INTRODUCTION to RADIATION BIOLOGY and RADIATION MEDICINE

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Goals

This session will introduce participants to the basic knowledge about radiation medicine. After a short introduction on the underlying physical and biochemical processes - with an focus on the interaction of radiation with matter - the biological and health effects of ionizing radiation will be discussed.

This paper will focus primarily on basic knowledge in "radiation biology" and "radiation medicine"; therefore it is neither sufficient nor intended to replace detailed education about radiation protection, radiation biology or the medical management of the acute radiation syndrome.

Generic issues of emergency response, like command & control (e.g. ICS), communication and registration etc. cannot be covered within this short overview.

Outcomes/Objectives

On completion of this session, participants will:

1. have a basic understanding on the nature of ionizing radiation and its interaction with matter,
2. understand the health effects of ionizing radiation and their categorization in **stochastic** and **deterministic** effects,
3. know the characteristics of the **acute radiation syndrome** and distinguish between **syndroms** (hematopoietic, gastrointestinal, and cerebrovascular) and **phases** (prodromal, latent, manifest illness),
4. know about the more recent approach of the "**METREPOL**" system, describing the acute radiation syndrome by the effects in four critical early reacting **organ systems** (neurovascular, haematopoietic, cutaneous and gastrointestinal),
5. be able to define and discriminate **exposition** and **contamination** and know about protection against,
6. be able to draw on available literature on all topics mentioned.

Core Content

1. Ionizing Radiation and its Health Effects

Part 1 will give an short overview about the nature of ionising radiation and describe the health effects of it.

If you need more information to improve your knowledge, you can consult the following resources provided by national and international organisations; they contain simple overviews as well as in-depth discussions (the latter are marked with * or **):

Ionizing Radiation:

http://www.who.int/ionizing_radiation/about/what_is_ir/en/index.html

http://www.ead.anl.gov/pub/doc/ionizing-radiation.pdf

http://www.osha.gov/SLTC/radiationionizing/

http://www.iaea.org/Publications/Booklets/RadPeopleEnv/radiation_booklet.html *

http://www.iaea.org/Publications/Booklets/RadPeopleEnv/index.html *

http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=484&tid=86 *

http://www.epa.gov/radiation/docs/402-f-06-061.pdf

Non-Ionizing Radiation:

http://www.epa.gov/rpdweb00/understand/index.html#nonionizing

http://www.osha.gov/SLTC/radiation_nonionizing/index.html

http://www.who.int/topics/radiation_non_ionizing/en/

Quantities and Units of Ionizing Radiation:

http://www.ccohs.ca/oshanswers/phys_agents/ionizing.html

Interaction of Radiation with Matter:

http://hyperphysics.phy-astr.gsu.edu/HBASE/mod4.html

Health Effects of Ionizing Radiation:

http://www.osha.gov/SLTC/radiationionizing/index.html

http://www.epa.gov/radiation/understand/health_effects.html

http://web.princeton.edu/sites/ehs/osradtraining/biologicaleffects/page.htm *

http://www.atsdr.cdc.gov/toxprofiles/tp149-c3.pdf **

A wide range of materials is available from the website of "Radiation Emergency Medical Management" (http://www.remm.nlm.gov/), which is recommended for further reading.

Part 1 is mainly based on ICRP Publication 60 from 1991 ("1990 Recommendations of the International Commission on Radiological Protection"); tables and illustrations are created by the author, if not indicated otherwise. Other references are given in the text.

1.1 Radioactivity and Ionising Radiation (modified from ICRP 60)

Atoms can be thought of as consisting of a positively charged nucleus surrounded by negatively charged electrons. The nucleus is made up of protons (positively charged) and neutrons (electrically neutral); the number of protons determines the nature of the atom and the number of neutrons determines the particular isotope. While many nuclides in nature are stable (depending on their ratio of neutrons to protons) and maintain their form and composition indefinitely, many others are unstable.

These **unstable nuclides** return to stability by the emission of a charged particle (alpha particle, beta particle or positron) from the nucleus at a defined, characteristic rate. They are then called radioactive nuclides or simply **radionuclides**. Many different radionuclides exist naturally especially among atoms of high atomic number.

The decay rate of radionuclide is characteristic of that radionuclide and is described by its **half life**. Half-lives range from fractions of a second to billions of years.

The new nucleus formed by the emission of a particle may still be radioactive and emit further particles or may be an excited state and may return to stability by emitting further radiation (gamma radiation) which leaves the nucleus stable but does not alter its composition.

Ionising radiations are radiations that are capable of causing ionisation in the atoms of any medium through which they may pass.

They consist either of high velocity **charged particles** (e.g. alpha particles, beta particles) which may be (primarily) **emitted from radionuclides** or which may arise **secondarily**.

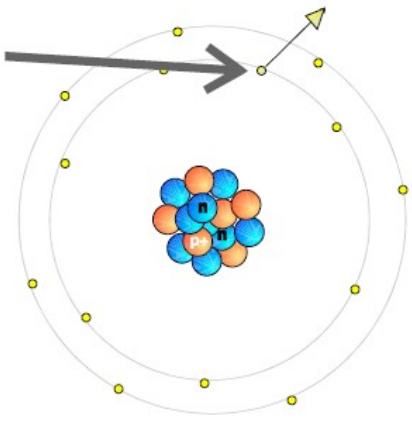
These secondary charged particles (usually electrons or protons) are created, when indirectly ionising radiations such as x-rays (generated artificially), gamma rays (from nuclear transitions) or neutrons expel them from the atoms of the medium. They will cause further ionisation or excitation in the same way as the primary charged particles do.

The processes by which photons (x and gamma rays) eject electrons from atoms include the photoelectric effect, the Compton effect and pair production.

1.2 Interaction of Radiation with Matter

1.2.1 Physical Processes (modified from ICRP Publication 60)

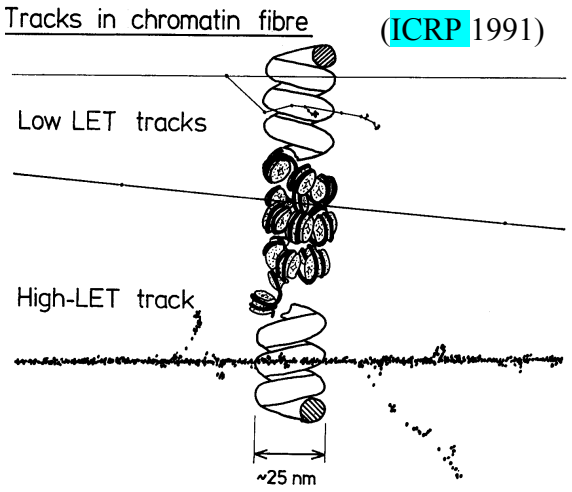
When ionising radiations traverse a medium, the resulting electrical interactions are random and follow the tracks of the charged particles (primary or secondary) bouncing from one interaction event to another as they pass through the medium.



The interaction results in an electron being removed from the atom, thus creating an **ion pair**. An ion pair consists of the removed electron (which may quickly attach itself to another atom to form a negative ion) and the residual nucleus with its complement of remaining electrons

constituting a positive ion. At low doses only a small number of the atoms of a medium will be ionised; most atoms will remain unaffected.

The **microdistribution** of the ionisations produced by ionising radiation depends on the type and energy of the radiation and determines its biological effectivity. The average energy deposited along the track of the particle per unit length is called the **linear energy transfer (LET)** and used to measure this microdistribution.



A sparsely ionising radiation producing few events per micron of track, is known as a "**low LET**" radiation (e.g., x or gamma rays) and will have relatively low biological effectivity.

