important if internalized. Absorption via the GI tract is usually of limited importance, but absorption from wounds can be medically significant.

(b) **Beta Particles**: electrons found in weapons fallout and emitted from isotopes such as tritium and strontium. Beta particles can travel a short distance in tissue. Large quantities deposited on the skin can damage the basal layer and cause radiation burns. Beta emitters also are important if internalized.

(c) **Bioassay**: Any procedure used to determine the nature, activity, location or retention of radionuclides in the body by direct (in vivo) measurement or by in vitro analysis of material excreted or otherwise removed from the body.

(d) **Bio dosimetry**: The use of a biological response as an indicator of radiation dose.

(e) **Biological Half-Life**: The time taken for the quantity of a material in a specified tissue, organ or region of the body (or any other specified biota) to halve as a result of biological processes.

(f) **Chelation:** Process of an organic or inorganic compound binding metal ions/radionuclide forming ‘chelates’ (complex ring-like structures) which is readily voided by kidneys, intestines etc. E.g., Diethylenetriamine-Pentaacetate (DTPA)

(g) **Contamination**: Radioactive substances on surfaces or within solids, liquids or gases (including the human body), where their presence, or the process giving rise to their presence, is unintended or undesirable.

(h) **Cytogenetic Bio dosimetry:** It is a widely accepted method for dose assessment following acute whole- or partial-body irradiation. The various methods of cytogenetic bio dosimetry are dicentric analysis, cytokinesis block micronucleus assay, premature chromosome condensation, electron paramagnetic resonance, and molecular markers in body fluids and tissues.

(i) **Decontamination**: Action taken to remove radionuclides from clothing and the external surfaces of the body, from rooms, building surfaces, equipment or other items.

(j) **Decorporation**: The action of the biological processes, facilitated by chemical or biological agents, by means of which incorporated radionuclides are removed from the human body. It is also described as a process of treatment for persons with internally deposited radionuclides that aims to reduce the internal dose of exposure and hence the risk of health effects. It can be accomplished by reducing absorption, preventing incorporation and internal deposition of radionuclides within organs, and promoting elimination or excretion of absorbed nuclides.

(k) **Deposition**: is the ingress of the radionuclide into the cells of its target organ or tissue (e.g., the thyroid for radioiodine) after uptake or the contact of radioactive materials with regions of the respiratory tract in the case of inhalation as an intake process.

(l) **Deterministic Effect**: A health effect of radiation for which, generally, a threshold level of dose exists above which the severity of the effect is greater for a higher dose. Such an effect is described as a 'severe deterministic effect' if it is fatal or life threatening or results in a permanent injury that reduces the quality of life.

(m) **Displacement**: A non-radioactive element competes for the uptake sites, displacing the attached radioisotope. E.g., Calcium gluconate for Radiostrontium in Bone, or Technetium-99m displaced by stable iodine.

(n) **Dose**: A measure of the energy deposited by radiation in a target.

(o) **Dose Assessment**: Assessment of the dose(s) to an individual or group of people.

(p) **Early Reacting Organ System**: Organ systems involved in the development of the Acute Radiation Syndrome (ARS), in particular the neurovascular system (NVS), the haematopoietic system (HS), the cutaneous system (CS) and the gastrointestinal system (GIS).

(q) **Excision:** Removal of contaminated tissue/foreign material by surgical exploration with assistance of a radiation safety professional using a wound probe under local or general anaesthesia.

(r) **Exposure**: The act or condition of being subject to irradiation. Exposure can be either external exposure (due to a source outside the body) or internal exposure (due to radioactive material within the body).

(s) **Gamma Rays**: photons emitted during a nuclear detonation, by fallout, and in many instances of nuclear decay. They are highly energetic and pass-through matter easily. Because of high penetrability, gamma radiation can result in whole-body exposure and damage to deep organs.

Gamma-emitting nuclides are medically important in external exposure and if internalized.

(t) **Grading**: Classification of the radiation induced damage for each of the early reacting organ systems on the basis of characteristic clinical symptoms and their degree of severity

(u) **Improvised Nuclear Device** (IND): device designed to produce a nuclear explosion, at full or partial yield. An IND exposes people to high-level external dose, trauma, inhalation of radioactive materials, particulate contamination, and ingestion of radioactive materials in the food chain.

(v) **Individual Monitoring**: Monitoring using measurements by equipment worn by individual workers, or measurements of quantities of radioactive material in or on their bodies.

(w) **Intake**: It is the radioactive material taken into the body by inhalation, ingestion, absorption through the skin, injection or via a wound.

(x) **Ion Exchange:** Radioactive caesium recycles from the blood into the gut; therefore, ferric hexacyanoferrate, known as Prussian Blue, is useful to capture recycling caesium through an ion exchange mechanism even a long time after contamination has occurred. Prussian Blue was extensively and successfully used for caesium-137 decorporation in the Goiânia accident.

(y) **Isotopic Dilution:** Stable isotope given in quantities facilitating radionuclide elimination. E.g., Increased fluid ingestion for treating Tritium contamination.

(z) **Large-Scale Incident**: Incident where relatively large quantities of radionuclides occurs with possible exposure or contamination of multitude, e.g., terrorist attacks with radiological weapons, nuclear weapons detonation, and large-scale nuclear power plant disasters.

(aa) **Late Effect Phase**: In this phase, organ specific radiation induced effects may develop that are not attributable to either the prodromal or the manifest illness phase of ARS.

(bb) **Manifest Illness Phase**: Covering the time period from the end of the prodromal phase up until day 60; includes development of the complete picture of ARS and/or first signs of recovery.

(cc) **Mobilization:** Releasing radionuclides from body tissues resulting in its excretion. E.g., Radiostrontium excretion by Ammonium Chloride.

(dd) **Multi-Parameter Biodosimetry**: No single assay is sufficiently robust to address all potential radiation scenarios, including management of mass casualties and diagnosis for early medical treatment. Recommendations for use by first responders and first receivers involve a prioritized multiple-

assay biodosimetric-based strategy. The National Council on Radiation Protection & Measurements (NCRP) Commentary No. 19 (NCRP, 2005) recommends multi-parameter triage (i.e., time to vomiting, lymphocyte kinetics, and other biodosimetry and biochemical indicators) as the current best early assessment of a victim's absorbed dose. Early, approximate assessment of dose is not intended to replace more established, but more time-consuming, techniques of health physics dose reconstruction.

(ee) **Neutrons**: Uncharged particles emitted from the fission process in a nuclear reaction. Neutrons can cause 2–20 times as much damage to tissue as gamma rays.

(ff) **Partial Body Irradiation**: Exposure to penetrating external radiation, clearly limited to a large part of the body while the rest remains unexposed.

(gg) **Prodromal Phase**: Covering a time period of up to the first week after exposure, crucial for an initial assessment of the extent of damage to the individual on the basis of prodromal symptoms.

(hh) **Protective Environment**: Induction of a patient environment free of bacteria or other microbial elements by appropriate methods (lamina flow situation, physical barrier, etc.). Also known as "gnotobiotic state" in experimental settings.

(ii) **Radiation Exposure Device**: Radioactive material, in a sealed source or within a container, intended to expose people in the vicinity of the device to a high-level external dose. Some materials used in military equipment and supplies contain radioactive components that, if improperly handled, could function as an RED. Industrial radiography sources as shown above constitute the most prevalent REDs in the civilian sector.

(jj) **Radioactive Half-Life**: For a radionuclide, the time required for the activity to decrease, by a radioactive decay process, by half.

(kk) **Radiological Dispersion Device**: A device intended for spreading radioactive material in absence of a nuclear detonation. An RDD can cause organ dose through inhalation of radioactive material in a dispersal plume or ingestion of materials in the food chain. An RDD would cause conventional casualties to become contaminated with radionuclides and the contaminated area would complicate medical evacuation.

(ll) **Radionuclide**: Naturally occurring or artificially produced instable ion that transforms to a stable or unstable atom and releases radiations in the process.

(mm) **Small-Scale Incident**: Incident occurring in laboratories, hospitals, etc., involving small amounts of radionuclides with the potential exposure and/or contamination of one or a few individuals.

(nn) **Stochastic Effect**: A radiation induced health effect, the probability of occurrence of which is greater for a higher radiation dose and the severity of which (if it occurs) is independent of dose. Stochastic effects may be somatic effects or hereditary effects and generally occur without a threshold level of dose. Examples include thyroid cancer and leukaemia.

(oo) **Target Organ/Tissue**: Organ or tissue in which, for physiological and physicochemical reasons, a specific radionuclide is preferentially deposited.

(pp) **Uptake**: The processes by which radionuclides enter the systemic circulation (body fluids) from the respiratory tract, from the GI tract or directly through the skin, especially through wounds. In other words, the fraction of an intake entering the systemic circulation is referred to as the uptake.

CHAPTER 4

Medical Response to Radiological Accident

MEDICAL RESPONSE TO RADIOLOGICAL ACCIDENT

Medical Management General Principles:

9. Adequate and appropriate medical response at the scene of radiation emergency will ensure mitigation of contamination risk both external and internal. The victim's presence relative to the incident site and its zones i.e., Red with its Safety Perimeter and the Yellow Zone with its Security Perimeter and the outer Green Zone OR the Light Damage (LD) zone, Moderate Damage (MD) zone and Severe Damage (SD) zone which will exemplify the radiation exposure and the ill effects thereof. Incremental grades of physical injuries along with thermal burns and radiation exposure will be found in victims as one enters the affected zone.

Approach to the Scene

10. First responders and all other health care providers must use universal precautions (disposable gowns, gloves, masks, etc) for personal protection and should confirm the radioactivity levels before venturing into the affected zone and dynamic radioactivity monitoring while undertaking during the rescue operations.

11. Zoning of the impact area will help in judicious deployment of medical resources resulting in desirable outcome of saving precious lives with limited detrimental exposure of the rescuers. LD zone will primarily have ambulatory patients who after initial evaluation can be directed to the nearest health care facility. The MD zone will primarily be the place of maximum rescue efforts, however regular monitoring of radioactivity by first responders to avoid areas with dangerous fallout is imperative. The SD zone will initially be inaccessible to the first responders due to the high levels of radiations and extreme caution is to be taken in approaching it. A guide to zoning as adapted from IAEA guidelines is given at ***Table 4***.

Zone Designation	Color Code	Perimeter Designation	Radiation exposure level	Activities & Guidelines
Inside the Inner Cordoned Area	Red	--	Areas with > 100 mSv/h	▪ Only life saving actions should be performed in this area ▪ Limit staying time to < 30 Minutes, or less, depending on measured level of radiation
Inner Cordoned Area ("Hot Zone")	Yellow	Safety Perimeter	> 0.1 mSv/h	▪ Area around dangerous radioactive source where precautions should be taken to protect the responders and the

				public from potential external exposure and contamination
Outer Cordoned Area	Green	Security Perimeter	--	▪ Access controlled, secure zone around the inner cordoned area. ▪ Ambient dose rates in this area need to be at levels very close to background levels. ▪ Activities undertaken ▪ Triage ▪ Registration ▪ Monitoring ▪ Decontamination ▪ Temporary Morgue area ▪ Waste Storage Area

Table 4. Zoning of Radiation Accident Site.
(Reprinted from: International Atomic Energy Agency (IAEA). Manual for First Responders to a Radiological Emergency. Vienna; 2006. https://www-pub.iaea.org/MTCD/publications/PDF/EPR_First Responder web.pdf. Accessed 12 Sep 2020. & International Atomic Energy Agency (IAEA). Generic Procedures for Medical Response During a Nuclear or Radiological Emergency. Vienna; 2005. https://www.iaea.org/publications/7213/ generic-procedures-for-medical-response-during-a-nuclear-or-radiological-emergency. Accessed 12 Sep 2020)

TRIAGE:

12. As in any emergency, a triage system is needed in a resource scarce radiological accident environment to correctly identify casualties with serious and life-threatening conditions so that immediate attention can be directed to them. Most casualties may not require immediate medical attention and the “worried well” might form a large number. Forward triaging before hospital control lines will help to identify the casualties which are suitable to undergo time consuming radiation surveys and decontamination.

Onsite Triage:

13. Early management in the field and also at the emergency room should follow basic triage principles. *Firstly*, life-threatening injuries should be treated (even before assessing exposure). Unless a confirmed information is available each victim should be assumed to be originating from the Red Zone and irrespective of being in Immediate (P1), Delayed (P2) or Minimal (P3) category each patient is externally and internally contaminated. (i.e., by absorption of radiation through the skin after being physically covered by radioactive material or by ingestion or inhalation of radioactive material). Urgent treatment for victims with traumatic injuries should be undertaken at the Public Processing Area of the Yellow Zone. (The Public Processing Area is a

designated area in the outer cordoned area and is used to undertake triage & decontamination, provide first aid and registration of reporting casualties followed by their evacuation using ambulances).
Stabilized victims should be transported to a medical facility with “Immediate” (P1) cases transferred on priority without decontamination with intimation to the transporting medics/paramedics and the hospital staff. A lag of 10-12 hrs on cases to case basis is acceptable in “Delayed” (P2) cases with onsite decontamination before transfer to the hospital. The walking wounded i.e., “Minimal” (P3) are either decontaminated at the incident venue or at their home and are subsequently treated at the hospital OPD.

14. *Secondly*, injured victims should be treated by standard triage guidelines. Preliminary decontamination (removal of clothing, washing of the victim, etc) should be performed before or during transport to a medical facility. The external contamination is reduced by 80-90% on removal of outer garments.

