

Acute Radiation Effects

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Human data generated primarily from:

- ✱ Atom Bomb survivors
- ✱ Marshallese accident victims
- ✱ Accidents at nuclear installations, e.g., Chernobyl

Acute Radiation Effects

- ✱ The Radiation Accident Registry maintained by the Radiation Emergency Assistance Center at Oak Ridge National Library has documented 403 radiation accidents from 1944-1999
- ✱ Of these, 19 involved nuclear reactors, 303 involved radiation devices, and 81 isotopes
- ✱ Resulted in 120 deaths; 30 in the US, 2 in GB, 32 in the former USSR

Prodromal Radiation Syndrome

- ✦ Refers to early symptoms seen after exposure to high-intensity radiation
- ✦ Vary with respect to time of onset, severity, and duration
- ✦ Doses of ~ 30 Gy individuals will exhibit all phases of the syndrome within 5-15 min of exposure
- ✦ Severe prodromal syndrome usually associated with poor prognosis

Prodromal Radiation Syndrome

Signs and symptoms divided into 2 main groups

A. Gastrointestinal:

anorexia, nausea, vomiting etc.

B. Neuromuscular:

easy fatigability, fever, and hypotension.

Prodromal Radiation Syndrome

Neuromuscular

Signs and Symptoms to be expected at ~ 50% Lethal Dose

Easy fatigability

Gastrointestinal

Anorexia

Vomiting

Additional Signs to be expected after Supralethal Doses

Fever

Immediate diarrhea

Hypotension

Characteristics of Prodromal and Latency Periods as Function of Dose

<u>Dose (Gy)</u>	<u>Onset (h)</u>	<u>Duration (h)</u>	<u>Latency</u>
0.5-2.0	6 or more	<24	3 weeks or longer
2.0-3.5	2-6	12-24	2-3 weeks
3.5-5.5	1-2	24	1-2.5 weeks
>5.5	Minutes to 1	48	2-4 days

- Time of onset of prodromal syndromes inversely related to dose
- Duration and severity of prodromal syndromes directly dose-dependent

Cerebrovascular Syndrome

Total body dose of approx. 100 Gy γ rays will cause death in a few hours

N.B. All organs severely damaged and would cause death if the person survived long enough

- ✱ Cerebrovascular damage occurs rapidly, causing death within 24-48h. See severe nausea and vomiting within minutes, followed by disorientation, respiratory distress, diarrhea, seizures, coma, and death
- ✱ Pathogenesis thought to be massive edema leading to severe brain dysfunction

Cerebrovascular Syndrome

1964: 38 year-old-man working in a ^{235}U recovery plant was involved in nuclear accident; received total dose of ~88 Gy (22 Gy neutrons, 66 Gy γ rays)

Recalled seeing a flash, hurled backwards but did not lose consciousness. Ran from scene of accident to another building 200 yards away

Complained of abdominal cramps and headaches, vomited, was incontinent with bloody diarrheal stools. Next day patient comfortable but restless