Radiations producing dense ionisations along the track are known as "**high LET**"-radiation (e.g., alpha particles, protons and recoil nuclei from neutrons, heavy ions) and show higher biological effectivity than low-LET radiation.

radiation			place of origin	place of interaction	ionisation direct / indirect	LET high / low	ω_R	range	examples	consequences in the body
alpha $2p^+, 2n$		particles, charged	atomic nucleus	atomic shell	direct	high	**20**	very short	natural radioactivity	high dose in critical organ (incorporation)
beta e^-		particles, charged	atomic nucleus	atomic shell	direct	low	**1**	short	natural radioactivity	skin damage "beta-burn" (exposition, contamination) high dose in critical organ (incorporation
gamma		photons (electro-magnetic wave)	atomic nucleus	atomic shell	indirect	low	**1**	pene-trating	natural radioactivity	total body irradiation
X-ray		photons	atomic shell "brems-strahlung"	atomic shell	indirect	low	**1**	pene-trating	natural radioactivity, x-ray tube	total body irradiation
n **neutrons**		particles, uncharged	nuclear fission	atomic nucleus (!) ➔activating	indirect	high	**5 - 20** [1)]	pene-trating	nuclear power plant, cosmic radiation	total body irradiation

Table - most important kinds of lonising radiation

[1)] ω_R is energy dependent for neutrons

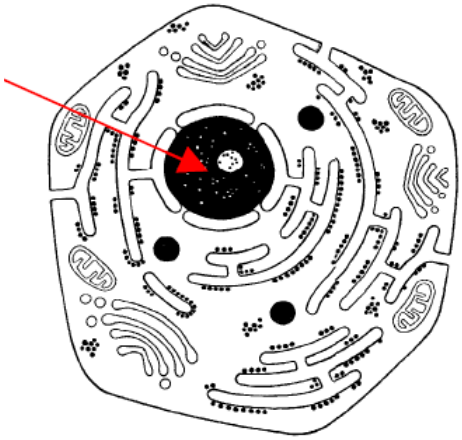
You will be able to assess the biological significance of an irradiation in almost all cases, when you keep in mind, that the **absorption** of radiation energy by matter (or tissue) is the indispensable precondition of any radiation effect. Being penetrated by radiation is not harmful by itself; the portion absorbed by the body is what creates damage.

The process of ionisation necessarily changes atoms, at least transiently, and may thus alter the structure of the molecules containing them. That leads us on to the next step of the process: the chemical effects.

1.2.2 Chemical Processes (modified from ICRP Publication 60)

Molecular changes in form of **breakage of chemical bonds** are the consequence of ionisation. lf the affected molecules are in a living cell, the cell itself will be damaged, if the molecule is critical to the cell's function.

Molecules can be damaged directly (by direct hits). The **most important target** within the cell is the **DNA**. Given the microscopic structure of it you will understand, that direct hits are not very probable. However there is the possibility of indirect chemical damage by induction of free **radicals.**



These can move rapidly in the medium some distance from the site of the original event and cause further chemical changes in the molecules of the medium before they are inactivated.

1.2.3 Biological Processes (modified from ICRP Publication 60)

The molecular changes will manifest themselves over various periods of time and in a variety of ways. The damage to the DNA is the most important consequence of the steps so far.

If the **DNA damage** can be **repaired** (and cells have good repair mechanisms, for life on earth developed in an hostile environment from the beginning), there will be no implications at all.

If the DNA damage prevents the survival or reproduction of the cell, there may be problems for the body in its whole; If enough **cells** in an organ or tissue **are killed**, clinical symptoms and disease will arise.
This type of effect is called "**deterministic**": it is in most cases well known, what symptoms will be produced by what dose, they are "predictable."
This group comprises the ***"acute radiation syndrome" (ARS)*** as well as ***local tissue or organ damage*** and ***teratogenetic*** effects (malformations after irradiation of the embryo in the uterus).

If the repair succeeds only partially and produces a viable but **modified cell** (**misrepair**), this might eventually result in ***cancer*** (if a somatic cell was modified) or in ***mutagenetic*** effects in the offspring (if incorrect information is transmitted by a modified germ cell in the gonads).
These are called the "**stochastic** effects", which cannot predicted for single persons, but only estimated statistically for a population ("stochastic" = involving or containing random variables).

Drawing conclusions about and assessing the risk of stochastic effects is not straightforward, because epidemiological studies cannot provide exactly the information needed (for detailed discussion see ICRP Publication 60). Especially the response of the body to the development of a clone of modified somatic cells (cancer) is complex and influenced by many factors.

Life-shortening found in exposed human populations and in experimental animals after **low doses** has been shown to be caused by excess radiation induced **cancer mortality**; therefore the risk of cancer has emerged as the primary concern at low doses.

The probability or frequency of cancer is related to the received dose, while the severity of a particular cancer is influenced only by the type and location of the malignant condition.
Cancer probability can be reduced by lowering the received dose (even if it cannot be abolished entirely since stochastic effects appear to have no threshold).
Exposure limits for occupational and environmental exposures are therefore a principal component of all radiation protection regulations.

1.3 Deterministic Effects

Stochastic effects express themselves long after the exposure: *cancer* has typically a latency of years (or decades); *hereditary disorders* can only arise if offspring is generated after irradiation. *Teratogenetic* effects (malformations after intrauterine irradiation, which are deterministic) will be visible only after birth of the child.

For these **time** related **characteristics** only the "*acute radiation syndrome" (ARS)* as well as *local tissue or organ damage* can be of (emergency or disaster medicine related) interest after an radiation accident, even if they still have a latency of days or weeks.
That is what is meant, if the term "deterministic effects" is used in context with accidents or with side-effects of radiotherapy.

In many organs and tissues of the body there is a continuous process of **loss and replacement of cells**. There is a wide range of **sensitivities** - the **gonads** and the (blood producing) **bone marrow** are the most sensitive systems.
A minor increase in the rate of loss will be compensated for by an increase in the replacement rate, but if the decrease is large enough - above some level of dose called "threshold" (more strictly: the "**threshold for clinical effect**") - there will be clinically observable pathological conditions caused by loss of tissue function or by the consequential reactions (as the body attempts to repair the damage).

This can result in the death of the individuum, if the affected tissues are essential and the damage is pronounced enough.

Loss of functional cells is the pathophysiological mechanism of radiation damage in an tissue with cell replication ("early reacting organs"). In addition to that, damage to supporting blood vessels may also occur, leading to secondary tissue damage.
The latter mechanism causes damage also in tissues or parenchymatous organs without cell replication ("late reacting"), mainly in form of subacute/chronic **inflammation** or fibrosis (especially in lungs and kidneys).

The severity of acute illness due to effects in early reacting organs will increase with dose, reflecting the number of cells damaged, and **may be reversible**, provided that the damage is not too severe (ICRP Publication 60).

Deterministic effects are avoided in radiation protection procedures by limiting doses to below the threshold dose; the exposure limits intended to reduce the stochastic risk to an acceptable level (see above: 1.2.2) are far below the threshold dose, which makes radiation sickness a very rare event.

1.3.1 Acute Radiation Syndrome (ARS)

The **ARS** occurs after whole-body or significant partial-body irradiation of greater than 1 Gy delivered at a relatively high-dose rate. The **cells with the highest replication rate** are the most sensitive; particularly spermatocytes, lympho-hematopoietic elements, and intestinal crypt cells.
The inherent sensitivity of these cells results in a constellation of **clinical syndromes** that predominates within a predictable range of doses of whole-body or significant partial-body exposure.

The clinical components of the acute radiation syndrome include the ***hematopoietic, gastrointestinal, and cerebrovascular syndromes.*** Each syndrome can be divided into ***4 phases: prodromal, latent, manifest illness***, and ***recovery or death*** (Waselenko et al. 2004)**.**

Depending on the absorbed dose, symptoms appear within hours to weeks, following a **predictable clinical course**. The **prodromal** phase of the acute radiation syndrome usually occurs in the first 48 hours but may develop up to 6 days after exposure. The **latent** phase is a short period characterized by improvement of symptoms, as the person appears to have recovered. Unfortunately, this effect is transient, lasting for several days to a month. Symptoms of **manifest illness** then appear and may last for weeks. This stage is characterized by intense immunosuppression and is the most difficult to manage. If the person survives this stage, recovery is likely. Individuals exposed to a supralethal dose of radiation may experience all of these phases over a period of hours, resulting in early death (Waselenko et al. 2004).