15. *Thirdly*, persons who are only externally contaminated (without other injury) should be relocated (to a facility other than the hospital) in order to decongest the hospital care system. Assessment of basal radiation level at the management facility prior to arrival of the patients must be undertaken. Thereafter, assessment and prevention of contamination, treatment of minor injuries, and evaluation and treatment of internal contamination should be addressed. Major management decisions to be made in the triage phase are shown in ***Figure 2***.

16. A ready guide to first responders is “Triage Score” (T) which depicted by the formula T = N/L + E where E is Emesis and N/L is the Neutrophil/Lymphocyte ratio. Emesis scoring is 0 for absent emesis and 2 if emesis is present and actual value of the Neutrophil/Lymphocyte (N/L) ratio (normal being around 2.1). If the calculated “Triage Score” T > 3.7 the patient warrants assessment.

17. Algorithmic approach to onsite management of casualty as promulgated by IAEA is reproduced at ***Figure 3***.

18. Scarce resource setting warrants judicious triage for optimum utilization of resources with desirable outcomes benefitting the multitude. ***Table 5. and 6***. give the approach to triaging in scarce resource setting when only radiation exposure is expected and in cases where combined injury i.e., trauma and radiation exists. The initial decision making based on clinical manifestations as given by IAEA is reproduced in ***Table 7***.

19. After arrival in the emergency department, victims should be classified and graded as explained in detail above. Depending on the situation, a Trauma Surgeon, Burn Specialist, Dermatologist, and/or Neurologist may be consulted, in addition to Haematologist. Detailed clinical assessment as outlined in preceding paragraphs should be done at the earliest after receiving the patient. For larger incidents, a national system requires to be in place. Hospitals must develop radiation response plans that coordinate their efforts with those of local response teams. First responders and all other health care providers must use universal precautions (disposable gowns, gloves, masks, etc) for personal protection.

TRIAGE CATEGORY AFFECTED BY RADIATION DOSE AND RESOURCE AVAILABILITY				
Radiation Dose* (Gy)	RADIATION ONLY			
> 10* Likely fatal (In higher range)	Expectant[3] / Immediate[2]	Expectant[3]	Expectant[3]	Expectant[3]
6-10* Gy (Severe)	Immediate[2]	Immediate[2]	Delayed[2]	Expectant[3]
>2-6* Gy (Moderate)	Immediate[2]	Immediate[2]	Immediate[2]	Immediate[2]
> 0.5 - <2* Gy (Minimal)	Minimal B[3]	Minimal B[3]	Minimal B[3]	Minimal B[3]
< 0.5* Gy (Minimal)	Minimal A[3]	Minimal A[3]	Minimal A[3]	Minimal A[3]
Resource Availability	Normal	Good	Fair	Poor
Standard of Care**	Conventional	Contingency	Crisis	Crisis

Legend – Radiation Only

* Radiation dose received by the whole body or a significant portion of the whole body

** Crisis standards of care IOM letter Report 2009

Minimal B: Consider repeating both biodosimetry and clinical reassessments, especially at high end of this dose range.

Minimal A: < 0.5 Those with physical dose estimates based on location below 0.5 Gy need not report for medical evaluation. Joining a registry may be suggested after the incident.

The red/black split triage category for >10 Gy indicates that some victims may receive aggressive treatment at discretion of physician, especially if 10 Gy is received over prolonged time period.

Resource availability below NORMAL:

GOOD **conditions allow for maintenance of "functionally – equivalent"** care through contingency operations

FAIR conditions require delaying care for severe injuries after moderate injuries

POOR conditions require classifying severe injuries as expectant

Myeloid Cytokine Category	G-CSF Recommendation
1	G-CSF indicated
2	G-CSF indicated, lower priority than Category 1
3	G-CSF not indicated

Table 5. Triage Protocol: Radiation Dose & Resource Availability.

(Reprinted from: Coleman CN, Knebel AR, Hick JL, Weinstock DM, Casagrande R, Caro JJ, DeRenzo EG, Dodgen D, Norwood AE, Sherman SE, Cliffer KD, McNally R, Bader JL, Murrain-Hill P. Scarce Resources for Nuclear Detonation: Project Overview and Challenges. Disaster Med Public Health Prep. 2011 Mar;5 Suppl 1:S13-9)

TRIAGE CATEGORY FOR TRAUMA AND COMBINED INJURY AFFECTED BY INJURY SEVERITY, RADIATION DOSE AND RESOURCE AVAILABILITY				
Injury Severity	**Trauma* + Radiation** = Combined Injury**			
≥ Moderate trauma* + radiation > 2 Gy**	Immediate	Delayed Immediate	Expectant Delayed	Expectant
	Trauma Only	BURN > 20% BSA worsens triage category (lowers priority) 1 level		
Severe trauma*	Immediate	Immediate	Delayed	Expectant
Moderate trauma*	Delayed	Delayed	Immediate	Immediate
Minimal trauma*	Minimal	Minimal	Minimal	Minimal
Resource Availability	Normal	Good	Fair	Poor
Standard of Care***	Conventional	Contingency	Crisis	Crisis

Legend – Trauma and Combined injury

* Adding > 20% total body surface area burn to trauma worsen priority by 1 category (*puts them lower on the priority list*)

** Radiation dose received by the whole body or a significant portion of the whole body

At higher radiation doses (>6 Gy), triage category may worsen as on Combined Injury card

*** Crisis standards of care, IOM letter report 2009

Trauma category	Description
Combined injury	▪ Radiation dose of > 2 Gy to whole body or significant portion of whole body ***plus*** moderate or severe trauma and /or burn injury
Severe trauma	▪ Stabilization requires complex treatment; ▪ ≥20% chances of death with stabilization and treatment
Moderate trauma	▪ Without stabilization, potential for death within hours ▪ < 20% chance of death with stabilization and treatment
Minimal trauma	▪ Injuries pose no significant risk to life and limb in next 3-4 days ▪ Limited or no treatment prior to referral in the next 3-4 days

Table 6. Triage Protocol: Trauma and Combined Injury affected by Injury Severity, Radiation Dose & Resource Availability.

(Reprinted from: Coleman CN, Knebel AR, Hick JL, Weinstock DM, Casagrande R, Caro JJ, DeRenzo EG, Dodgen D, Norwood AE, Sherman SE, Cliffer KD, McNally R, Bader JL, Murrain-Hill P. Scarce Resources for Nuclear Detonation: Project Overview and Challenges. Disaster Med Public Health Prep. 2011 Mar;5 Suppl 1:S13-9)

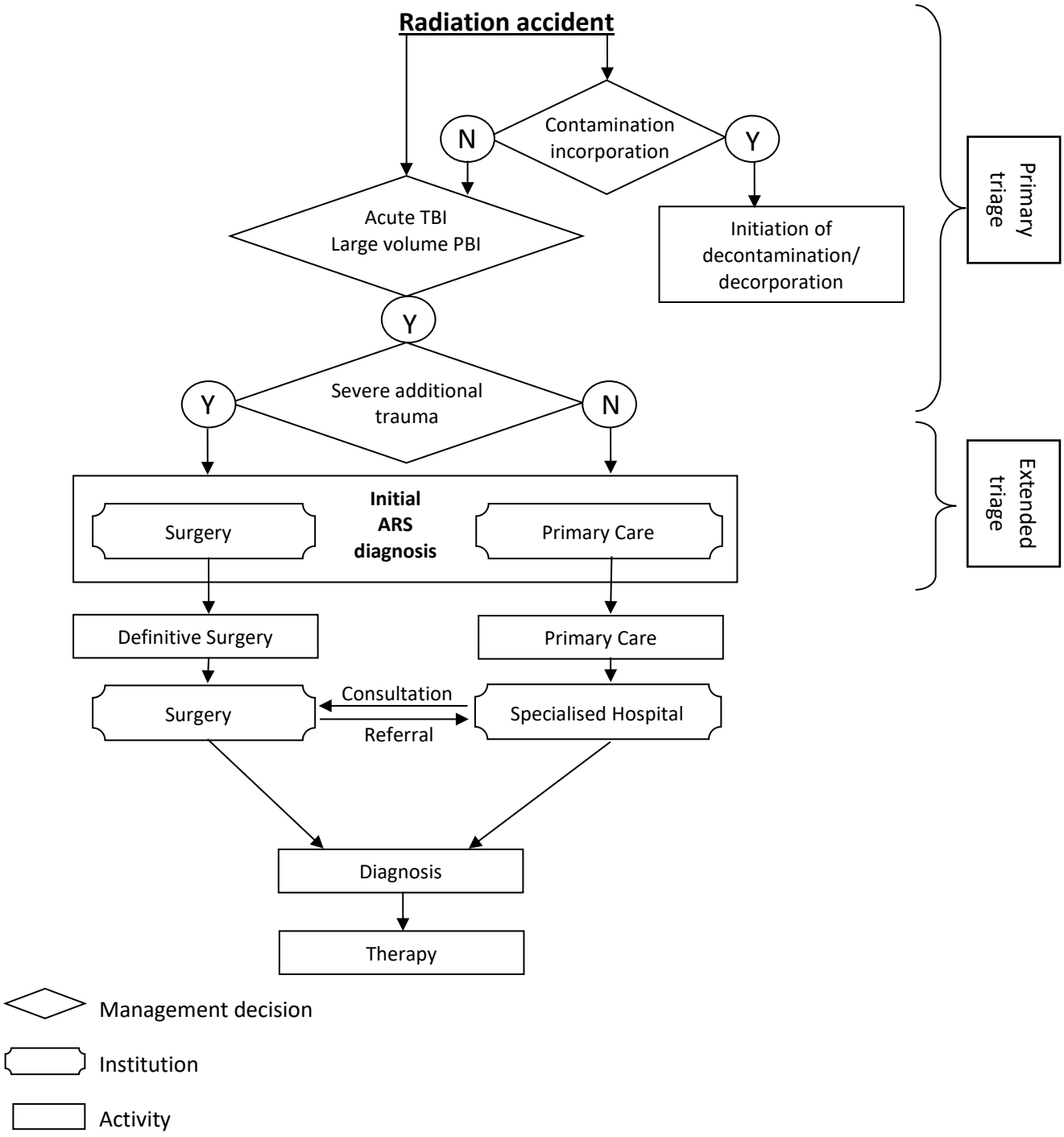

Figure 2. Major Management Decisions to be made in the Triage Phase. (Y = yes; N = no)

(Reprinted from: Fliedner 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.)

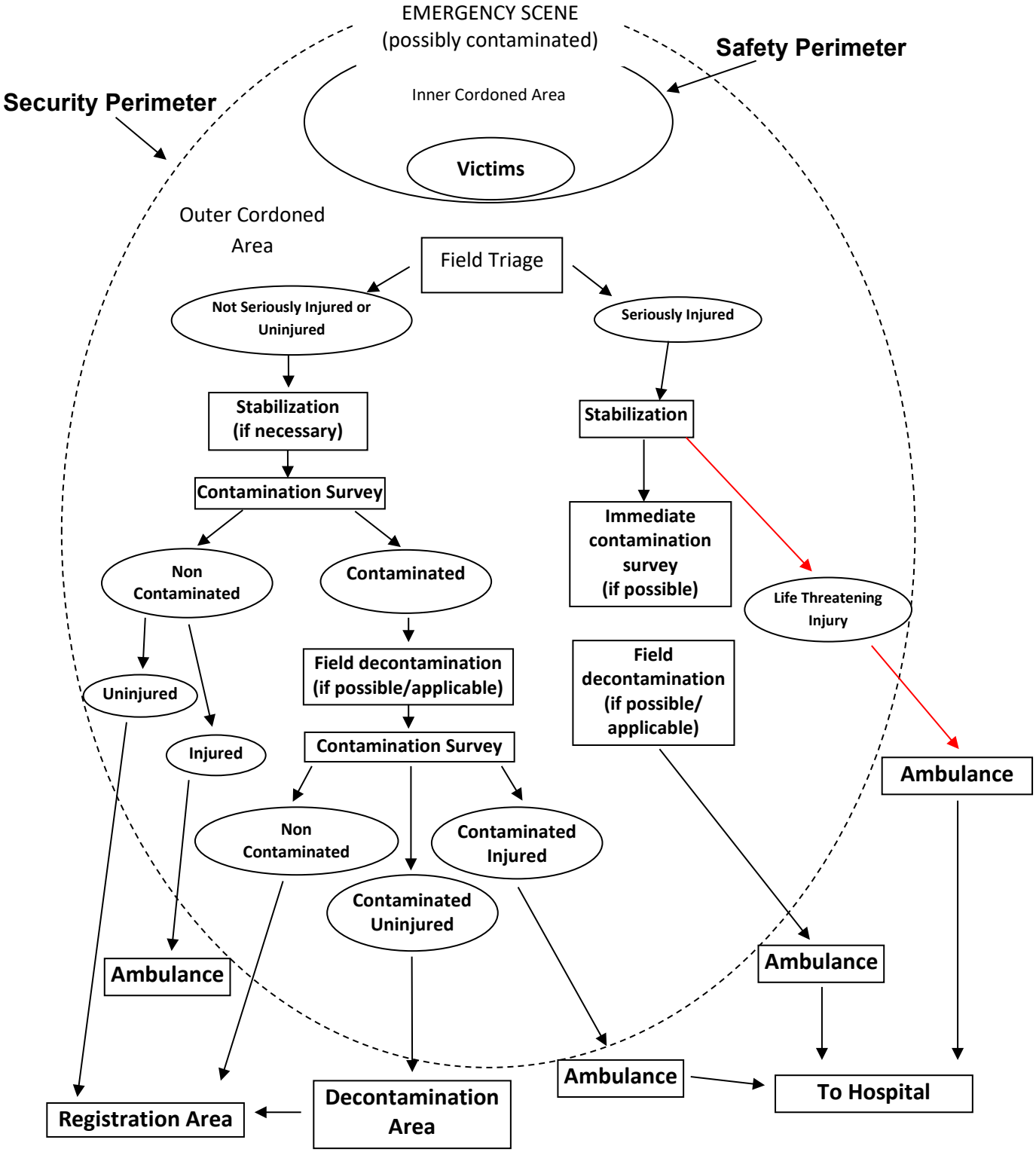

Figure 3. Onsite Emergency Management of Radiation Accident Victims.
(Adapted from: International Atomic Energy Agency (IAEA). Generic Procedures for Medical Response During a Nuclear or Radiological Emergency. Vienna; 2005. https://www.iaea.org/publications/7213/ generic-procedures-for-medical-response-during-a-nuclear-or-radiological-emergency. Accessed 12 Sep 2020)

