European approach for the medical management of mass radiation exposure

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

Therapeutical management according to the European consensus conference*

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.

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 an 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: 2x10^6 CD34 cells.kg^-1 (peripheral blood);
  - 2x10^6 nucleated cells.kg^-1 (bone marrow);
  - 3x10^7 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.

All blood products should be irradiated

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


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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 abberations 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 ^14Na 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

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

Depletion of blood lymphocytes

<table>
<thead>
<tr>
<th>Lymphocytes per µl</th>
<th>Time (days)</th>
<th>Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td>2000</td>
<td>1</td>
<td>Moderate</td>
</tr>
<tr>
<td>1000</td>
<td>2</td>
<td>Severe</td>
</tr>
<tr>
<td>500</td>
<td></td>
<td>Critical</td>
</tr>
<tr>
<td>100</td>
<td></td>
<td>Lethal</td>
</tr>
</tbody>
</table>

At 24 hours
- Above 1 500 / µl
- Below 1 500 / µl
- Below 500 / µl

At 48 hours
- Above 1 500 / µl
- Below 1 500 / µl
- Below 100 / µl

Outpatient monitoring
Hospitalisation for curative treatment
Hospitalisation (MOF predicted)

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