People exposed to radiation will get ARS only if:

- The radiation dose was high
  (doses from medical procedures such as chest X-rays are too low to cause ARS; however, doses from radiation therapy to treat cancer may be high enough to cause some ARS symptoms),
- The radiation was penetrating (that is, able to reach internal organs),
- The person's entire body, or most of it, received the dose, and
- The radiation was received in a short time, usually within minutes (CDC 2005).

The following table (from CDC 2005) provides an overview about syndromes and phases of ARS:

Syndrome	Dose*	Prodromal Stage	Latent Stage	Manifest Illness Stage	Recovery
Hematopoietic (Bone marrow)	> 0.7 Gy *(mild symptoms may occur as low as 0.3 Gy)*	• Symptoms are anorexia, nausea and vomiting. • Onset occurs 1 hour to 2 days after exposure. • Stage lasts for minutes to days.	• Stem cells in bone marrow are dying, although patient may appear and feel well. • Stage lasts 1 to 6 weeks.	• Symptoms are anorexia, fever, and malaise. • Drop in all blood cell counts occurs for several weeks. • Primary cause of death is infection and hemorrhage. • Survival decreases with increasing dose. • Most deaths occur within a few months after exposure.	• In most cases, bone marrow cells will begin to repopulate the marrow. • There should be full recovery for a large percentage of individuals from a few weeks up to two years after exposure • Death may occur in some individuals at 1.2 Gy (120 rads). • The $LD_{50/60}$† is about 2.5 to 5 Gy (250 to 500 rads).
Gastrointestinal (GI)	> 10 Gy *(some symptoms may occur as low as 6 Gy)*	• Symptoms are anorexia, severe nausea, vomiting, cramps, and diarrhoea. • Onset occurs within a few hours after exposure. • Stage lasts about 2 days.	• Stem cells in bone marrow and cells lining GI tract are dying, although patient may appear and feel well. • Stage lasts less than 1 week.	• Symptoms are malaise, anorexia, severe diarrhoea, fever, dehydration, and electrolyte imbalance. • Death is due to infection, dehydration, and electrolyte imbalance. • Death occurs within 2 weeks of exposure.	• The LD_{100}‡ is about 10 Gy (1000 rads).
Cardiovascular (CV) **Central Nervous System** (CNS)	> 50 Gy *(some symptoms may occur as low as 20 Gy)*	• Symptoms are extreme nervousness and confusion; severe nausea, vomiting, and watery diarrhoea; loss of consciousness; and burning sensations of the skin. • Onset occurs within minutes of exposure. • Stage lasts for minutes to hours.	• Patient may return to partial functionality. • Stage may last for hours but often is less.	• Symptoms are return of watery diarrhoea, convulsions, and coma. • Onset occurs 5 to 6 hours after exposure. • Death occurs within 3 days of exposure.	• No recovery is expected.

Table - Acute Radiation Syndromes (from CDC 2005)

* The absorbed doses quoted here are "gamma equivalent" values. Neutrons or protons generally produce the same effects as gamma, beta, or X-rays but at lower doses. If the patient has been exposed to neutrons or protons, consult radiation experts on how to interpret the dose.

† The $LD_{50/60}$ is the dose necessary to kill 50% of the exposed population in 60 days.

‡ The LD_{100} is the dose necessary to kill 100% of the exposed population.

If you want more information about ARS, you can consult the following resources:

http://www.bt.cdc.gov/radiation/ars.asp

http://www.bt.cdc.gov/radiation/pdf/arsphysicianfactsheet.pdf (CDC 2005) *

http://www.annals.org/cgi/content/full/140/12/1037 (Waselenko et al. 2004) **

A more recent publication ("**METREPOL**" **approach** described by Fliedner et al. 2001) identifies four critical early reacting organ systems in which effects can be expected after acute exposure to ionising radiation: the **neurovascular (N), haematopoietic (H), cutaneous (C) and gastrointestinal system (G)**.

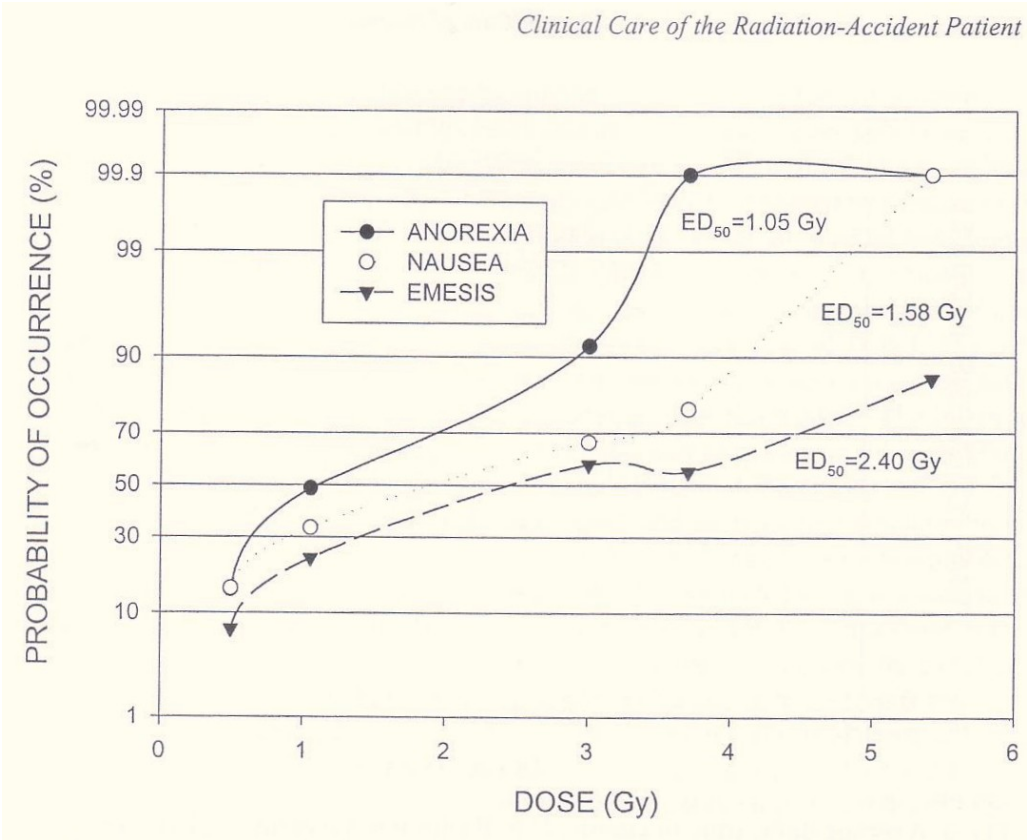
For each system a list of observable characteristic signs and symptoms is used to assess the clinical manifestation of ARS as a function of time; semi-quantitative criteria (see Annex for overview tables) are used to establish an organ specific grading, a grading code and a corresponding **Response category (RC)** to express the overall state and outcome of the radiation accident victim.

A "Patient Accompanying Documentation Sheet" (PADS) is available for standardised documentation (Fliedner et al. 2001; similar: Waselenko et al. 2004); it is reproduced in the Annex to this chapter.

The "latent phase" preceding the "manifest illness" lasts days or weeks.

During the "prodromal phase" right after the irradiation typical symptoms can be observed. Knowledge of these **prodromi** is of critical importance for the recognition of an radiation accident.

Emesis and nausea, which are regarded as neurovascular symptoms, are more frequent and the onset is earlier, the higher the dose (see next page for figures from Ricks et al. 2001).