Clinical Manifestations		Estimated Dose		Initial Decision
Whole Body Exposure	**Local Exposure**	**Whole Body Exposure**	**Local Exposure**	
No vomiting	No erythema	<1 Gy	< 3 Gy	Outpatient with five-week surveillance (blood, skin)
Vomiting 2-3 h after exposure	Primary erythema 12-24 h after exposure	1-2 Gy	>3-8 Gy	Monitoring in a general hospital
Vomiting 1-2h after exposure	Primary erythema 8-15 h after exposure	2-4 Gy	>15 Gy- <25 Gy	Hospitalization in a haematology or surgical department or specialized surgical department (ideally in a room with laminar air flow and air filtering, and with a plastic surgery team trained in radiation injuries).
Vomiting earlier than 1 h after exposure	Primary erythema within 3-6 h (or less) associated with itching, oedema and pain	>4 Gy	>25 Gy	Hospitalization in a haematological or specialized surgical department (ideally in a room with laminar air flow and air filtering, and with a plastic surgery team trained in radiation injuries). Specialized counselling is necessary.

Table 7. Initial Decision Making for Managing Radiation Injuries Based on Vomiting and Erythema.

(Reprinted from: International Atomic Energy Agency, Vienna. Medical Management of Radiation Injuries. International Atomic Energy Agency (IAEA), Vienna; 2020. Safety Reports Series No. 101. https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1891_web.pdf. Accessed 31 Oct 2020.)

Medical Management During Transportation

20. The radiation casualty is carried by the team of first responders from the cordoned region to the area just beyond the outer cordon line where the ambulance team is waiting with a stretcher with a clean blanket or sheet over it. The casualty is passed over lying on a backboard which is kept on the stretcher and the blanket/sheet is covered over the casualty. Now the patients will be required to be transported to the most appropriate hospital for the first basic assessment and care. “Appropriate” in this context means finding a compromise between the nearest and the best equipped hospital capable of handling such emergencies. While in ambulance regular monitoring of the casualty is undertaken (with due precautions wearing Personal

Protective Equipment) and any alteration in its status is intimated to the receiving hospital. After handing over the casualty at the designated hospital area, the designated radiation monitoring group screens the Medical Transport Team and facilitates decontamination prior to putting them back into operation unless their emergent move is warranted. Each member carrier a personal dosimeter to record individual exposure.

Medical management at Hospital

21. The prearrival preparation starts with intimation of occurrence of a radiological emergency and despatch of casualties to the hospital from the site. Preferably the hospital desk which receives the call should try and elicit the following information about the casualties for planning a judicious response:

(a) Exact number despatched to the hospital
(b) Health status
(c) Contamination status
(d) Radiological source and the radioisotope
(e) Mode of transport and expected travelling time to the hospital

Ideally the hospital medical response team is composed as per ***Figure 4.***

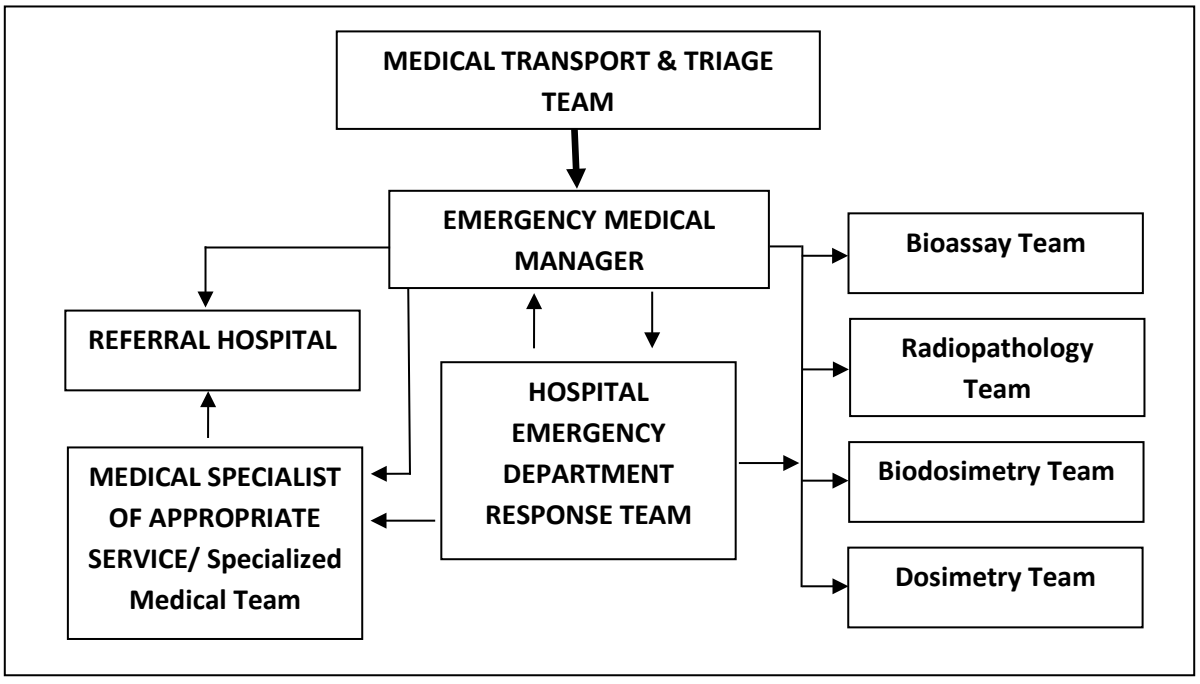

Figure 4. Hospital Level Medical Response Organization in Radiation Emergency.

(Reprinted from: International Atomic Energy Agency (IAEA). Generic Procedures for Medical Response During a Nuclear or Radiological Emergency. Vienna; 2005. https://www.iaea.org/publications/7213/ generic-procedures-for-medical-response-during-a-nuclear-or-radiological emergency. Accessed 12 Sep 2020)

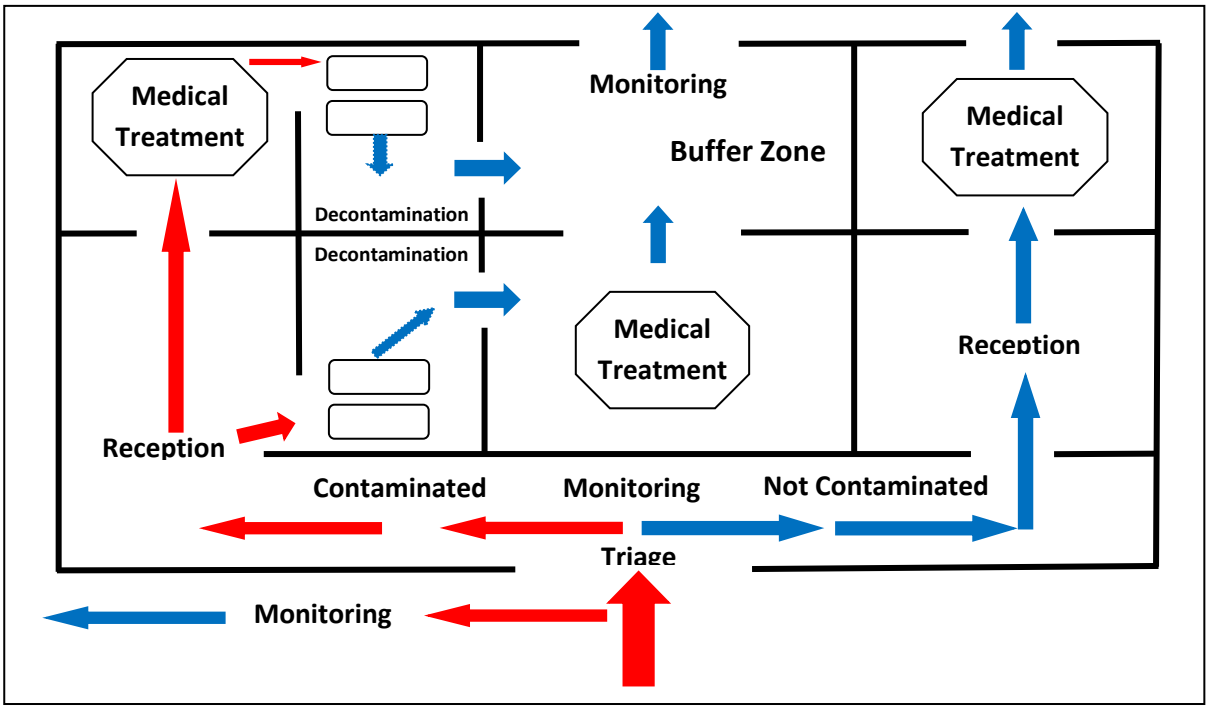

Figure 5. Proposed Layout of Reception Area of Hospital for Radiation Emergency.
(Reprinted from: Palma CR, Liland A, Jerstad AN, Etherington G, Pérez MR, et al. TMT Handbook. Triage, Monitoring and Treatment of people exposed to ionizing radiation following a malevolent act. Norway: Norwegian Radiation Protection Authority (NRPA); 2009. https://www.remm.nlm.gov/tmt-handbook-20091.pdf. Accessed 15 Sep 2020)

22. On receipt of information about the impending arrival of radiation incidence casualties to the hospital activation, briefing of the Emergency Response Team along with preparation of the Medical Transport and Patient Reception and Treatment area must be undertaken. The proposed layout of the hospital reception area which can be used as a guideline for customizing the available infrastructure is given at ***Figure 5***.

23. The route from the ambulance bay to the emergency department if time permits must be covered with plastic sheets or freezer paper properly fixed with tape. Similar action should be taken for nonessential equipment too. Proper demarcation of the decontamination region, treatment region, Contaminated and uncontaminated zone must be undertaken for seamless movement of the casualties.

24. Containment control zone at the hospital demarcates the transition of the patient from the medics transporting the patient to the hospital team. A trauma triage and necessary lifesaving intervention (if required) followed by radiological triage must be undertaken. Segregation of contaminated and uncontaminated cases is done, and their necessary management is undertaken in hot and cold hospital areas respectively.

25. On or prior to admission, the doctor in charge should familiarize himself with the patient's problems and then brief the entire hospital staff. This doctor should preferably be trained in Internal Medicine with basic knowledge in all other medical specialties. Patient's clinical status if permitting the attending physician can undertake an urgent radiological assessment for contamination status followed by a detailed assessment on stabilization. Cloths if not removed at the site of accident, should be

removed now without compromising the clinical condition of the patient and should be kept in a plastic bag for further disposal. A detailed end to end approach to a patient in the emergency department is given at ***Figure 6***. Hospital Response Card highlighting the actions required to be primarily undertaken during management of the patient as advised by IAEA are reproduced at ***Table 8a. and 8b.***

Local Hospital Actions in Radiological Emergency (Page 1)
• Operate under the IC. Follow personnel protection guidelines. • Brief health care staff on negligible risk in treating contaminated patients if appropriate precautions are followed. • Have law enforcement provide a cordoned area around the hospital(s) to redirect worried-well to the secondary location. • Prepare ambulance reception area and treatment area. • Set up a controlled area and control lines. • Prepare the medical staff. Use universal precautions. • Assess and manage injuries (assumed to be contaminated): (1) Medical stabilization first; (2) Radiological survey (if possible); (3) Physical examinations and blood tests (CBC with differential) promptly. If internal contamination is suspected take nasal swabs.

Table 8a. Local Hospital Response Cards (Page 1).
(Reprinted from: International Atomic Energy Agency (IAEA). Manual for first responders to a radiological emergency. Vienna; 2006. https://www-pub.iaea.org/MTCD/publications/PDF/epr_Firstresponder_web.pdf. Accessed 12 Sep 2020)

Local Hospital Actions in Radiological Emergency (Page 2)
• If the patient could not be checked for contamination, have him/her take a shower and change clothing as soon as possible (if will not adversely affect patient's medical status). • If the patient is contaminated — perform full decontamination. • Survey and transfer the uncontaminated patient to the clean area. • Control the spread of contamination: Before exiting /removing from contaminated area (1) Survey staff, remove contaminated clothing and shower. (2) Survey equipment. • Conduct clean up under direction of radiological assessor. • Don't release areas and ambulance for normal use until approved by radiological assessor. • Assess needs and request additional resources.