Cerebrovascular Syndrome

On second day condition deteriorated

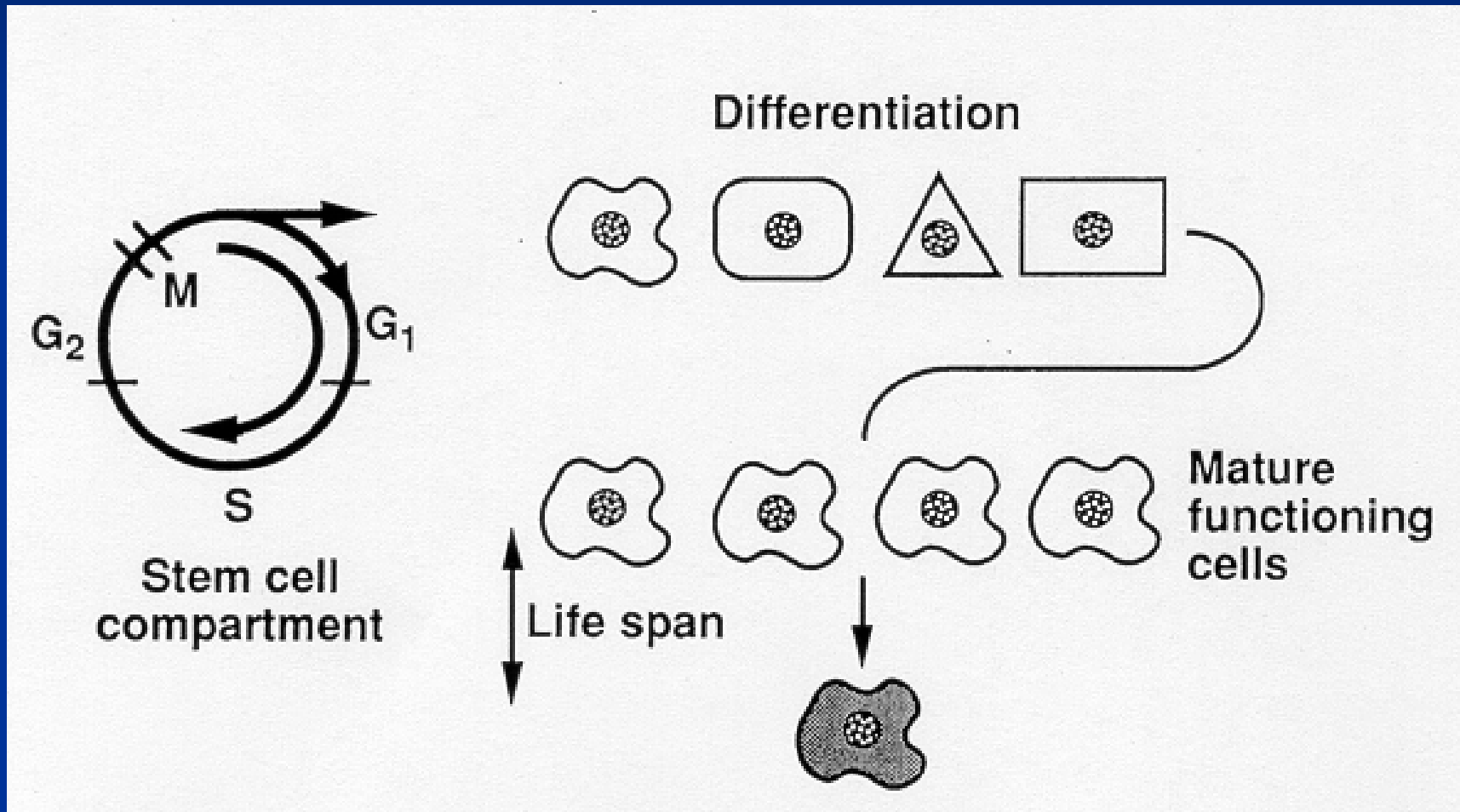
- ✱ Victim became restless, fatigued, apprehensive, short of breath, greatly impaired vision, hypotensive
- ✱ Six hours before death became disoriented, blood pressure could not be maintained
- ✱ Died 49 h after accident

Gastrointestinal Syndrome

Total body exposure of approx. 10 Gy γ rays leads to the GI syndrome

- ✱ Symptoms: nausea, vomiting and severe diarrhea
- ✱ Seen within 3-10 days of irradiation. Prolonged diarrhea indicates poor prognosis, with death occurring in a few days
- ✱ No human has survived a dose of >10 Gy

