

Therapeutical management

according to the European consensus conference*

European approach for the medical management of mass radiation exposure



Beyond the first 48 hrs, a second patient scoring is done by organs (Neurovascular, Hemopoiesis, Cutaneous, Gut) 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: - every day for 6 days, - then once a week for 2 months.

Score II: Cytokines (curative)

- G-CSF+ KGF should be used as early as possible for 14-21 days. TPO and agonists, EPO and stem cell factor questionable.
- 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 hematopoietic recovery.

Score III: Cytokines (until reappraisal of score)

- Palliative/Symptomatic treatment.
- Re-evaluation during the first week based on laboratory or clinical symptoms revealing irreversible organ damage or multi organ dysfunction.

All blood products should be irradiated

Severe radiological skin lesions have a peculiar torpid evolution and require specialist treatment.

* N.C. Gorin *et al.*, Consensus conference on European preparedness for haematological and other medical management of mass radiation accidents, *Ann Hematol*, 85 : 671- 679, 2006.

** T.M. Fliedner *et al.*, Medical Management of Radiation Accidents – Manual of the acute radiation syndrome, published by BIR, 2001.

Hematopoietic 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 a hematopoietic stem cell (HSC) transplantation is discussed.

Criteria to transplant

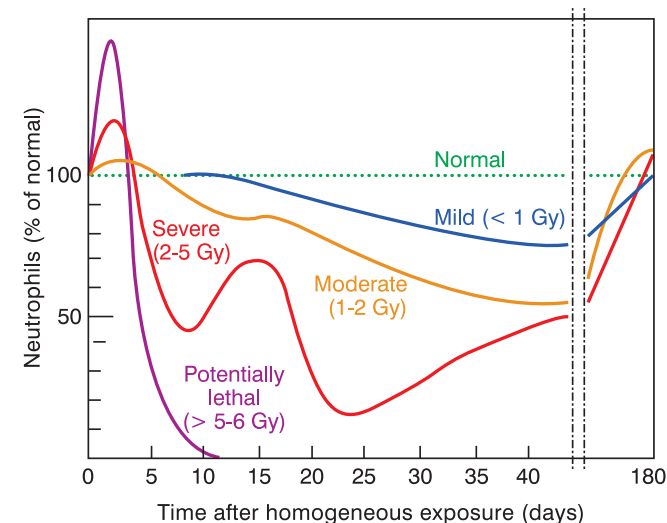
- Severe marrow aplasia persisting 14 - 21 days.
- No residual hematopoiesis.
- No irreversible organ damage (GI tract, lungs...).

Graft

- **Type of graft:**
 - Bone marrow.
 - Peripheral blood HSC (depleted or not).
 - Cord blood.
- **Donor in the following order of priority:**
 - HLA-identical sibling or 7/8 matched.
 - HLA-identical unrelated donor or 9/10 matched.
 - Cord blood > 4/6 matched.
- **Doses of cells to be grafted:**
 - At least: - 2×10^8 CD34 cells.kg⁻¹ (peripheral blood);
 - 2×10^9 nucleated cells.kg⁻¹ (bone marrow);
 - 3×10^7 nucleated cells (cord blood).

Conditioning and GVHD prevention

- **Non myelotoxic conditioning:**
 - Fludarabine (30 mg.m⁻².d⁻¹ for 3 days) ± anti-lymphocyte globulins.
- **GVHD prevention:**
 - No Methotrexate.



M. Akashi, B. Allenet-Le Page, D. Blaise, JF. Bottollier-Depois, A. Bushmanov, JM. Cosset, T. de Revel, T. Fliedner, F. Frassoni, A. Ganser, MH. Gaugler, NC. Gorin, P. Gourmelon, N. Griffiths, D. Lloyd, V. Meineke, D. Niederwieser, A. Nikiforov, R. Powles, AR. Oliveira, I. Resnick, G. Seitz, J.Sierra, B. Sirohi and L. Stenke.

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European group for Blood Marrow Transplantation.



Ulm University - Germany.



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The first 48 hours

Life-threatening wounds and burns should be treated first

Irradiation is not contamination – An irradiated person is not a source of radiation – In case of additional contamination, decontamination comes first

Beware of Multiple Organ Failure (MOF)

The severity of prodromal clinical features is of major importance.

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

Physical dosimetry

- Inquiry: circumstances of the accident, source characteristics, source-victim geometry, duration of exposure, daily dose rate, shielding, homogeneous/heterogeneous irradiation.
- Labelling and storage of personal belongings and clothes, biological material (hair, nails).

Urgent sampling

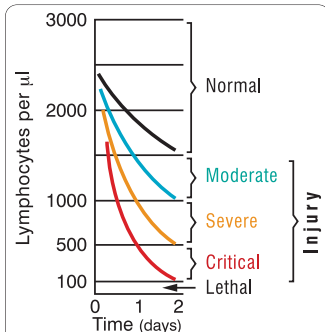
- Blood cell counts (+ differentials) every 4-8 hours for the 1st 24 hours, 12-24 h after.
- Chromosome aberrations on blood lymphocytes (biodosimetry) (15 ml + heparin).
- Red cell group typing.
- Store serum and cells or DNA for further analyses including HLA typing.
- Standard biochemistry + amylasemia.
- Blood (20 ml) to measure ²⁴Na if exposure to neutrons.
- Urine and faeces if radionuclide contamination is suspected.

Primary scoring

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

| | Score I | Score II | Score III |
|---|----------------------|--------------------------------------|---|
| <i>Average delay before symptoms appear</i> | Less than 12 hours | Less than 5 hours | Less than 30 minutes |
| Cutaneous erythema | 0 | +/- | +++; before 3 rd hour |
| Asthenia | + | ++ | +++ |
| Nausea | + | +++ | (-) |
| Vomiting per 24 hrs | Maximum 1 | 1 to 10 | Above 10; intractable |
| Diarrhea / Number of stools per 24 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 |

Depletion of blood lymphocytes



At 24 hours

At 48 hours

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)

Do not forget recording in parallel neutrophils and platelets

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 MED A (radiation accident) to : (+33)1 40 46 96 07