Table 8b. Local Hospital Response Cards (Page 2).
(Reprinted from: International Atomic Energy Agency (IAEA). Manual for first responders to a radiological emergency. Vienna; 2006. https://www-pub.iaea.org/MTCD/publications/PDF/epr_Firstresponder_web.pdf. Accessed 12 Sep 2020)

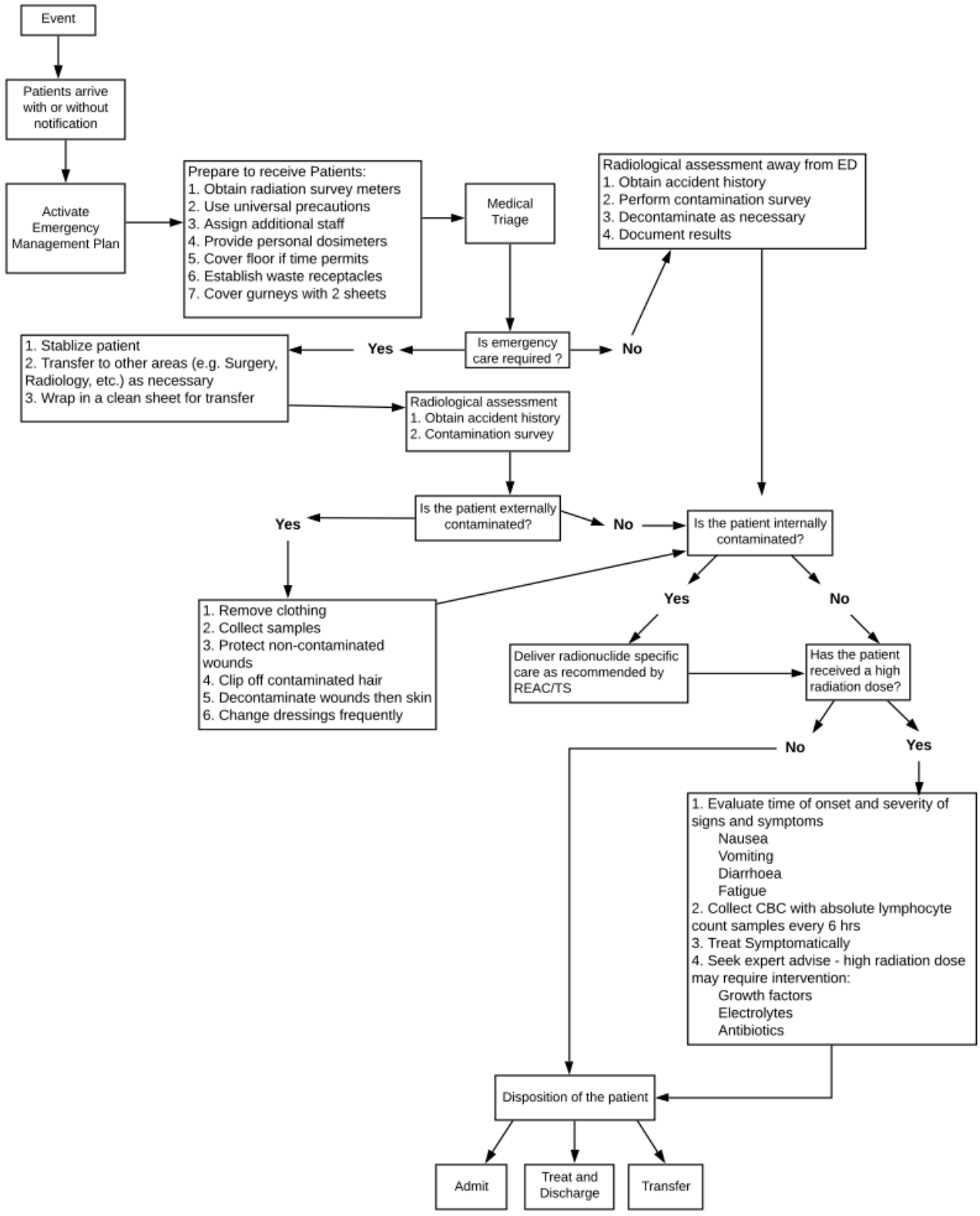

Figure 6. Patient flow through the Emergency Department.
(Reprinted from: Bushberg JT, Kroger LA, Hartman MB, et al. Nuclear/radiological terrorism: emergency department management of radiation casualties. J Emerg Med. 2007;32(1):71-85.)

Laboratory Evaluation

26. Primarily determination of the dose of radiation to which an individual is exposed determines the subsequent onset of various clinical symptoms. The various methods available for dose estimation are:

(a) Physical Dosimetry – wherein the whole body dosimetry determines the radiation exposure.
(b) Biological markers – Lymphocyte depletion kinetics
(c) Clinical marker – Onset of emesis
(d) Chromosomal aberration (Dicentric analysis, Chromosomal rings)

Basic indications and the tests recommended are given in ***Table 9.***

S.No.	Indication	Sample type	Collection Procedure	Collection Material	Analysis	Objective
(a)	Patient with suspected radiation injury	Blood	Select uncontaminated skin for venepuncture. Cover venepuncture location after the procedure	EDTA Tube (Purple top)	Complete Blood Count	Assess chronological change in counts is a denoter of level of radiation exposure
				Lithium heparin tube (Light Green top)/ EDTA (Purple Top)	Chromosomal Analysis/ Karyotyping	Gauge level of radiation exposure
		Urine			Routine analysis	Baseline kidney function
(b)	Detection of External Contamination	Nasal, Oral, Aural swab	A saline/water moist swab each for each nostril, ear canal and oral cavity	Swab moistened with saline/water	Radiation level using Giger muller counter, Gamma or liquid scintillation counter or Multichannel analyzer (MCA)	Identification of contaminant and gauge internal contamination
		Wounds		Discarded dressing, wound secretion using swab, foreign object/ debris		
(c)	Detection of Internal Contamination	Urine	24 hr urine sample	Standard Specimen containers	Bioassay	Gauge internal contamination
		Faeces	24 hrs faecal sample			

Table 9. Samples and Lab Tests Recommended.

(Reprinted from: Oak Ridge Institute for Science and Education. Radiation Emergency Assistance Center/Training Site (REAC/TS). Guidance for radiation accident management. http://orise.orau.gov /reacts/guide/index.htm. Accessed 13 Sep 2020.)

27. Initial investigations which are recommended based on European consensus, within the first 48 h are: -

(a) Repeated blood cell counts (lymphocytes, granulocytes and platelets) if possible, every 4–8 h for the first 24 h, then every 12–24 h (+reticulocytes).
(b) Chromosome aberration analysis on blood lymphocytes (biodosimetry).
(c) Red cell group typing.
(d) Store serum and cells for DNA for future analyses including HLA typing upon request from clinical teams.
(e) Standard biochemical tests (+amylasemia).
(f) If there is suspicion of a neutron exposure, a blood sample of 20ml should be taken to measure the content of radioactive sodium (24Na).
(g) Urine and feces if radionuclide contamination is suspected.
(h) Imaging studies which include but not limited to X-Ray Chest, CT scans and MRI to assess major organ systems involvement

28. Radiation dose from external exposure can be assessed by physical, biological, and clinical dosimetric techniques ***(Table 10.)***. Physical dosimetry can provide an estimate of individual dose, using a whole-body radiation dosimeter. Physical dosimeters can also measure dose in common materials (including air, soil, water, brick, etc.). It has been shown that frequency of chromosome aberrations in lymphocytes correlates well with radiation dose. The formation of dicentrics involves an interchange between 2 separate chromosomes, while ring formation involves a break in the arm of a single chromatid, followed by rejoining to form a ring and a fragment ***(Figure 7)***. The frequency of these asymmetric aberrations in circulating lymphocytes correlates with radiation dose. At low doses, chromosome breaks result from passage of a single charged particle, the consequence of which is a linear function of dose. At high doses, chromosome breaks are caused by the passage of multiple charged particles, resulting in an interaction that is a quadratic function of dose. Chromosomal aberrations have become the “gold standard” for biodosimetry. Their detection is facilitated by the application of hybridization probes for centromeres and automated metaphase detectors. For triage of victims of terrorist events, as few as 20 metaphases may be scored to provide a preliminary estimate of dose. Other forms of biological dosimetry include lymphocyte depletion kinetics, interphase aberrations (detected by premature chromosome condensation induced by agents such as okadaic acid and p34cdc2/cyclin B kinase, and electron spin resonance of dental enamel).

29. To assign risk from radiation exposure it is important to document clinical signs and symptoms. These include the time of onset and intensity of nausea and vomiting, the appearance and type of skin changes, the development of anorexia and fatigue and the severity of depression in circulating blood counts, including the polymorphonuclear cell count, lymphocyte count and platelet count. Three key elements i.e., time to onset of vomiting, lymphocyte depletion kinetics, and chromosome aberrations are essential for assignment of prognosis and selection of therapy.

Dosimetry	Method	Utility
Biological	Whole-body counting	Not generally available, impractical
	Chromosomal aberrations (dicentrics, ring forms)	The "gold standard." Typically requires 4–5 days processing time.
	Lymphocyte depletion kinetics	Inexpensive but requires 2–4 days for decline at doses of 4–6 Gy and 4–6 days at 2–4 Gy
	Interphase aberrations	Under development
	Electron spin resonance (dental enamel)	Permanent record of exposure but requires removal of tooth
Clinical	Symptoms and signs	Practical but loses sensitivity at low doses.

Table-10 Selected Methods for Estimating Radiation Dose.
(Reprinted from: Dainiak N, Waselenko JK, Armitage JO, MacVittie TJ, Farese AM. The hematologist and radiation casualties. Hematology Am Soc Hematol Educ Program. 2003;473-496.)

30. Of these methods, monitoring for a decrease in absolute lymphocyte count has been found to be a reliable and practical method for early assessment (within hours or days, depending on dose) after a radiation exposure. ***Table 11.*** highlights its correlation with the severity grade of ARS and prognosis.

Absolute lymphocyte count per µL	Severity grade of ARS	Survival Prognosis
700-1000	Mild	Good
400-700	Moderate	Probable
100-400	Severe	Possible at a highly specialized treatment centre
<100	Very Severe	Poor

Table 11. Absolute Lymphocyte Count 48h after Whole Body Exposure and Survival Prognosis.
(Reprinted from: International Atomic Energy Agency, Vienna. Medical Management of Radiation Injuries. International Atomic Energy Agency (IAEA), Vienna; 2020. Safety Reports Series No. 101. https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1891_web.pdf. Accessed 31 Oct 2020.)

31. Additional suggested tests are as under

(a) Plasma Flt-3 ligand: Bone marrow damage marker
(b) Serum Amyloid A: Prognostic indicator
(c) Plasma Citrulline: Small bowl epithelial loss marker

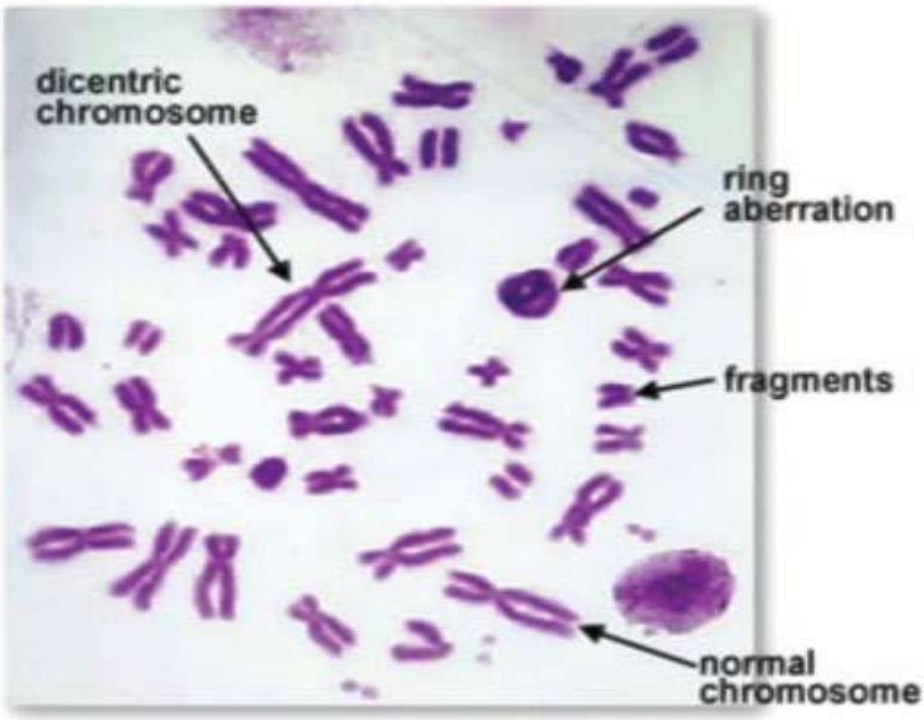

Figure 7 . Chromosomal Aberrations Post Radiation Exposure.
(Reprinted from: Goans RE, Military Medical Operations Staff. Medical Management of Radiological Casualties. 4th ed. Armed Forces Radiobiology Research Institute; 2013. Available at https://www. usuhs.edu/sites/default/files/media /afrri/pdf/ 4edmmrchandbook.pdf. Accessed 11 Sep 2020.)

LOCAL RADIATION INJURY (LRI)

Clinical Manifestation:

32. Exposure of a limited area of skin and sub-cutaneous tissue results in LRI manifesting as primary erythema as a result of capillary dilatation within hours of exposure. Early appearance and severity signifies higher radiation dose. It is different from the Cutaneous Radiation Syndrome (CRS) where there is excessive involvement of skin after exposure of the complete body to high doses of radiation.