Mechanism of Gastrointestinal Syndrome



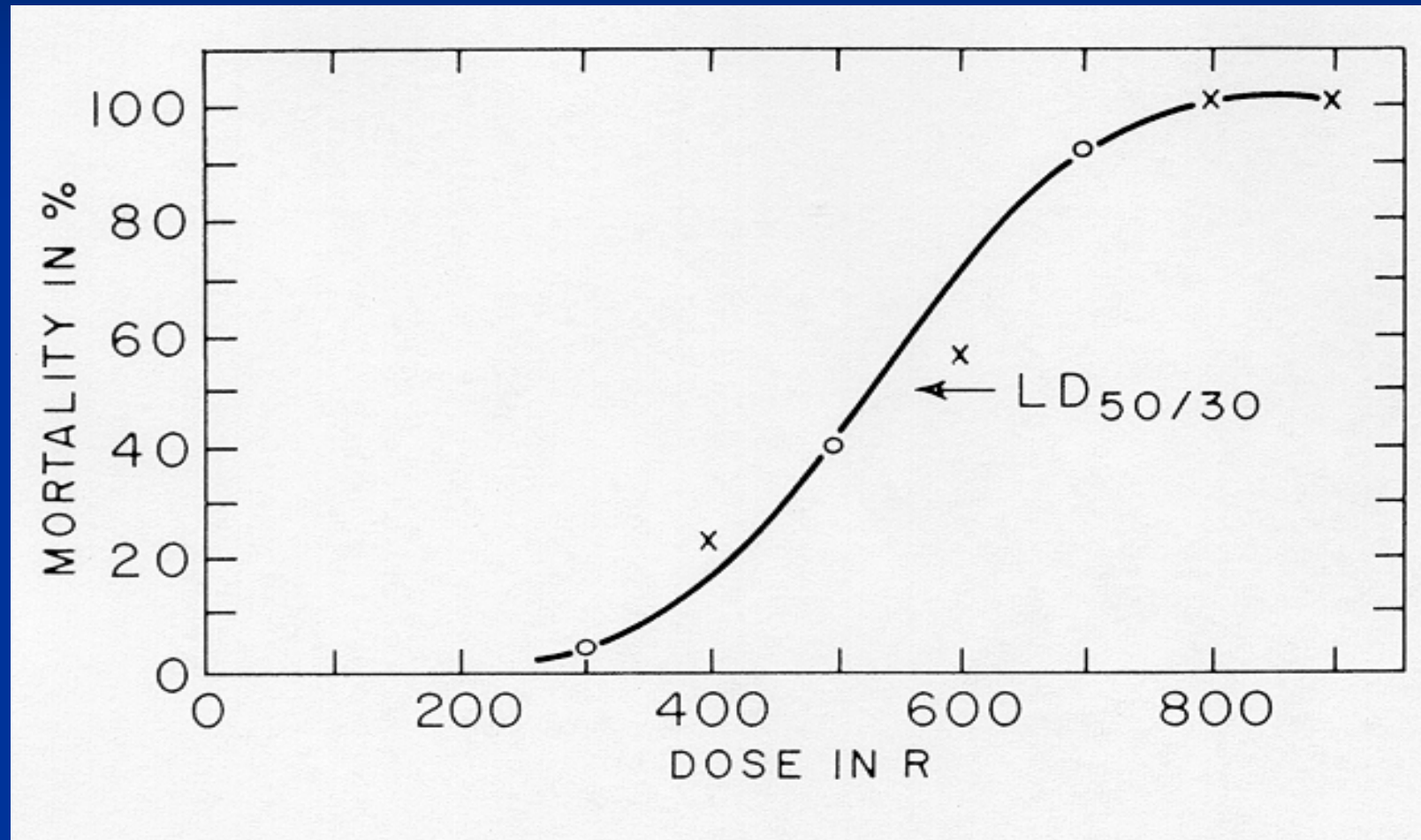
Hematopoietic Syndrome

- ✱ Total body exposure of 3-8 Gy leads to expression of the hematopoietic syndrome
- ✱ Dose limiting organ is the bone marrow
- ✱ Again have sterilization of precursor cells, leading to diminished supply of mature blood cells
- ✱ Critical period not seen for several weeks, due to lag between the natural turn-over time of the mature cells and subsequent inadequate supply from reduced precursor cell population.