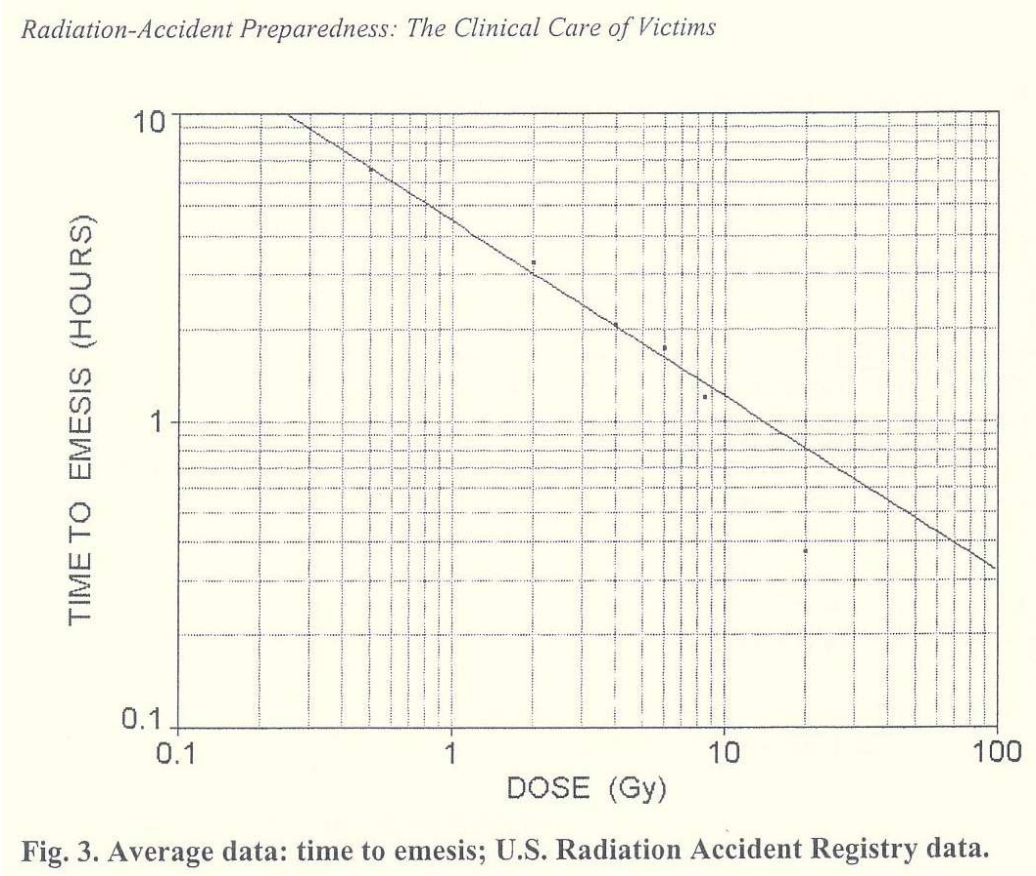


Fig. 3. Average data: time to emesis; U.S. Radiation Accident Registry data.

Figures "Probability of Nausea and Emesis" and "Time to Emesis", from: Ricks et al. 2001

Lymphocyte and granulocyte counts show characteristic response patterns within hours after significant irradiation and can therefore be used to prove or disprove radiation sickness or to predict its severity (see Figure 11 from Fliedner et al. 2001).

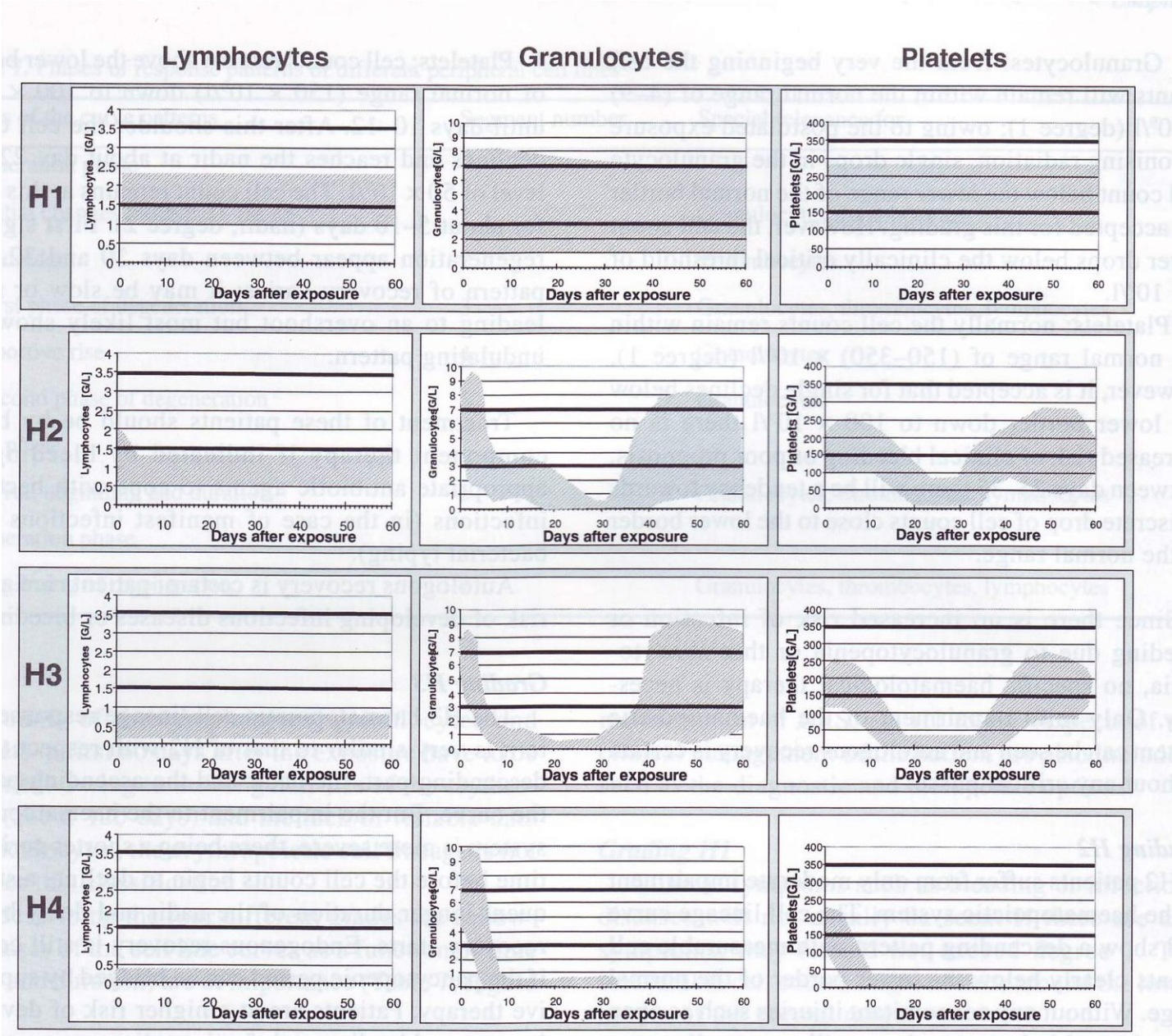


Figure 11. Schematic illustration of different cell line response patterns as a function of time for H1–H4.
from: *Medical Management Of Radiation Accidents - Manual on the Acute Radiation Syndrome,* edited by T M Fliedner, I Friesecke and K Beyrer, The British Institute of Radiology (BIR), London, 2001

Skin lesions ("burns") due to ionising radiation may have an similarity in appearance to thermal burns, their temporal progression is however completely different, for they have also a latency of days or weeks.

Radiation should be considered as possible causation, if a skin lesion with desquamation and epilation is observed, if an erythema was observed in the same location 2 to 4 weeks ago and if there is no history of chemical or thermal burn, insect bite, or known skin disease or allergy (IAEA/WHO 2000).