33. Pathophysiology involves temporal and superimposed cytokine mediated antiproliferative, local/systemic inflammatory reactions and microcirculation damage. Primary erythema is succeeded by secondary erythema and dry desquamation. Subsequent dose related moist desquamation, blistering, ulcers and radionecrosis follows. Associated adjoining muscle and bone damage is also anticipated. Clinical diagnosis at times in absence of definitive history is a challenge.

34. Laboratory evaluation includes
    (a) Serial complete blood count (CBC)
    (b) Serial standardized high resolution color photography.
    (c) Ultrasonography
    (d) CT Scan and MRI
    (e) Thermography
    (f) Physical dose reconstruction (Monte Carlo simulation)

35. Plastic and reconstructive surgery intervention is imperative. Pain management, infection control, Pentoxyphyllin, antioxidants, hyperbaric oxygen are generally the line of management. Local tissue dosimetery guided conventional surgery is the preferred line of management for severe LRI to curb intervention aggravated inflammation wave. Serial local injection of Mesenchymal Stem Cell (MSCs) during and after dosimetery guided surgery promises desirable outcomes. Post-surgical physiotherapy promotes rehabilitation.

ACUTE RADIATION SYNDROME

Clinical Manifestation:

36. It is acute manifestation as a result of whole body or partial body ionizing radiation exposure beyond the threshold dose of 1 Gy. The exposure could short duration i.e., upto a few hours to a prolonged one i.e., lasting for days. Early symptoms generally in the first 48 hours after the acute total-body radiation exposure constitute the prodromal radiation syndrome. The clinical progression from prodromal phase is to latent phase (2-3 days to 3 weeks), followed by critical phase (the illness phase) progressing to recovery or death. Severity and duration of symptoms and signs and mortality rate are dependent on the magnitude of radiation dose and the presence of additional injury (such as trauma or burns). Invariably all individuals receiving a dose of 10–20 Gy or higher develop prodromal signs and symptoms within 1–72 hours after exposure. The prodromal symptoms include anorexia, nausea, vomiting, diarrhoea, fever, fluid loss, and electrolyte imbalance. These symptoms gradually progress to loss of consciousness, hypotension, and at times death due to cerebrovascular syndrome and cardiovascular collapse. Toxicity of other organ systems such as the gastrointestinal and hematopoietic systems can also develop. Death may occur within a few days after exposure to 10–20 Gy. A rapid, severe prodromal response is the predictor of a poor clinical outcome that is complicated by severe neutropenia, thrombocytopenia, and anemia with reticulocytopenia (bone marrow failure), accompanied by haemorrhage, infection, and death. At lower doses (2–10 Gy), it is difficult to establish a prognosis based on the prodromal syndrome. The prodromal phase is followed by illness specific to various organ systems. Four major organ systems which are critical in the development of Acute Radiation Syndrome are the Neurovascular System, the Gastrointestinal System, the Cutaneous System, and the Hematopoietic System. Evaluation of system-specific signs and symptoms are important for triage of victims, selection of therapy, and determination of prognosis.

37. **Neurovascular Syndrome**. Low doses of radiation result in localized, transient changes in the central nervous system. These changes include impaired capillary circulation, damage to the blood-brain barrier, interstitial edema, acute inflammation, petechial hemorrhages, meningitis, and hypertrophy of perivascular astrocytes. Paroxysmal spike and wave discharges may be evident on EEGs, and the presence of swelling and edema may be documented by head CT scans and MRIs. The presence of transient nausea, anorexia, vomiting, and fatigue augers a relatively good prognosis. Moderate damage to the Central Nervous System presents with persistent and more severe nausea and vomiting, and is accompanied by headache,

neurological deficits, and abnormal cognition. The presence of severe nausea and vomiting, severe headaches, drowsiness, fever and hypotension predicts a poor prognosis. Clinical grading corresponding to damage to the Neurovascular System (NVS) and the respective prognostic probabilities are shown in ***Table 12***. Major manifestations of NVS and their onset have been summarized in ***Table 13***.

Grading	Extent of impairment	Prognosis
N1	Mild damage	Recovery certain
N2	Moderate damage	Recovery with possible deficit
N3	Severe damage	Recovery with severe deficit
N4	Fatal damage	Recovery impossible

Table 12. Overall Prognostic Aspects of the NVS on the basis of the Clinical Grading.
(Reprinted from: Fliedner 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.)

Symptoms	Time of onset after exposure
Nausea and vomiting	Immediate – Hours
Anorexia	Immediate – Hours
Fatigue	Immediate – Hours
Fever	Hours – Days
Hypotension	Hours – Days
Headache	Hours – Days
Neurological deficits	Hours – Weeks
Cognitive deficits	Hours – Weeks

Table 13. Neuro Vascular Syndrome (NVS) Symptoms after Radiation Exposure.
(Reprinted from: Fliedner 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.)

38. The diagnostic methods which are relevant for verification of the organ specific grading are listed in ***Table 14***. It may also act as a starting point for further control and follow up examinations. The ideal time for an examination depends on the characteristics of the symptom and the selected diagnostic method.

Method	Relevance for the NVS
EEG	Non-invasive method for the assessment of changes in brain electrical activity. Brain electrical activity displays an increase in paroxysmal spikes, wave discharges and disappearance of

	biorhythm. These brain electrical modifications are roughly linked to the dose: slowing of brain electrical activity is a sign of high dose. The duration of the recording must be at least 1 h.
Ophthalmoscopy	Non-invasive method for the detection of brain oedema. Papilloedema is a sign of increased intracranial pressure.
Laboratory	Routine screening for the early assessment of electrolyte loss or imbalance as well as fluid loss. Important for the exclusion of other reasons for CNS perturbations (such as infectious diseases).
Cranial CT	Method for the assessment of swelling and oedema of the brain. In the late effect phase of ARS, atrophy and calcification can be detected if there is suspicion of structural cerebral lesions.
MRI	Method for the assessment of swelling and oedema of the brain. In the late effect phase of ARS, if there is suspicion of structural cerebral lesions it may be possible to detect white matter changes and dystrophic cerebral calcification.

Table 14. Neuro-Vascular System: Diagnostic Methods
(Reprinted from: Fliedner 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.)

39. **Gastrointestinal Syndrome.** At doses of between 05 and 12 Gy, mild gastrointestinal symptoms limited to mild diarrhea with associated abdominal pain are accompanied by almost certain recovery. Intermittent diarrhea and bleeding are associated with extensive sloughing of the epithelial cell layer (Mucositis), leading to denudation of the bowel. More severe damage to the gastrointestinal tract is associated with persistent diarrhea, gastrointestinal bleeding, and crampy abdominal pain, resulting in abnormalities of fluid and electrolyte balance and sepsis. Impaired barrier function of the gastrointestinal tract results in the passage of bacterial toxins through the intestinal wall into the bloodstream. Severe complications include ulceration and necrosis of the bowel wall, leading to stenosis, ileus, and perforation. Clinical symptoms associated with GIS have been summarized in ***Table 15***.

Symptom	**Time of onset**
Diarrhea	Hours-Days
Profuse and/or bloody diarrhea	Days-Weeks
Abdominal cramps	Hours-Weeks

Table 15. Clinical Symptoms Associated with GIS.
(Adapted from: Fliedner 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.)

40. **Cutaneous Syndrome.** After early exposure (within 1-2 days) or may take years before becoming fully manifest. Early lesions include erythema and moist desquamation of the skin. Such lesions may be isolated or may appear simultaneously in several locations, depending on the amount of skin receiving direct exposure. Target

cells of radiation reside at multiple levels (i.e., epidermis, dermis, hair follicle canals and subcutaneous tissues) within the skin; hence, the severity of the cutaneous reaction depends upon the “depth dose distribution” of the radiation source. Signs and symptoms include pruritus, blisters, and bullae (with or without haemorrhage), ulceration (limited to the epidermis or involving the dermis, subcutaneous tissue, muscle and/or bone), hair loss, and onycholysis. Blisters and bullae with or without necrosis appear 1-3 weeks after localized exposure to doses of > 3 Gy. The clinical manifestation and time course of the Cutaneous Syndrome are shown in ***Table 16***.

Symptom	**Time of onset**
Erythema	Hours–30 Days–10 Weeks
Loss of sensation/itching	Hours–30 Days
Blistering	5 Days–3 Weeks
Swelling and oedema	5 Days–8 Weeks
Desquamation	5 Days–8 Week
Ulcer/necrosis	5 Days–>12 Weeks
Hair loss	2–8 Weeks
Onycholysis	2–8 Weeks
Hyperpigmentation or depigmentation	>12 Weeks
Atrophy	>12 Weeks
Onychodystrophy	>12 Weeks
Keratosis	>12 Weeks
Fibrosis	>12 Weeks
Telangiectasia	>12 Weeks

Table 16. Clinical Appearance and Time Course of CS Symptoms. (As they may cause the development of characteristic late effects, symptoms of this phase are listed in the lower part of the table)
(Reprinted from: Fliedner 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.)

41. 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 17.*** as a ready reckoner for the treating teams.

Symptom	**Degree 1**	**Degree 2**	**Degree 3**	**Degree 4**
Neurovascular System				
Nausea	Mild	Moderate	Intense	Excruciating
Vomiting	Occasional, 1/day	Intermittent, 2–5/day	Persistent, 6–10/day	Refractory >10/day
Anorexia	Able to eat	Intake decreased	Minimal intake	Parenteral nutrition
Fatigue	Able to work	Impaired work	Assistance for ADLs	No ADLs
Fever	< 38°C	38–40°C	> 40°C < 24 h	> 40°C > 24 h
Headache	Minimal	Moderate	Intense	Excruciating
Hypotension	HR > 100 / BP > 100/170	BP < 100/70	BP < 90/60; transient	BP < 80/?; persistent

Neurological deficits	Barely detectable	Easily detectable	Prominent neurological impairment	Life threatening, LOC
Cognitive deficits	Minor loss	Moderate loss	Major impairment	Complete impairment
Gastrointestinal System				
Diarrhea Frequency Consistency Bleeding Abdominal Cramps/Pain	 2–3 stools/d Bulky Occult Minimal	 4–6 stools/d Loose Intermittent Moderate	 7–9 stools/d Loose Persistent Intense	 > 10 stools/day Watery Persistent with large amount Excruciating
Cutaneous System				
Erythema	Minimal and transient	Moderate, < 10% BSA	Marked; 10–40% BSA	Severe; > 40% BSA
Sensation/Itching	Pruritus	Slight & intermittent pain	Moderate & persistent pain	Severe & persistent pain
Swelling/Edema	Present; asymptomatic	Symptomatic; tension	Secondary dysfunction	Total dysfunction
Blistering	Rare, sterile fluid	Rare, hemorrhage	Bullae, sterile fluid	Bullae, hemorrhage
Desquamation	Absent	Patchy dry	Patchy moist	Confluent moist
Ulcer/Necrosis	Epidermal only	Dermal	Subcutaneous	Muscle/bone involvement
Hair loss	Thinning, not striking	Patchy, visible	Complete and reversible	Complete and irreversible
Onycholysis	Absent	Partial	Partial	Complete

ADLs: activities of daily living; LOC: loss of consciousness; BSA: body surface area

Table 17. Grading System to Guide Evaluation of Neurovascular, Gastrointestinal and Cutaneous Systems

(Adapted from: 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.)

42. **Haematopoietic Syndrome (HS).** As with all tissues composed of short-lived cells, hematopoietic tissue is directly and indirectly affected by radiation. Depending upon the dose and dose rate, effects are primarily exerted through cell renewal, apoptosis, and redistribution of lymphohematopoietic cells. Hematopoietic Stem Cells (HSC) are extremely sensitive to radiation injury. However, some HSCs appear to be extremely radioresistant, surviving doses as high as 6 Gy. Radio resistant stem cells may play a role in the hematopoietic response that is observed in individuals receiving cytokine therapy after exposure to external radiation. In addition, hematopoietic reconstitution may occur from unirradiated (or relatively “under-irradiated”) areas of bone marrow that have been “shielded” from the source of radiation by physical materials, heavy clothing, or other body tissues. The carcinogenic effects of radiation occur after a prolonged and variable delay (or latency) after exposure.

43. Disturbances in haematopoiesis owing to significant radiation exposure (> 2 Gy) in almost all cases lead to clinical symptoms that can be gathered under the term Haematopoietic Syndrome (HS). HS occurs following radiation induced damage of the haematopoietic tissue in the bone marrow. Hematopoietic effects following radiation are well known to hematologists as Total Body Irradiation (TBI) is widely used as a

part of conditioning regime prior to Hematopoietic Stem Cell Transplant (HSCT). Significant radiation exposure leads to hypoplasia or aplasia of the bone marrow, leading to peripheral blood cytopenia which are responsible for the typical clinical signs and symptoms of HS in a patient. Ionising radiation (IR) exposure directly damages hematopoietic stem cells and alters the capacity of bone marrow stromal elements to support and/or maintain hematopoiesis in vivo and in vitro. At lower doses (< 2 Gy) radiation induces mild cytopenia without significant bone marrow damage, while very high dose (> 10 Gy) leads to complete myeloablation without any chance of autologous recovery. Peripheral blood lymphopenia may develop within the first 6–24 hours after a moderate- to high-dose exposure. Based on the level of depletion of lymphocyte, polymorphonuclear leukocyte, and platelet counts, as well as the presence of infection and/or blood loss, the relative severity of hematotoxicity has been graded from degree 1 to degree 4 ***(Table 18)***. Critical phase in HS has been defined as 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 secondary to low absolute cell counts the management depends on severity of involvement of haematological toxicity.

