

THERAPEUTICAL MANAGEMENT

According to the European consensus conference « *European approach for the medical management of mass radiation exposure* » updated in October 2017

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

Score I: Monitoring. No cytokine

- Outpatient clinical monitoring.
- Blood count day 1 - 2 and then once a week for 2 months.

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 10⁹/L). EPO and TPO agonists 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.

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 of score during the first week based on laboratory or clinical symptoms revealing irreversible organ damage or MOF.

ALL BLOOD PRODUCTS SHOULD BE IRRADIATED.

SEVERE RADIATION SKIN LESIONS HAVE A PECULIAR EVOLUTION. CONSIDER MESENCHYMAL STEM CELLS AT SPECIALIST CENTRES.

References:

- Gorin NC *et al* – *Ann Hematol*, 85 : 671-679, 2006.
- Fliedner TM *et al* – Medical Management of Radiation Accidents - Manual of the acute radiation syndrome, published by BIR, 2001.
- Powles R *et al* – *Health Phys*, 98 : 810-814, 2010.

Haematopoietic stem cell (HSC) transplantation

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).

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

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:
 - 2x10⁶ CD34 cells.kg⁻¹ (peripheral blood).
 - 2x10⁸ nucleated cells.kg⁻¹ (bone marrow).
 - 3x10⁷ nucleated cells (cord blood).

Conditioning and GVHD prevention (as per current transplant criteria):

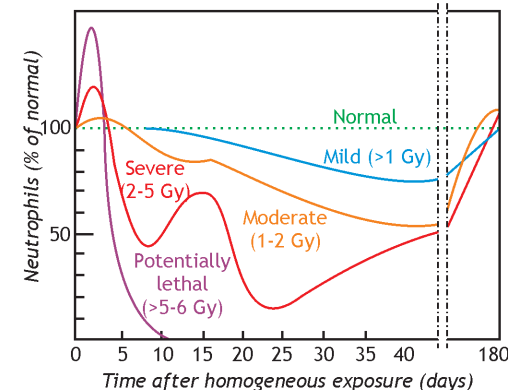
- Reduced intensity conditioning.
- No Methotrexate.



What can the European Blood and Marrow Transplant Group (EBMT) offer ?

Advice on :

1. Secondary Triage and Treatment
2. Ongoing feedback from experts on how the clinical scenario is evolving
3. Optimizing care outside of national borders
4. Skilled network of 500 BMT Centres
5. Generating prospective database of event



The amount of energy absorbed by the organs of the body is measured in Gray (Gy); the effects of this radiation is given by the equivalent dose which is measured in Sievert (Sv).

For x-rays, gamma rays, and beta particles 1 Gray ≈ 1 Sievert.

Contacts

- M Benderitter** (France): marc.benderitter@irsn.fr
- N Gent** (United Kingdom): Nick.Gent@phe.gov.uk
- N C Gorin** (France): gorinclaude@gmail.com
- M Port** (Germany): matthiasport@bundeswehr.org
- R Powles** (United Kingdom): myeloma@clara.co.uk
- B Sirohi** (United Kingdom): bhawna.sirohi13@gmail.com
- L Stenke** (Sweden): leif.stenke@ki.se

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

- 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).

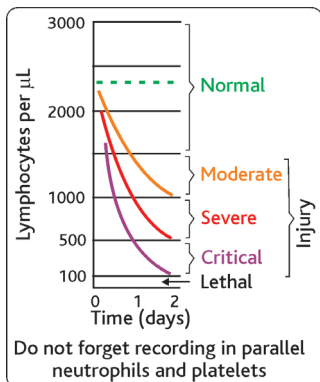
Urgent sampling

- 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

Record all clinical symptoms on a date and hour-stamped chart

	Score I Less than 12 hours	Score II Less than 5 hours	Score III Less than 30 minutes +++ ; before 3 rd hour
Average delay before symptoms appear	0	+/-	+++
Cutaneous erythema	0	+/-	+++ ; before 3 rd hour
Asthenia /Weakness	+	++	+++
Nausea	+	+++	(-)
Vomiting per 24 hrs	Maximum 1	1 to 10	Above 10; intractable
Diarrhea / Number of stools per 20 hrs	Maximum 2 - 3; bulky	2 - 9; soft	Above 10; watery
Abdominal pain	Minimal	Intense	Excruciating
Headaches	0	++	Excruciating; Signs of intra-cranial HT
Temperature	Below 38°C	38 - 40°C	Above 40°C
Blood pressure	Normal	Normal - Possible temporary decrease	Systolic below 80
Temporary loss of consciousness	0	0	+ / Coma



At 24 hours
At 48 hours

Depletion of blood lymphocytes

Above 1 500 / µL
Above 1 500 / µL

Below 1 500 / µL
Below 1 500 / µL

Below 500 / µL
Below 100 / µL

Outpatient monitoring

Hospitalisation for curative treatment

Hospitalisation (MOF predicted)
Multiple Organe failure (MOF)

WARNING: the symptoms and values indicated above are reliable only in case the whole body or large parts of the body have been externally exposed to a high radiation dose delivered within few minutes or few hours. Fill and fax EBMT MED A to : (+33)1 71 97 04 88
To download EBMT MED A: www.ebmt.org in Data-Management/Registry structure/data collection forms & manuals