Epilation or bleeding problems (such as petechia, gingival or nose bleedings) with a history of nausea and vomiting 2 to 4 weeks previously also should ring the alarm bells (IAEA/WHO 2000).

It is important to have a clear picture, **what radiation can do**:

Radiation **can** cause:

- nausea and emesis within hours
- changes in the blood cell count within hours
- severe clinical illness and death within days
- severe skin "burns" within days

Radiation **cannot** cause:

- immediate death
- immediate skin burns

A good summary of the facts, which a medical doctor should remember even if aroused in the middle of the night, is given by the IAEA in cooperation with the WHO (IAEA/WHO 2000): "**How to recognize and initially respond to an accidental radiation injury**", http://www.who.int/entity/ionizing_radiation/a_e/IAEA-WHO-Leaflet-Eng%20blue.pdf or http://www-pub.iaea.org/MTCD/publications/PDF/IAEA-WHO-L-Eng.pdf.

The management of a radiation accident has its difficulties not because of the acuity of the situation - radiation sickness is not an medical emergency demanding immediate lifesaving action. Hazards other than radiation (e.g., fires, explosives, chemicals) represent a much greater immediate health risk.

The patient will however require an unusual and combined **interdisciplinary effort** of many specialties to receive sufficient treatment.

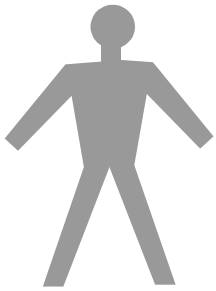
Secondly - there is a **risk to caregivers** that needs to be considered and to be managed. This risk does not exist in all situations; hence it must be determined, in what way a patient was "exposed" to radiation.

1.4 How Radiation affects the Body - and what we can do against it

Radioactive materials present two hazards: **external and internal**.

A radioactive material emitting gamma radiation, which is enclosed by some kind of container, is called a **sealed source**.

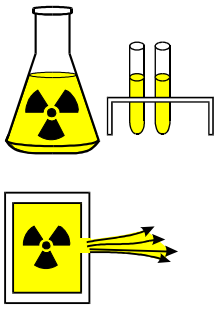
If you come near this source, you will be exposed to radiation, but you will have no direct contact to the radioactive substance itself.
This is called (**external) exposure**.



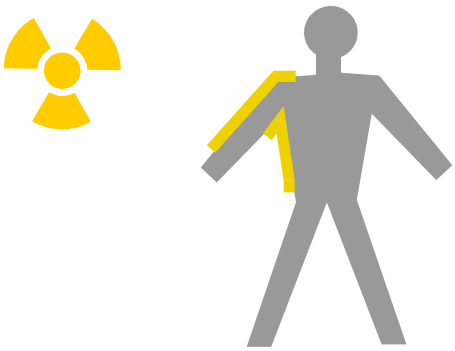
The closer a person comes to the source and the longer time spent near the source is, the greater is the hazard. Picking up a dangerous source is particularly hazardous. Analysis of past emergencies showed that severe deterministic health effects have resulted from holding or carrying (e.g. in a pocket) a dangerous source for just a few minutes (IAEA 2006).

The most important protection for responders is therefore, to keep distance and keep the time spent near the source as short as possible ("**time, distance, shielding**").
As soon as the vicinity of the source is evacuated, there is no risk to caregivers; no special protective clothing or equipment is needed.

If the radioactive substance is uncontained
or if a sealed source is opened e.g. by mechanical force or by fire,
it is possible to have direct contact with the substance.

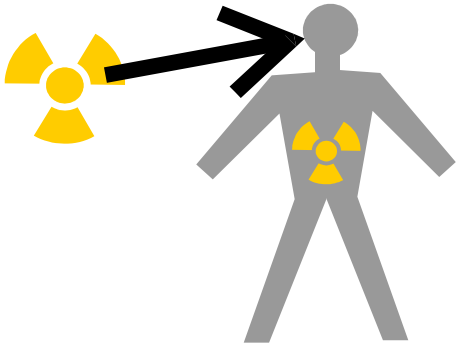


If that radioactive substance arrives at your skin, you are **contaminated** (externally).
A (external) **contamination** leads to irradiation of the skin and must therefore be removed; however contamination is unable to cause acute (deterministic) health effects (like skin burns or radiation sickness).



The main risk of contamination is, that the substance could reach the inside of your body (via mouth, nose or skin). A contaminated person must therefore be **decontaminated**; washing with water and soap usually is sufficient.

All published experience shows, that **caregivers will not receive significant external exposure** (BUMED 2003). They must however protect themselves from contamination by covering their body surface as completely as possible (single use protective suit, gloves, goggles etc.).
As protective suits in radiation protection are never intended to shield the radiation - only to keep the substance away from the skin - it is possible to achieve sufficient protection also with medical supplies (operation room gowns and masks). **Barrier nursing principles** are fully adequate for protection against radioactive contamination.



If radioactive material gets into a person's body, via inhalation, ingestion or through open wounds, this is called **internal contamination**.

The substance may accumulate in tissues and organs ("**critical organ**") following the biochemical pathways and according to its chemical properties (e.g. iodine => thyroid, radionuclides similar to calcium => bone).

Internal contamination does usually not cause acute health effects - except in exceptionally high doses like in the Litwinenko case. A chronic deposition in the body will increase cancer risk and can lead to late deterministic effects like fibrosis.

For radiation protection and laboratory safety purposes radionuclides have been divided in **radiotoxicity** categories (depending on type and energy of rays, absorption in the organism, residence time in the body; IAEA Technical Reports Series No. 15 1963 and ICRP Publication No. 5 1964), which describe, how nocuous to health a radionuclide is in case of intake.

*1.5 Summary on **protective measures** against ionising radiation:*

Keep external exposure as low as possible:

- keep **distance** from the source
- keep the **time** near the source as short as possible
- use every **shielding** available

Keep external contamination as low as possible and remove it as soon as possible:

- use **personal protective equipment** to **cover the body** as completely as possible
- do not touch suspicious substances
- avoid to stir up or to spread suspicious substances
- perform own **decontamination** (undress, shower, now clothing) after the incident

Avoid internal contamination:

- **no eating, drinking or smoking** during the incident
  (you may eat and drink after decontamination; you should abandon smoking at all !)
- avoid inhalation - do not stir up substance, keep containers closed

(You may compare "Protection of Responders and the Public" in IAEA 2006).

References

BUMED: Bureau of Medicine and Surgery (2003) *Initial Management of Irradiated or Radioactively Contaminated Personnel*, BUMEDINST 6470.10B, Washington DC, Department of the Navy, www.deploymentlink.osd.mil/pdfs/bumedinst_6470-10B.pdf

CDC: Centers for Disease Control and Prevention (2005) *Acute Radiation Syndrome: A Fact Sheet for Physicians*, CDC, Atlanta, http://www.bt.cdc.gov/radiation/arsphysicianfactsheet.asp

Fliedner TM, Friesecke I, Beyrer K. (2001) *Medical management of radiation accidents. Manual on the acute radiation syndrome*. The British Institute of Radiology, London

IAEA / WHO: International Atomic Energy Agency / World Health Organization *(2000) How to recognize and initially respond to an accidental radiation injury,* IAEA, Vienna, www.who.int/ionizing_radiation/a_e/IAEA-WHO-Leaflet-Eng%20blue.pdf

IAEA: International Atomic Energy Agency (2006) *Identification of Radioactive Sources and Devices,* Nuclear Security Series No. 5, IAEA, Vienna, http://www-pub.iaea.org/MTCD/publications/PDF/Pub1278_web.pdf

ICRP: International Commission on Radiological Protection (1991) *1990 Recommendations of the International Commission on Radiological Protection*, ICRP Publication 60, Annals of the ICRP, Volume 21/1-3, Pages 11-16, 92-95, First edition 1991, ISBN 0 08 041144 4, Pergamon Press, Oxford