Blood counts/Symptoms	**Degree 1**	**Degree 2**	**Degree 3**	**Degree 4**
ALC	≥ 1.5 X 10^9/L	1-1.5 X 10^9/L	< 0.5-1 X10^9/L	< 0.5 X 10^9/L
ANC	≥ 2.0 X 10^9/L	1-2.0 X 10^9/L	0.5-1 X10^9/L	< 0.5 X 10^9/L
Platelet counts	≥ 100 X 10^9/L	50-100X10^9/L	< 20-50 X10^9/L	< 20 X 10^9/L
Hb	Normal Hb	<10% decrease in Hb	10-20% decrease in Hb	>20% decrease in Hb
Infection	Local; no antibiotics required	Local; only local antibiotics required	Systemic; oral antibiotics required	Sepsis: IV antibiotics required

ANC absolute neutrophil count, ALC absolute lymphocyte count, Hb Hemoglobin, IV Intravenous

Table 18. Severity of Hematotoxicity following Radiation Exposure according to Blood Counts.

(Adapted from: 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.)

44. Based on above mentioned severity of hematotoxicity grading of HS can be done from H1 to H4 for initial risk stratification and prognostication ***(Table 19)***.

Grading	**Extent of involvement and degree of severity**	**Prognosis**
H1	Mild damage, Degree 1	Autologous recovery certain without critical phase*
H2	Moderate damage, Degree 2	Autologous recovery certain with low risk critical phase*
H3	Severe damage, Degree 3	Autologous recovery certain with high risk critical phase*
H4	Fatal damage	Autologous recovery most unlikely

* Critical phase: see text

Table 19. Overall prognostic aspects of the Haematopoietic Syndrome on the Basis of the Degree of Severity

(Reprinted from: Fliedner 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.)

45. Estimations of the 50% lethal dose (LD50) have been made in various scenarios. Depending on the incident, the LD50 ranges from 1.4 Gy among atomic bomb survivors in Japan to 4.5 Gy based upon bone marrow for uniform total-body exposure to external photons. Based upon an analysis of all available data, it has been estimated that the LD50 at 60 days (LD50/60) for humans will be approximately 3.5 Gy for young healthy adults. Some other estimations have been that the LD50 will be approximately 4 Gy and if victims are receiving appropriate supportive care and antibiotics, the LD50 increases to 6-7 Gy. These data show that some victims if given appropriate care may survive a near fatal dose exposure.

46. To make early predictions of the clinical course and outcome of a patient after radiation exposure, it is necessary to differentiate between reversible and irreversible damage to the stem cell compartment of the bone marrow. This is possible by the pathophysiological interpretation of typical haematopoietic response patterns of peripheral blood cell lineages. The clinical grading summarizes the extent of the damage to the individual and the corresponding prognosis. Without or prior to any treatment, four different grades of the HS can be distinguished based on the extent of damage to haematopoiesis as well as on the prognosis for autologous recovery of the system.

47. The basic procedure is to assess the different cell lineage response patterns as a function of time after a radiation accident. To this end the peripheral blood cell counts of the lymphocytes, granulocytes and platelets in first 60 days after the exposure have to be examined. Owing to the long half-life of the erythrocytes (about 120 days) and the lack of reliable data on reticulocytes, the erythropoietic cell lineage is not used for this classification.

48. It should be stressed that the co-ordination of care and the selection of consultants is of critical significance, since physicians of different specialties are likely to be required for each patient. A haematologist should evaluate all patients in whom exposure is suspected. Depending on the presence of symptoms and their degree, a Dermatologist, Neurologist or Gastroenterologist may also be essential. In some cases, other consultants such as Ophthalmologists, and ENT specialists, to detect acute radiation induced effects and to assess a patient’s status for further follow-up examinations and to outline the basis for early detection of the development of late effects. The same approach is valid for investigations of the Cardiovascular, Respiratory and Endocrine systems. Further, it is necessary to have well trained nursing staff, since monitoring is essential for the care of hospitalised patients especially for those under intensive care. In addition, social workers or psychologists / psychiatrists may also play an important role in dealing with the psychological impact of the radiation exposure on the patients and their families.

49. The doctor in charge usually depends on systematic and well-planned policy and guidelines to avoid omission of any important medical procedures in the very early but decisive phases of ARS. In ***Figure 8*.,** a general flow chart was given for the medical management of a radiation accident victim.

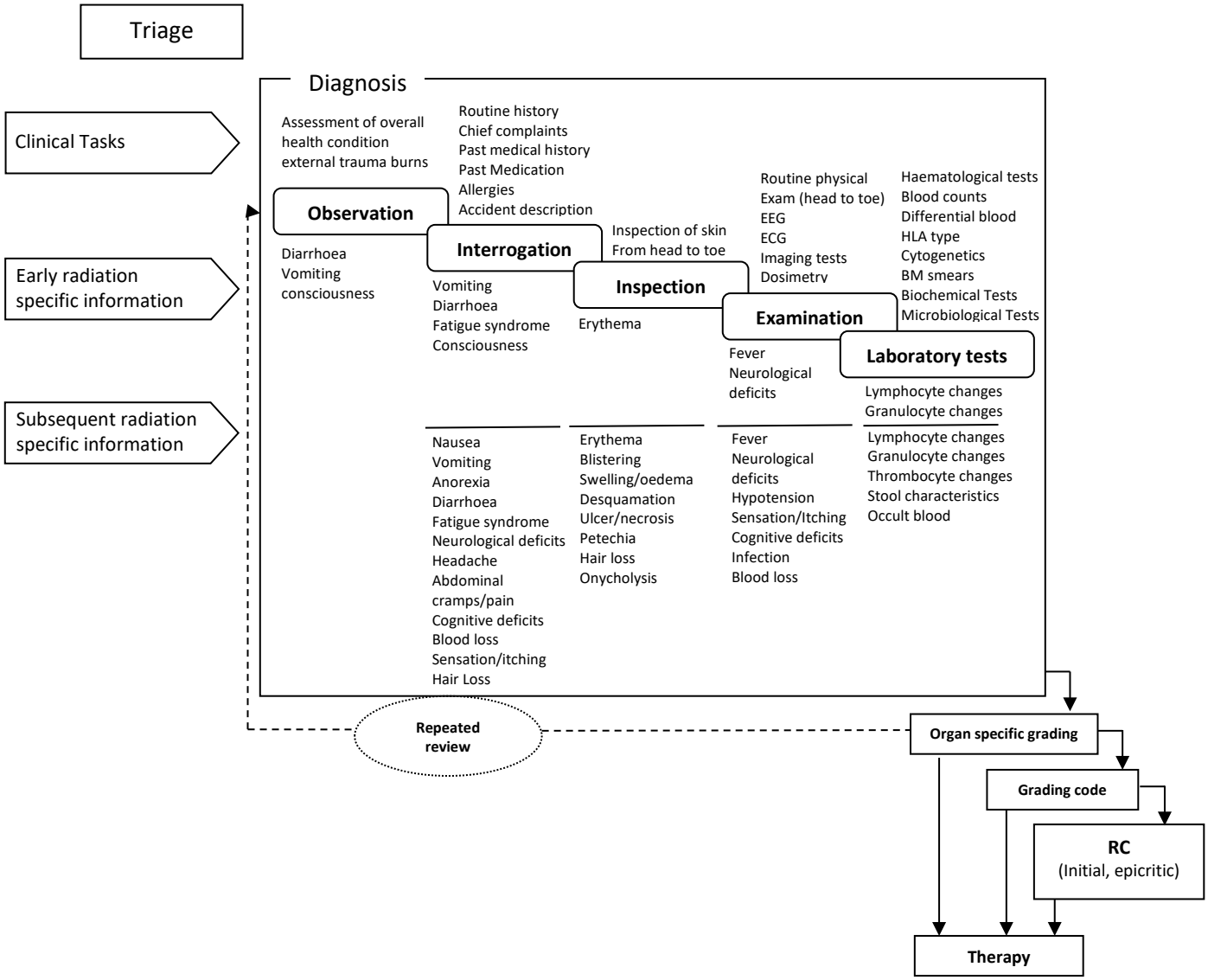

Figure 8. Schematic Representation of the Early Tasks for the Medical Team in the Diagnostic Phase of the Assessment of Characteristic Signs and Symptoms of ARS. (Some symptoms are listed several times as they can be verified in the different ways)**.**

(Reprinted from: Fliedner 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.)

50. As a guide to the clinician, one approach to the decision-making process that was developed by The European protocol METREPOL (Medical Treatment Protocols for radiation accident victims) is to assign a score based upon clinical and routine laboratory findings ***[Table 23 (page 71)]***. Integration of clinical information regarding the severity of signs and symptoms with changes in peripheral blood counts permits one to assess hazard in quantitative terms.

51. A “response category” is assigned to each victim, determined by the highest degree of severity in any of the signs or symptoms. Using this information and results of hematologic monitoring, victims can be triaged to the ambulatory setting, routine care medical/surgical floor, intensive care unit or transplantation unit.

52. Some psychological symptoms, ranging from insomnia and hypervigilance to social withdrawal will be there. Posttraumatic stress disorder may occur among victims, families, and friends. High-risk victims include children, pregnant women, mothers of young children and victims with a prior medical history of psychiatric disorders. Clinical psychologist/psychiatrist should be involved in counselling of these patients from the beginning for optimal results.

Management of ARS

53. Treatment of the ARS is not indicated when exposure dose is very low. Obtaining a history and physical examination, removal of external contamination, dose estimation, supportive care (including psychological support of the patient and family), symptomatic treatment, and replacement of fluids and electrolytes should be the earliest goals of medical management. Reverse isolation is needed for patients with whole body doses greater than 2–3 Gy. Antacids and H2 blockers should be avoided to maintain gastric acidity, with using of sucralfate to prevent stress ulcers. Patients of prolonged severe granulocytopenia with the increased risk of bacterial and fungal infection, supportive care should include the use of reverse barrier nursing (sterile rooms including mobile laminar air flow rooms) and prophylactic antimicrobials. Blood products support is required for patients with severe bone marrow damage resulting from radiation induced aplasia. Fortunately, this complication does not typically occur before 2-4 weeks, during which time blood donors may be rapidly identified. All cellular products should be leukoreduced and irradiated (25 Gy) to prevent transfusion-associated graft-versus-host disease (TA-GVHD), a life-threatening form of acute graft versus-host disease (aGVHD). In incident involving a nuclear power plant or a device explosion, it is probable that radioiodine will be released. Early prophylaxis with potassium iodide is indicated in the latter situation to protect thyroid which is very radiosensitive. Initial management based on METREPOL scoring has been summarized in ***Table 20***.

Score 1:	No cytokine Outpatient clinical monitoring. Blood count: every day for 6 days, then once a week for 2 months.
Score 2:	Cytokines (curative) G-CSF/KGF should be used as early as possible for 14–21 days. EPO and stem cell factor questionable. Symptomatic treatment for gastrointestinal damage. If severe aplasia: protected environment. Accidental radiation exposure is generally heterogeneous; some under-exposed/protected regions of bone marrow can give rise to endogenous hematopoietic recovery.

Score 3:	Cytokines (until reappraisal of score) Palliative/symptomatic treatment. Re-evaluation during the first week based on laboratory or clinical. Symptoms revealing irreversible organ damage/disfunction.

G-CSF Granulocyte Colony Stimulating Factor, KGF Keratinocyte Growth Factor, EPO Erythropoietin.

Table 20. Initial Therapeutic Management.
(Adapted from: Gorin NC, Fliedner TM, Gourmelon P, et al. Consensus conference on European preparedness for haematological and other medical management of mass accidents. *Ann Hematol* 2006;85:671–9)

SPECIFIC THERAPEUTIC APPROACHES

Use of Colony Stimulating Factor

54. Currently hematopoietic colony-stimulating factors which are available are recombinant forms of granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF), it's Pegylated form (PEG-G-CSF or pegfilgrastim), Erythropoietin (EPO), Thrombopoietin analogues and Thrombopoietin receptor agonists like Eltrombopag. The rationale for the use of CSFs in this setting is derived from three aspects: their enhancement of neutrophil recovery in oncology patients, their perceived benefit in a small number of radiation-accident victims, and, most importantly, the survival benefit observed in several carefully conducted, prospective trials in canines and nonhuman primates exposed to radiation. The value of CSFs in the treatment of radiation induced marrow suppression lies in their ability to increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils. G-CSF and GM-CSF have been shown to hasten neutrophil recovery by approximately 3-6 days in humans after intensely myelotoxic therapies, including bone marrow and stem cell transplantation. Both G-CSF and GM-CSF have been used in radiation accident victims, and neutrophil recovery appeared to have been hastened in 25 of 28 cases in the registry maintained by REAC/TS. It suggested that CSF should be initiated as early as possible in those exposed to a survivable whole-body dose of radiation who are at risk of the hematopoietic syndrome (> 3 but < 10 Gy) and in any patient who becomes neutropenic, defined as an absolute neutrophil count < 500. Use of these colony stimulating factors has been summarized in ***Table 21***. New directions are under evaluation which include novel cytokine therapies like interleukin-7, keratinocyte growth factor, and thrombopoietin or its analogues. Use of erythropoietin (EPO) anemia therapy after radiation injury is not recommended even though probably safe as anemia is not generally life-threatening in this situation.