Ricks RC, Berger ME, O'Hara FM (editors) (2001) *The Medical Basis for Radiation-Accident Preparedness - The Clinical Care of Victims,* Proceedings of the Fourth International REAC/TS Conference on The Medical Basis for Radiation-Accident Preparedness March 2001, Orlando, Florida; The Parthenon Publishing Group, Boca Raton

Waselenko JK, MacVittie TJ, Blakely WF et al (2004) *Medical Management of the Acute Radiation Syndrome: Recommendations of the Strategic National Stockpile (SNS) Radiation Working Group*, Ann Intern Med. 2004;140:1037-1051. www.annals.org

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(1) Need to read

IAEA / WHO: International Atomic Energy Agency / World Health Organization *(2000) How to recognize and initially respond to an accidental radiation injury,* IAEA, Vienna, www.who.int/ionizing_radiation/a_e/IAEA-WHO-Leaflet-Eng%20blue.pdf

BUMED: Bureau of Medicine and Surgery (2003) *Initial Management of Irradiated or Radioactively Contaminated Personnel*, BUMEDINST 6470.10B, Washington DC, Department of the Navy, www.deploymentlink.osd.mil/pdfs/bumedinst_6470-10B.pdf

good and practical overbiew on decontamination and medical management; based on extensive experience; emphasises priority of lifesaving measures because of low risk from contamination for medical personnel

(2) Nice to read

Fliedner TM, Friesecke I, Beyrer K. (2001) *Medical management of radiation accidents. Manual on the acute radiation syndrome*. The British Institute of Radiology, London

for detailed guidance on treatment of ARS and on the response category concept ("METREPOL")

Waselenko JK, MacVittie TJ, Blakely WF et al (2004) *Medical Management of the Acute Radiation Syndrome: Recommendations of the Strategic National Stockpile (SNS) Radiation Working Group*, Ann Intern Med. 2004;140:1037-1051. www.annals.org

as an alternative to Fliedner et al., available online

IAEA: International Atomic Energy Agency (2006) *Manual for First Responders to a Radiological Emergency*, Emergency Preparedness and Response, EPR-FIRST RESPONDERS, jointly sponsored by CTIR IAEA, PAHO and WHO; IAEA, Vienna, http://www-pub.iaea.org/MTCD/publications/PDF/EPR_FirstResponder_web.pdf

for discussion of response and tactics

IAEA: International Atomic Energy Agency (2006) *Identification of Radioactive Sources and Devices,* Nuclear Security Series No. 5, IAEA, Vienna, http://www-pub.iaea.org/MTCD/publications/PDF/Pub1278_web.pdf

for discussion of response and tactics

FEMA: Federal Emergency Management Agency (2003) *Don't be a Victim! Medical Management of Patients Contaminated with Chemical Agents*, Course Student Guide, Chemical Stockpile Emergency Preparedness Program, http://www.fema.gov

OSHA: Occupational Safety and Health Administration (2005) *Best Practices for Hospital-Based First Receivers of Victims from Mass Casualty Incidents Involving the Release of Hazardous Substances*, Washington DC: Department of Labor, http://www.osha.gov/

both very practical, good template for hospital planning

USAFRRI: US Armed Forces Radiobiology Research Institute (2003) *Medical Management of Radiological Casualties Handbook*, 2nd Edition, Bethesda MD, online available at https://ccc.apgea.army.mil/products/handbooks/books.htm

(3) Only for information

Ricks RC, Berger ME, O'Hara FM (editors) (2001) *The Medical Basis for Radiation-Accident Preparedness - The Clinical Care of Victims,* Proceedings of the Fourth International REAC/TS Conference on The Medical Basis for Radiation-Accident Preparedness March 2001, Orlando, Florida; The Parthenon Publishing Group, Boca Raton

comprehensive overview on medical treatment

IAEA and WHO *(1998) Diagnosis and Treatment of Radiation Injuries,* Safety Reports Series No. 2, IAEA, Vienna (to be found via Google)

slightly outdated, but classical overview in ARS treatment, much information on treatment of internal contamination

IAEA: International Atomic Energy Agency (2005) *Generic Procedures for Medical Response During a Nuclear or Radiological Emergency*, Emergency Preparedness and Response, EPR-MEDICAL; IAEA, Vienna, http://www-pub.iaea.org/MTCD/publications/PDF/EPR-MEDICAL-2005_web.pdf

information on medical treatment; however too generic to be of practical use; templates for working sheets for lab work might be of interest

UNSCEAR: United Nations Scientific Committee on the Effects of Atomic Radiation (2000) *Report: Sources and Effects of Ionizing Radiation*, UNSCEAR, Vienna, http://www.unscear.org/unscear/en/publications/2000_1.html

WHO (2007) *Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) Collaborating Centres and Liaison Institutions Members Directory*, WHO, Geneva, http://www.who.int/ionizing_radiation/a_e/rempan/REMPAN_directory_2007.pdf

ICRP: International Commission on Radiological Protection (1991) *1990 Recommendations of the International Commission on Radiological Protection*, ICRP Publication 60, Annals of the ICRP, Volume 21/1-3, Pages 11-16, 92-95, First edition 1991, ISBN 0 08 041144 4, Pergamon Press, Oxford

NCRP: National Council on Radiation Protection and Measurements: (1980) *Management of Persons Accidentally Contaminated with Radionuclides*; ISBN 0-913392-49-9, NCRP Report No. 65; Bethesda, MD,

IAEA Accident reports

US Army and NATO Field Manuals

Glossary

ARS	acute radiation syndrome
CBRN	chemical, biological, radiological and nuclear
NBC	nuclear, biological, chemical
METREPOL	Medical Treatment Protocols for Radiation Accident Victims as a Basis for a Computerised Guidance System

International organisations

IAEA International Atomic Energy Agency
http://www.iaea.org

ICRP International Commission on Radiological Protection
http://www.icrp.org

REMPAN Radiation Emergency Medical Preparedness and Assistance Network
http://www.who.int/ionizing_radiation/a_e/rempan/en/

UNSCEAR United Nations Scientific Committee on the Effects of Atomic Radiation
http://www.unscear.org/