Cytokine	Adult	Pediatric
G-CSF or Filgrastim	5 µg/kg per day as a SC injection started as early as possible and continued until ANC >1,000	5 µg/kg per day as a SC injection started as early as possible and continued until ANC >1,000

Pegylated G-CSF or Pegfilgrastim	Give 6 mg SC x 1 dose	For adolescents > 45 kg: Give 6 mg SC x 1 dose
GM-CSF or Sargramostim	250 µg/m^2 per day started as early as possible and continued until ANC > 1,000	250 µg/m^2 per day started as early as possible and continued until ANC > 1,000

G-CSF Granulocyte colony stimulating factor, GM-CSF Granulocyte macrophage colony stimulating factor, SC subcutaneous, ANC Absolute neutrophil count.

Table 21. Use of colony stimulating factors post radiation exposure (see text)
(Adapted from: Dainiak N, Waselenko JK, Armitage JO, MacVittie TJ, Farese AM. The hematologist and radiation casualties. Hematology Am Soc Hematol Educ Program. 2003;473-496.)

Role of Allogeneic Haematopoietic Stem Cell Transplant (HSCT)

55. In haematopoietic syndrome post radiation, HSCT seems to be lifesaving for patients with severe bone marrow aplasia. However, the use of HSCT in these patients is complicated by a variety of factors. Radiation exposure is often not homogeneous. For example, patients might have bone marrow ablative doses of radiation to parts of their body, but other bone marrow containing structures might be minimally or not irradiated. This can occur when the patient was partially shielded. Concomitant burns or traumatic injuries can greatly complicate the care of patients who also have bone marrow failure induced by radiation. Dainiak et al., in a compilation of 58 patients who had potentially lethal radiation exposure, the major causes of deaths were burns (55%), haemorrhage (41%), infection (15%), and acute respiratory distress syndrome (15%). In many patients, more than one major factor contributing to death was identified. It is important to emphasize that although a sample for HLA typing should be taken immediately and the search for a potential donor initiated early, the transplant itself should not be carried out before a minimum observational period of 14 to 21 days has elapsed. The final decision regarding transplant should be considered after taking into account the source of irradiation, individual circumstances, additional injuries and previous diseases.

56. Doses below 3 Gy of uniform total body exposure would usually not be fatal with excellent nursing care. The upper dose limit that can be survived without HSCT might be in the range of 7–8 Gy with prompt use of hematopoietic growth factors and aggressive supportive care. Doses in excess of 10 Gy are likely to be fatal because of injury to organs other than bone marrow. Thus, there is not a large “window” of opportunity for hematopoietic stem cell transplantation. All of this is complicated by the difficulty in accurately determining the patient’s dose of radiation. The most favourable situation would be a patient who had autologous stem cells stored for some other reason which in most of the time will not be there except in planned military scenario. Search for a HLA match donor either in family or in any registry may have its own inherent obstacles. However, these can be overcome in isolated small accidents where the logistics can be mobilised for selected few victims. Points to be considered for HSCT have been summarized in ***Table 22***.

- HSCT is not an emergency.
- If severe bone-marrow aplasia persists despite cytokines for more than 14 days, possibility of an HSCT is considered.
- Criteria for transplant:
  - Severe marrow aplasia persisting 14–21 days
  - No residual hematopoiesis
  - No irreversible organ damage
- Type of graft:
  - Bone marrow
  - Peripheral blood
  - Cord blood
- Donor in the following order of priority:
  - Identical twin
  - Family member matched for a minimum of 7/8 HLA antigens
  - Unrelated donor matched for 9/10 antigens
  - Cord blood matched for at least 4/6 antigens
- Source of stem cells (minimum doses of infusion):
  - 2×10^6 CD34/kg (peripheral blood)
  - 2×10^8 nucleated cells/kg (bone marrow)
  - 3×10^7 nucleated cells (cord blood)

Table 22. Key Points for Hematopoietic Stem Cell Transplantation (HSCT)
(Adapted from: Gorin NC, Fliedner TM, Gourmelon P, et al. Consensus conference on European preparedness for haematological and other medical management of mass accidents. *Ann Hematol* 2006;85:671–9)

57. Available data to treat radiation injury with HSCT are not encouraging. As reported by Densow D et al., 29 patients who underwent HSCT after accidental radiation overdose, the median survival was only 33 days. All 29 patients had some evidence of engraftment 14 days after the transplant, but in none of the surviving patients engraftment was stable. In 7 of the 29 patients (24%) graft-versus-host disease (GVHD) was the underlying cause of mortality.

CHAPTER 5

Radiological Accidents And Lessons Learnt

Chapter- 5

RADIOLOGICAL ACCIDENTS AND LESSONS LEARNT

58. Numerous Radiological accidents have taken place in the past and have resulted in grave local and global implications. An analysis of these events is essential to understand the evolution of these accidents and the chronological flow of detrimental events thereafter and how the detrimental effects were mitigated.

I. GOIÂNIA, BRAZIL (1987)

1. **Brief of Accident**

(a) Date 13 Sep 1987

(b) Location: Institute Goiano de Radioterapia (IGR) (a private radiotherapy institute)

(c) Medical application: Teletherapy

(d) Equipment: Cesapan F-3000 Radiotherapy Unit (***Figure 9.)***

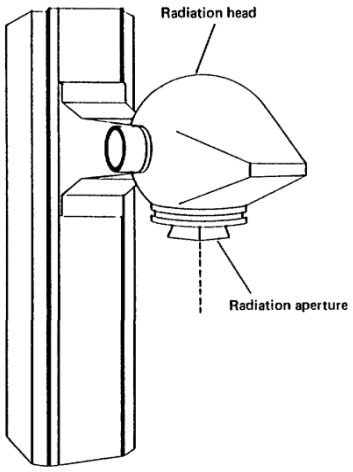

Figure 9. **Cesapan F-3000 Radiotherapy unit.**

(e) Radioactive Source: Cs^{137} (Radioactive Caesium Chloride (made from radioisotope Caesium-137)

(f) No of affected persons: 249 (contaminated of which 129 were Internally contaminated)

(g) No of fatalities: 4

2. **Chronology of events**

(a) The institute operated two radiotherapy units, a Co^{60} and Cs^{137}.

(b) Institute moved to a new location and only took the Co 60 unit and left the Cs137 radiotherapy unit behind as it ownership was disputed. The same was not informed to the National Nuclear Energy Commission (CNEN), Brazils regulatory authority. In the interim the building became delipidated ***(Figure 10)***.

(c) The abandoned Radiotherapy unit was stolen and dismantled the by Scrape dealers in their residential premises there by rupturing the source capsule on 13 Sep 1987.

(d) The same was sold to a junkyard owner (on 18 Sep 1987), who in turn exposed his family and friends to the source and also distributed the powder to many acquaintances. The blue glow emanating from the powder it was shared by many and even applied on the body. The source was then sold off to another junkyard.

(e) The two individuals who stole the radiotherapy unit initially developed symptoms of vomiting and diarrhea (on 13 Sep 1987) which aggravated with one of them also developing a reddish rash on the hand and reddish skin lesion appeared in the two individuals who had stolen and ruptured the source capsule. Medical consultation was taken and were diagnosed with food poisoning and allergic.

(f) Simultaneously many people who came in contact with the source/ powder started falling ill. The junkyard owner's wife who herself was not well took Dr Paulo Roberto Monteiro at Vigilancia Sanitaria (Hospital) (on 28 Sep 1987)

(g) Dr Paulo contacted a physician at Tropical Disease Hospital, where the patients presenting with symptoms after exposure to the source were already being seen, however were being diagnosed to have contracted a Tropical Disease. Finally, a doctor at the Department of Environment of Goias State was contacted who in turn asked a Licensed Medical Physicist, known personally and on a chance visit to Gioania, for help. The Physicist with a borrowed Scintillation detector found extensive contamination of the Junkyard and the surrounding areas.

Figure 10. The delipidated building of from where the radiotherapy unit was stolen.

(h) Government agencies including CNEN were informed. A coordinated response with multinational support was instituted.

(i) Hexacyanoferrate (Prussian Blue, Radiogardase) was used for decorporation for the first time.

3. **Contributing factors:**

(a) Inadequate safety of the abandoned radiological equipment.

(b) Lack of notification by the end user to the national regulatory authorities on relocation and leaving behind the radiotherapy unit.

(c) Lack of public knowledge about radiation source and illness.

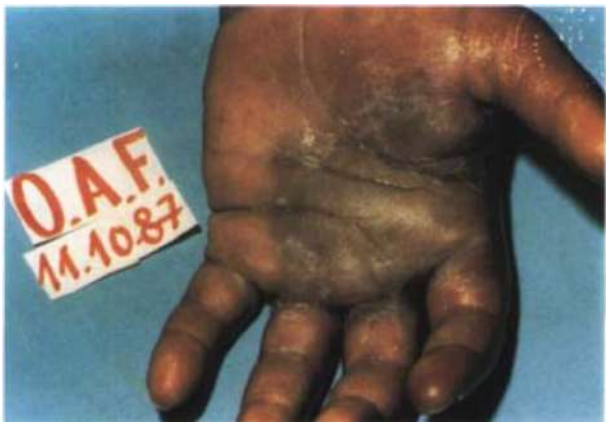

Figure 11. Lesion on the hand of one of the scrap scavengers who stole and broke open the radiotherapy unit.

4. **Strengths:**

(a) A radiological accidents cooperation program between IAEA and Brazil where in manpower training and response infrastructure were developed. This resulted in a well planned and coordinated response to the accident.

(b) Multinational cooperation from Argentina, France, Germany, Hungary, Israel, Netherlands, USSR, UK, USA along with experts from IAEA and WHO shared manpower and resources.

Figure 12. Demolition and Decontamination of the Scrap Dealer's House.

Figure 13. Temporary Storage of the Radioactive Waste Collected from the Incidence Site.

5. **Lessons learnt:**

(a) Regular inspection of radiological equipment by government agencies and timely information/ report returns by the end user of any alteration in status of radiological equipment.

(b) General awareness of the public about radiation emergencies.

(c) Adequate training of manpower and infrastructure development to respond to any radiological emergency.

(d) Regional centers to coordinate and deliver emergency response during radiological accidents in each continent.

(e) Directory/ record of resource persons/ experts to be contacted in any radiation emergency.

(f) Robust civil engineering infrastructure for decontamination process.

II. VENTANILLA, PERU (2014)

1. **Brief of Accident**

(a) Date 14 Feb 2014

(b) Location: Chemical Plant construction site, Ventanilla, Peru

(c) Industrial application: Non-destructive testing (NDT) of Pipe Joints using Industrial Radiography (Gammagraphy)

(d) Equipment: Sentinel Model 880 Delta, serial number D5188. ***(Figure 14.)***

Figure 14. Source projector used during the accident

(e) Radioactive Source: Ir^{192}

(f) Service provider: Industrial Radiography company (with valid license)

(g) No of affected persons: 03

(h) No of persons handling radiological equipment – 03

(i) Worker I – Licensed to handle radiography equipment

(ii) Worker II - Licensed to handle radiography equipment

Licensed as Radiation Protection Officer (License expired in 2013)

(ii) Worker III - Licensed to handle radiography equipment

Licensed as Radiation Protection Officer (License expired in 2013)

2. **Chronology of events**

(a) 'Worker 1' – hung the guide tube around his neck, with its distal part and collimater inside the left vest pocket ***(Figure 15)***. Pig tail containing radioactive source did not return to the safety position on the shielded radiography equipment, but instead remained in the collimator. Personal dosimeter did sound alarm but it was not heard due to noisy work

environment. On moving out of the noisy environment the worker heard the alarm, moved the source back to the safety position and informed the manager. Initial Medical evaluation undertaken at the Primary health Center. Worker I admitted at the hospital for further evaluation. Acute Radiation Syndrome (ARS) not expected as the estimated dose for worker 1 was less than 1 Gy.

Figure 15. Placement of Guide tube and Collimator in vest pocket.

(b) Local radiation injury (LRI) of area surrounding Lt Upper Thigh and Anatomical projection of Lt Hip.

(c) IAEA assistance under Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency requested by Peruvian authorities (24 Apr 2014).

(d) IAEA response and assistance network (RANET) through experts from Brazil, France and Biodosimetery from Argentina provided (28 Apr 2014). ISO 19238:2004 (now replaced by ISO 19238:2014) Radiation Protection — Performance criteria for service laboratories performing biological dosimetry by cytogenetics.

(e) Second request for IAEA assistance requested for treatment of Worker 1 (09 Jun 2014). Patient shifted to Brazil 21 Jul 2014. Underwent treatment through RANET (Experts from France, Brazil and IAEA). Local dose estimation was done by IRSN using radiation–material interaction MCNPX Monte Carlo computer code Multidisciplinary approach using dosimetry guided surgery, administration of mesenchymal stem cell (MSC) therapy, physiotherapy, hyperbaric oxygen therapy, nursing care and nutritional and psychological support. (“MSCs have been used in severe LRI cases, such as those related to the industrial radiography accidents in Nueva Aldea (2005) ; Dakar (2006); Francisco de Orellana (2009); Turmero (2010); and

Chilca (2012–2013); as well as the radiotherapy accident in Epinal (2007). These experiences were the basis for the use of MSCs in the treatment of Worker 1").

3. **Contributing factors:**

(a) Lack of safety and radiation protection procedures (equipment failure-failure of the pigtail to return to the safety opposition in the radiography equipment.