WHO World Health Organisation
http://www.who.int/en/

National organisations

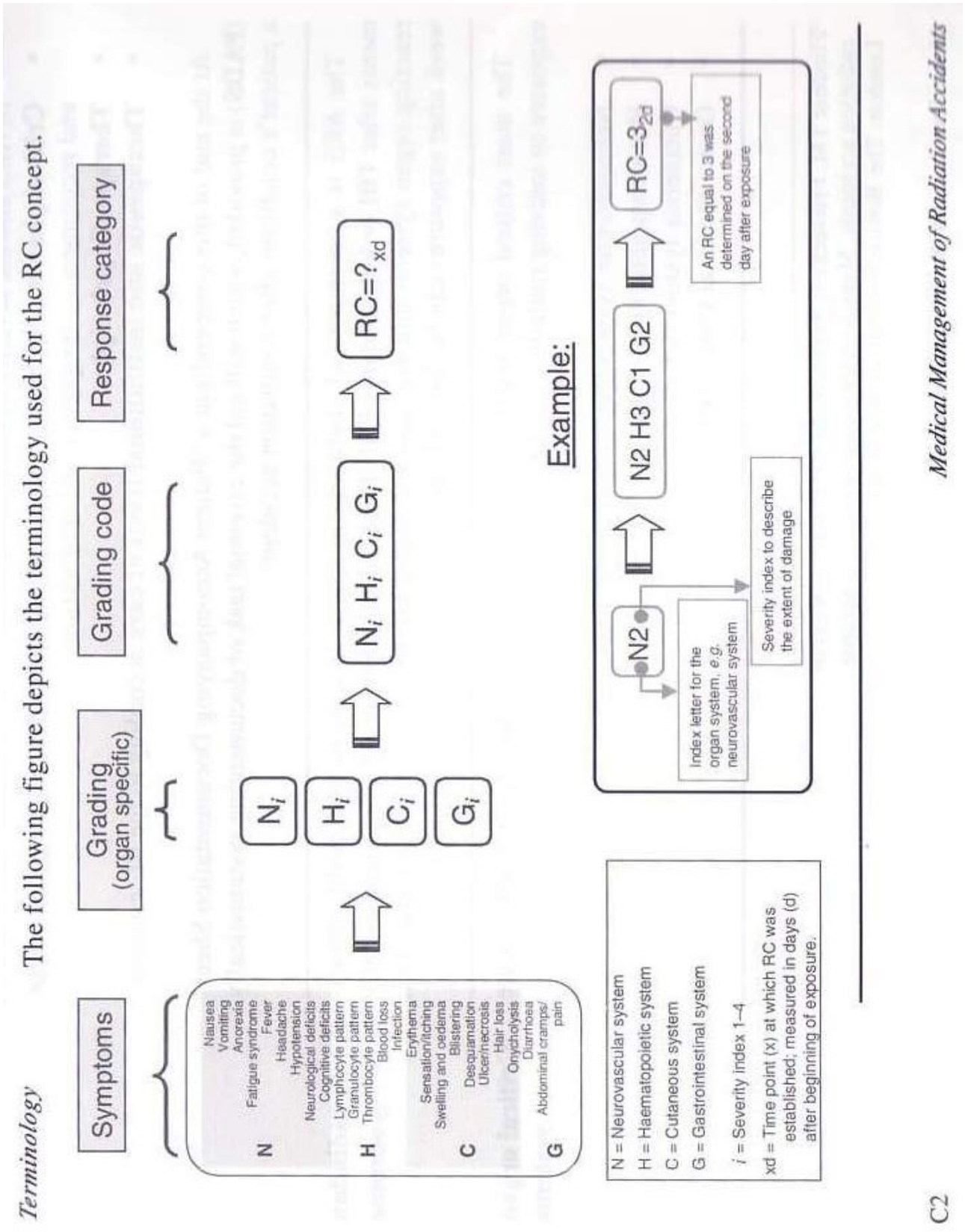
BUMED Bureau of Medicine and Surgery, US Navy
http://navymedicine.med.navy.mil/

NCRP National Council on Radiation Protection & Measurements
http://www.ncrponline.org

REAC/TS Radiation Emergency Assistance Center/Training Site
http://orise.orau.gov/reacts

Annex: Tables

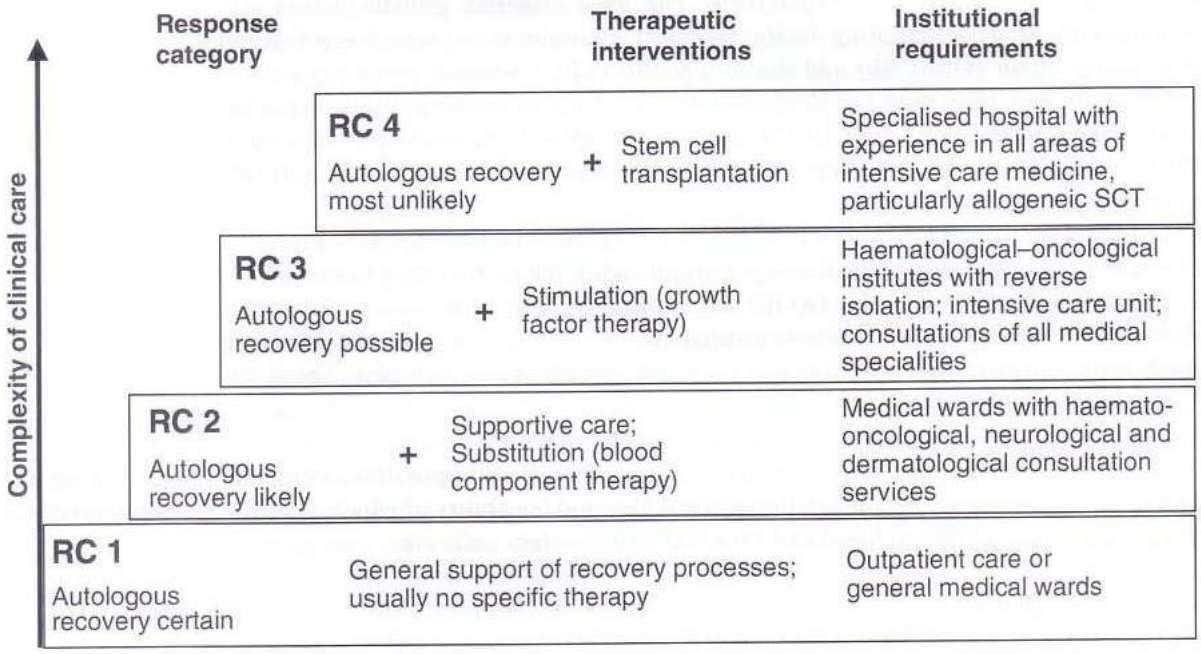
from: Fliedner et al. 2001 (*Medical management of radiation accidents. Manual on the acute radiation syndrome):*

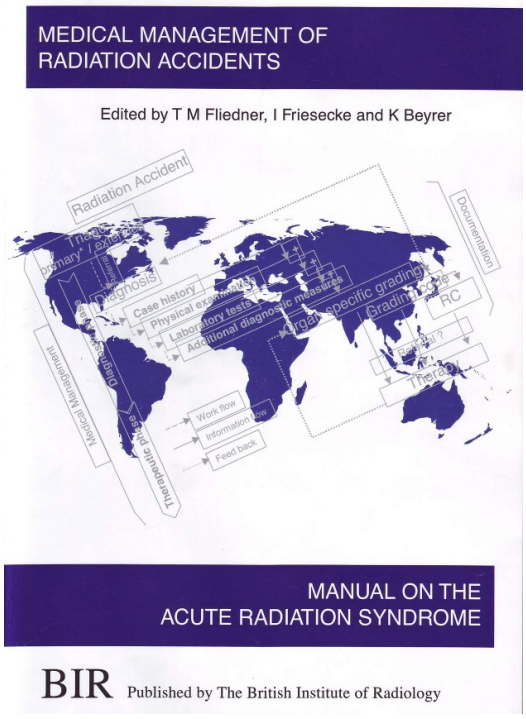


from: *Medical Management Of Radiation Accidents - Manual on the Acute Radiation Syndrome,* edited by T M Fliedner, I Friesecke and K Beyrer, The British Institute of Radiology (BIR), London, 2001

Therapeutic and institutional levels of care

The following figure gives a synopsis of the RC-dependent therapeutic and institutional levels of care for radiation accident victims.





from: *Medical Management Of Radiation Accidents - Manual on the Acute Radiation Syndrome,* edited by T M Fliedner, I Friesecke and K Beyrer, The British Institute of Radiology (BIR), London, 2001

Neurovascular system

Symptom	Degree 1	Degree 2	Degree 3	Degree 4
		N		
Nausea	mild	tolerable	intense	excruciating
Vomiting	occasional, 1/d	intermittent, 2–5/d	persistent, 6–10/d	refractory >10/d or parenteral nutrition
Anorexia	able to eat, reasonable intake	significantly decreased intake but able to eat	no significant intake	parenteral nutrition
Fatigue syndrome[a]	able to work or perform normal activity	interferes with work or normal activity	needs some assistance for self-care	prevents daily activity
Fever	<38 °C	38–40 °C	>40 °C for less than 24 h	>40 °C for more than 24 h or accompanied by hypotension
Headache	minimal	tolerable	intense	excruciating
Hypotension	HR>100/BP>100/70	BP<100/70	BP<90/60; transient	BP<80/?; persistent
Neurological deficits[b]	barely detectable neurological deficit; able to perform normal activity	easily detectable neurological deficit, no significant interference with normal activity	prominent neurological deficit, significant interference with normal activity	life threatening neurological signs, loss of consciousness
Cognitive deficits	minor loss of memory, reasoning and/or judgement	moderate loss of memory, reasoning and/or judgement	major intellectual impairment since accident	complete memory loss and/or incapable of rational thought

HR, heart rate; BP, blood pressure.