(b) Inadequate use of radiation detector survey meters.

(c) Inadequate use of personal alarm dosimeters.

4. **Strengths:**

(a) Complete integration of medical efforts and mobilization of resources coordinated by IAEA.

(b) Coordinated sharing and transfer of knowledge among international community.

5. **Lessons learnt:**

(a) Cultivate safety culture

(b) Protocols to be followed religiously

(c) Supervised hands on training of equipment handlers

(d) Ensure safety equipment availability

(e) Periodic retraining and assessment of human resource

(f) Preventive equipment maintenance

(g) Regulatory authorities' empowerment

(h) Mandatory Comprehensive Health for radiation workers

(i) Capability development for specialized tests (Biodosimetry)

(j) Seamless regional, national and international coordination [under Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency, INFCIRC/336, IAEA, Vienna (1986)].

III. MAYAPURI, DELHI, INDIA (2010)

1. **Brief of Accident**

(a) Date : Mar 2010

(b) Location: Scrap Market, Mayapuri, New Delhi

(c) Scientific application: Research

(d) Equipment: Gamma Cell Model 220 ***(Figure 16.)***

Figure 16. Gamma Cell Model 220

(e) Radioactive Source: Co^{60}

(f) No of affected persons: 08

(g) No of fatalities: 01

2. **Chronology of events**

(a) Dept of Chemistry, Delhi University had acquired a Gamma Cell Model 220 from the Atomic Energy of Canada Limited (AECL) in 1969.

(b) The equipment was sold to a scrap dealer of Mayapuri scrap market in 2010, who dismantled it. He found pencils of Co^{60} inside it and kept them in his shop thinking them to be of value ***(Figure 17.)***. The scrap shop owner and his 07 workers received variable exposure over a period of end march to early April 2010 while working in the shop.

(c) The Scrap Shop owner reported to the Emergency Department of a government tertiary care hospital with symptoms of upper limbs hyperpigmentation, loss of hair, nausea and weakness. Acute Radiation Syndrome was provisionally diagnosed. Though the patient subsequently reported to a tertiary hospital, the national agencies were alerted.

(d) Proactive action was taken to identify the coworkers who too were symptomatic after the exposure. All were transferred and managed at tertiary care hospital.

(e) Bhabha Atomic Research Center (BARC) and Defense Research and Development Organization (DRDO), National Disaster Management Authority (NDMA) the three government agencies played a key role in the management. Dept of Hematology, Army Hospital Research & Referral (AH R&R) played a key role in providing much needed clinical expertise to facilitate the medical management of the cases.

Figure 17. The Scrap Shop where the Source Radioactive Scrap was Stored.

(f) Elaborate measures were undertaken to ensure decontamination of the contaminated areas in the Mayapuri Scrap Market.

Figure 18. Shielded Flask Used for Safe Collection and Transport of Radiological Material.

3. **Contributing factors:**

(a) Inadequate protocol for disposing radiological equipment.

(b) Lack of public knowledge about radiation source and illness.

4. **Strengths:**

(a) Timely diagnosis and management of the patients.

(b) Well coordinated collective efforts by the regulatory, healthcare and disaster management authorities.

5. **Lessons learnt:**

(a) Regular updating of radiation source inventory nationally.

(b) General awareness of the public about radiation emergencies.

(c) Adequate training of staff at academic centers on safety and administrative aspects of radiation source management.

(d) eLORA (e-Licensing of Radiation Applications) an automated regulatory process developed by the Atomic Energy Regulatory Board.

CHAPTER 6

Protection of Health Care Providers

Chapter- 6

PROTECTION OF HEALTH CARE PROVIDERS

59. All medical personnel working in the emergency department tending to radiation victims will invariably be exposed to radiation and likely to get contaminated. Necessary training at a regular interval will ensure their desirable response at the time of need for availability of radiation safety officers will not be forthcoming in dire situations. Each medical professional must know the three basic concepts of protection from radiation i.e., time, distance and shielding. It must be reiterated that the exposure will be limited but a likely possibility with either or both external, internal contamination which in turn can be spread to others in the ER. All individuals must have a personal dosimeter in situ and must be monitored by the radiation safety officer frequently. Ready availability of decontamination facility must be there to tide over any mal occurrence.

60. Liberal availability of Personal protective equipment as under should be there:
- (a) Coveralls or surgical scrub suits
- (b) Plastic aprons
- (c) Surgical caps
- (d) Plastic or rubber gloves
- (e) Shoe covers
- (f) Respiratory protection devices (e.g. N95 mask or any other that filters 95% or more of airborne particulates, surgical masks and full-face masks can be used but these have lower filtering rates)
- (g) Eye protection equipment
- (h) Tape to close open ends of clothing
- (i) Personal dosimeters

61. Radiation detectors should be invariably available for ready monitoring of medical personnel. The following can be part of the inventory:
- (a) Geiger–Müller survey meter (for beta/gamma radiation)
- (b) Zinc sulphide scintillation survey meter (for alpha radiation)
- (c) Ion chamber (for gamma radiation)
- (d) Sodium iodide scintillation survey meter (for gamma radiation)
- (e) Spectrometers (for identification of radionuclides)
- (f) Whole body counters, lung and thyroid counters.

62. To ensure contamination control the following should be available:
- (a) Plastic sheets and paper sheets for covering floor
- (b) Tape
- (c) Rope
- (d) Radiation area signs (e.g., ‘Do not Enter’)
- (e) Radiation tags, radiation tape for marking areas
- (f) Plastic bags (various sizes) for collecting waste or contaminated clothes
- (g) Adhesive labels and tags for labelling contaminated samples.
- (h) Decontamination
- (i) Scissors (not used for cutting hair)
- (j) Soap, detergents, shampoo
- (k) Soft brushes or sponges

(l) Physiological saline solution
(m) Water or solution for wound irrigation
(n) Eyewash solution
(o) Nail brushes
(p) Nail clippers
(q) Hair clippers
(r) Drapes and masking tape for covering non-contaminated skin or area during decontamination
(s) Indelible felt pens for marking contaminated spots
(t) Data forms (e.g., decontamination forms)
(u) Large towels and clean patient gowns or clothing

63. Equipment and supplies used for decontamination have to be isolated and kept in plastic bags or containers with radiation labels and appropriately checked for radiation dose rate, both at the surface and at different distance levels. If possible, medical equipment can be decontaminated for safe re-utilization; otherwise, it will have to be dealt with as radioactive waste and stored in accordance with the local legislation.

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Important Contacts/Resources

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2. IAEA Regional Office in Japan
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3. IAEA, Division of Human Health
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4. WHO Headquarters
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5. WHO Regional Office for the Western Pacific
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6. National Council on Radiation Protection and Measurements
   7910 Woodmont Avenue, Suite 400,
   Bethesda, MD 20814-3095
   Tel: (301) 657-2652
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   Email: NCRPpubs@NCRPonline.Org

7. Radiation Emergency Assistance Center/Training Site REACTS/TS
   Tel: 865-576-3131
   After-hours number865-576-1005 (Ask for REAC/TS)
   Email: reacts@orau.org

8. The European Society for Blood and Marrow Transplantation (EBMT)
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Ready Reckoner

The following Videos may be reviewed for better understanding at the following link https://orise.orau.gov/resources/reacts/guide/procedure-demonstrations.html accessed on 13 Aug 2020.

1. Personal Protective Equipment – Donning
2. Removing Contaminated Clothing
3. Wound Decontamination
4. Intact Skin Decontamination
5. Removing Personal Protective Equipment: Doffing

METREPOL (MEDICAL TREATMENT PROTOCOLS FOR RADIATION ACCIDENT VICTIMS) SCORING GUIDE

	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	0	+/-	+++; before 3 h
Asthenia	+	++	+++
Nausea	+	+++	++++
Vomiting per 24 h	Maximum 1	1–10	Above 10; intractable
Diarrhea/number of stools per 24 h	Maximum 2–3; bulky	2–9; soft	Above 10; watery
Abdominal pain	Minimal	Intense	Excruciating
Headache	0	++	Excruciating; signs of raised ICP*
Temperature	Below 38 °C	38–40 °C	Above 40 °C
Blood pressure	Normal	Normal; possible temporary decrease	Systolic below 80 mm hg
Temporary loss of consciousness	0	0	+/coma
Depletion of blood lymphocytes At 24 h At 48 h	 Above 1500/µl Above 1500/µl Outpatient monitoring	 Below 1500/µl Below 1500/µl Hospitalization for curative treatment	 Below 500/µl Below 100/µl Hospitalization multi-organ

* ICP Intra Cranial Pressure

Table 23. Primary Scoring Based on METREPOL During First 48 h (para 50, page 44).

(Adapted from: Gorin NC, Fliedner TM, Gourmelon P, et al. Consensus conference on European preparedness for haematological and other medical management of mass accidents. *Ann Hematol* 2006;85:671–9)

ALGORITHM : THERAPEUTIC MANAGEMENT ACUTE RADIATION SYNDROME

Beyond the first 48 hrs, a second patient scoring is done by organs (Haematopoietic, Gastrointestinal, Cutaneous, Neurovascular) according to the METREPOL document for therapeutical management and Multiple Organ Failure (MOF) prediction.

CYTOKINES	HEMATOPOEITIC STEM CELL TRANSPLANT (HSCT)
SCORE-I : Monitoring, No Cytokine - Outpatient clinical Monitoring - Blood count day 1-2 and then once a week for 2 months	**Background** - HSC transplantation is not an emergency. - It is crucial to avoid GVHD in order not to compromise an endogenous recovery. - If severe aplasia persists under cytokines for more than 14 days, the possibility of an haematopoietic stem cell (HSC) transplantation is discussed (as below).
SCORE II : Cytokines (curative) - G-CSF (Pegylated or not) should be used within 48 hrs or as soon as possible until neutrophil recovery (ANC > 0.5 x 10^9 /L). EPO and TPO agnoists can be used if needed. Routine marrow failure support with antibiotics, blood products as per routine haemato-oncology care. - Symptomatic treatment of gastrointestinal damage. - If severe aplasia Protected environment. - Accidental radiation exposure is generally heterogeneous. Some under-exposed/protected regions of bone marrow can give rise to endogenous haematopoietic recovery	**Criteria to Transplant** - Severe marrow aplasia persisting 14 - 21 days despite cytokines. - No residual haematopoiesis on bone marrow biopsy. - No other irreversible organ damage. - Treated or controlled infection, if present
SCORE III : Cytokines (Until reappraisal of score) - Patients to be treated as score II until it is clear that they are score III. - Palliative and end of life care to be initiated. - Re-evaluation during the first week based on laboratory or clinical symptoms revealing irreversible organ damage or multi organ failure	**Graft** **Type of graft:** **-** Bone marrow. - Peripheral blood HSC (depleted or not). - Cord blood. **Donor in the following order of priority** (as per current transplant criteria): - HLA-identical sibling. - HLA-identical unrelated donor. - Cord blood > 4/6 matched. - Haplo-identical. **Doses of cells to be grafted:** At least: - $2x10^6$ CD34 cells. kg^{-1} (peripheral blood). - $2x10^8$ nucleated cells.kg^{-1} (bone marrow). - $3x10^7$ nucleated cells (cord blood). **Conditioning and GVHD Prevention (as per current transplant criteria):** **-** Reduced intensity conditioning. No Methotrexate

Adapted from European group for Blood Marrow Transplantation (EBMT). European approach for the medical management of mass radiation exposure. [Internet]. 2017 [updated 2017; cited 01 Nov 2020]. Available from: https://www.ebmt.org/sites/default/files/2018-03/EBMT%20Nuclear%20Accident%20Committee%20Pocket%20Guide%202017.pdf

The First 48 hours

Decontamination after stabilisation.

Life-threatening wounds and burns should be treated first.

Radiation dose review comes later – Irradiation is not contamination – An irradiated person is not a source of radiation.

Acute Radiation Injury

The severity of prodromal clinical features is indicative of probable significant injury.

- Extensive and immediate erythema.
- Early Transient Incapacitation Syndrome
- (temporary loss of consciousness).
- High fever.
- Hypotension; Early Vomiting.
- Immediate diarrhoea.

Accident Characterisation

- Extensive and immediate erythema.
- Inquiry: circumstances of the accident (is irradiation +/-contamination present; use contamination monitoring device), source characteristics, source-victim geometry, duration of exposure, shielding, homogeneous / heterogeneous irradiation.
- Labelling and storage of personal belongings and clothes, biological material (hair, nails).

Urgent Sampling

- Extensive and immediate erythema.
- Blood cell counts (+ differentials) every 4-8 hours for the 1st 24 hours, 12-24 h every day after.
- Red cell group typing
- Standard biochemistry + amylasemia.
- Urine and faeces if radionuclide contamination is suspected
- Store serum and cells or DNA for further analyses including HLA typing.
- Chromosome aberrations on blood lymphocytes (biodosimetry) (15 ml + heparin). Seek advice from national / international biodosimetry networks as soon as possible.

Primary Scoring (See Table-20)

Score -I	Score -II	Score -III
Outpatient monitoring	**Hospitalisation for curative**	**Hospitalisation (MOF predicted)**

Adapted from European group for Blood Marrow Transplantation (EBMT). European approach for the medical management of mass radiation exposure. [Internet]. 2017 [updated 2017; cited 01 Nov 2020]. Available from: https://www.ebmt.org/sites/default/files/2018-03/EBMT%20Nuclear%20Accident%20Committee%20Pocket%20Guide%202017.pdf