[a]Fatigue: self-recognised state of overwhelming, sustained exhaustion and decreased capacity for physical and mental work—not relieved by rest. Typical descriptions are drained, finished off, lethargic, beaten, exhausted or worn out, prostration, drowsiness. Components are physical, cognitive, emotional/affective.

[b]Neurological deficits: reflex status including reflexes of the eye, ophthalmoscopy (oedema of papilla), fainting, dizziness, ataxia and other motor signs, sensory signs.

Haematopoietic system

Symptom	Degree 1	Degree 2	Degree 3	Degree 4
		H		
Lymphocyte changes[a]	$\geq 1.5 \times 10^9$/l	$(<1.5–1) \times 10^9$/l	$(<1–0.5) \times 10^9$/l	$<0.5 \times 10^9$/l
Granulocyte changes[b]	$\geq 2 \times 10^9$/l	$(<2–1) \times 10^9$/l	$(0.5–1) \times 10^9$/l	$<0.5 \times 10^9$/l or initial granulocytosis
Thrombocyte changes[c]	$\geq 100 \times 10^9$/l	$(<100–50) \times 10^9$/l	$(<50–20) \times 10^9$/l	$<20 \times 10^9$/l
Infection	local; no antibiotic therapy required	local; only local antibiotic therapy required	systemic; p.o. antibiotic treatment sufficient	sepsis; i.v. antibiotics necessary
Blood loss	petechiae; easy bruising; normal Hb	mild blood loss with <10% decrease in Hb	gross blood loss with 10–20% decrease in Hb	spontaneous bleeding or blood loss with >20% decrease in Hb

[a]Reference value: $(1.5–4) \times 10^9$/l.

[b]Reference value: $(4–9) \times 10^9$/l.

[c]Reference value: $(140–400) \times 10^9$/l.

from: *Medical Management Of Radiation Accidents - Manual on the Acute Radiation Syndrome,* edited by T M Fliedner, I Friesecke and K Beyrer, The British Institute of Radiology (BIR), London, 2001

Cutaneous system

Symptom	Degree 1	Degree 2	Degree 3	Degree 4
		C		
Erythema[a]	minimal and transient	moderate; isolated patches <10 cm^2; not more than 10% of body surface (BS)	marked; isolated patches or confluent; 10–40% of BS	Severe[b]; isolated patches or confluent; >40% of BS; erythroderma
Sensation/itching	pruritus	slight and intermittent pain	moderate and persist pain	severe and persistent pain
Swelling/oedema	present; asymptomatic	symptomatic; tension	secondary dysfunction	total dysfunction
Blistering	rare, with sterile fluid	rare, with haemorrhage	bullae with sterile fluid	bullae with haemorrhage
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 most likely reversible	complete and most likely irreversible
Onycholysis	absent	partial	Ø	complete

Changes in the skin pigmentation may also occur. However, given the lack of reference data describing depigmentation or hyperpigmentation, this symptom is not included in the grading. Nevertheless it should be recorded systematically, as it may be helpful in future radiation accidents.

Ø, not defined.

[a]The extent of the skin area affected is decisive and should be documented for all skin changes.

[b]Only for penetrating irradiation.

Gastrointestinal system

Symptom	Degree 1	Degree 2	Degree 3	Degree 4
		G		
Diarrhoea				
Frequency	2–3 stools/d	4–6 stools/d	7–9 stools/d	≥10 stools/d; refractory diarrhoea
Consistency	bulky	loose	sloppy	watery
Mucosal loss/d	intermittent	intermittent with large amount	persistent	persistent with large amount
Bleeding/d	occult	intermittent	persistent	gross haemorrhage
Abdominal cramps/pain	minimal	tolerable	intense	excruciating

from: *Medical Management Of Radiation Accidents - Manual on the Acute Radiation Syndrome,* edited by T M Fliedner, I Friesecke and K Beyrer, The British Institute of Radiology (BIR), London, 2001

List of the degrees of severity of organ specific symptoms

Symptom	Degree 1	Degree 2	Degree 3	Degree 4
		N		
Nausea	mild	tolerable	intense	excruciating
Vomiting	occasional, 1/d	intermittent, 2–5/d	persistent, 6–10/d	refractory >10/d or parenteral nutrition
Anorexia	able to eat, reasonable intake	significantly decreased intake but able to eat	no significant intake	parenteral nutrition
Fatigue syndrome[a]	able to work or perform normal activity	interferes with work or normal activity	needs some assistance for self-care	prevents daily activity
Fever	<38 °C	38–40 °C	>40 °C for less than 24 h	>40 °C for more than 24 h or accompanied by hypotension
Headache	minimal	tolerable	intense	excruciating
Hypotension	HR>100/BP>100/70	BP<100/70	BP<90/60; transient	BP<80/?; persistent
Neurological deficits[b]	barely detectable neurological deficit; able to perform normal activity	easily detectable neurological deficit, no significant interference with normal activity	prominent neurological deficit, significant interference with normal activity	life threatening neurological signs, loss of consciousness
Cognitive deficits	minor loss of memory, reasoning and/or judgement	moderate loss of memory, reasoning and/or judgement	major intellectual impairment since accident	complete memory loss and/or incapable of rational thought
		H		
Lymphocyte changes[c]	$\geq 1.5 \times 10^9$/l	$<1.5–1 \times 10^9$/l	$<1–0.5 \times 10^9$/l	$<0.5 \times 10^9$/l
Granulocyte changes[d]	$\geq 2 \times 10^9$/l	$<2–1 \times 10^9$/l	$0.5–1 \times 10^9$/l	$<0.5 \times 10^9$/l or initial granulocytosis
Thrombocyte changes[e]	$\geq 100 \times 10^9$/l	$<100–50 \times 10^9$/l	$<50–20 \times 10^9$/l	$<20 \times 10^9$/l
Infection	local; no antibiotic therapy required	local; only local antibiotic therapy required	systemic; p.o. antibiotic treatment sufficient	sepsis; i.v. antibiotics necessary
Blood loss	petechiae; easy bruising; normal Hb	mild blood loss with <10% decrease in Hb	gross blood loss with 10–20% decrease in Hb	spontaneous bleeding or blood loss with >20% decrease in Hb
		C		
Erythema[f]	minimal and transient	moderate; isolated patches <10 cm^2; not more than 10% of body surface (BS)	marked; isolated patches or confluent; 10–40% of BS	severe[g]; isolated patches or confluent; >40% of BS; erythroderma
Sensation/itching	pruritus	slight and intermittent pain	moderate and persistent pain	severe and persistent pain
Swelling/oedema	present; asymptomatic	symptomatic; tension	secondary dysfunction	total dysfunction
Blistering	rare, with sterile fluid	rare, with haemorrhage	bullae with sterile fluid	bullae with haemorrhage
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 most likely reversible	complete and most likely irreversible
Onycholysis	absent	partial	Ø	complete
		G		
Diarrhoea				
Frequency	2–3 stools/d	4–6 stools/d	7–9 stools/d	≥10 stools/d; refractory diarrhoea
Consistency	bulky	loose	sloppy	watery
Mucosal loss/d	intermittent	intermittent with large amount	persistent	persistent with large amount
Bleeding/d	occult	intermittent	persistent	gross haemorrhage
Abdominal cramps/pain	minimal	tolerable	intense	excruciating

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from: *Medical Management Of Radiation Accidents - Manual on the Acute Radiation Syndrome,* edited by T M Fliedner, I Friesecke and K Beyrer, The British Institute of Radiology (BIR), London, 2001