Hematopoietic Syndrome

- ✦ Peak incidence of death from hematopoietic syndrome occurs at ~ 30 days after exposure
- ✦ Death can be observed up to 60 days
- ✦ Thus, express LD_{50} for humans as $LD_{50/60}$
- ✦ Dose appears to be in the order of 4 Gy

Hematopoietic Syndrome: Experimental Data



Treatment of Radiation Accident Victims

Treatment options depend on exposure dose

< 4-5 Gy:

Observation

Treat specific symptoms e.g., antibiotics
for infections

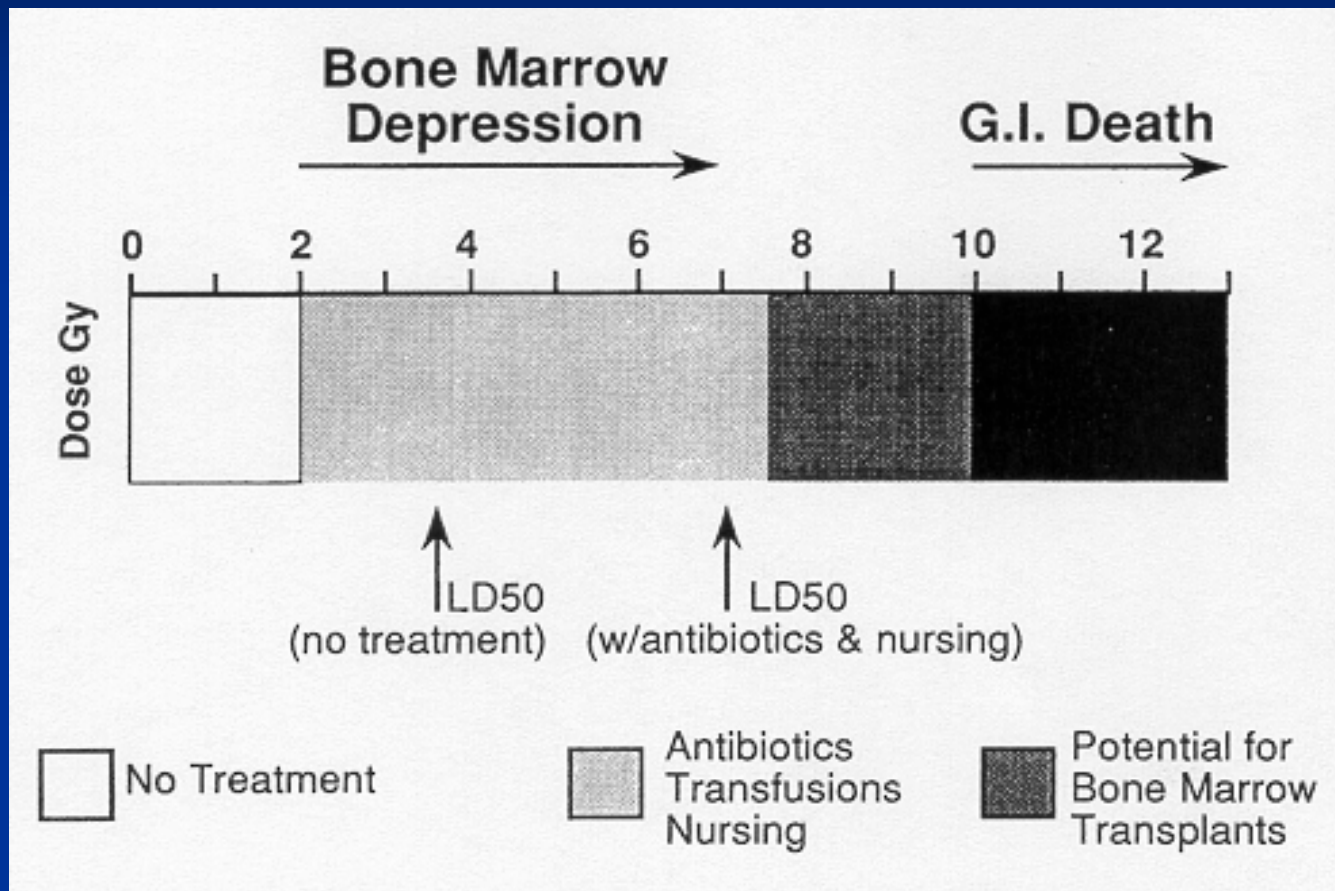
Blood transfusions if required

Treatment of Radiation Accident Victims

Dose > 5 Gy:

- ✱ Person will likely die from hematopoietic syndrome if untreated
- ✱ Use antibiotics and keep patient in isolation to prevent infection
- ✱ Animal studies suggest using antibiotics can increase LD₅₀ twofold
- ✱ Aim to provide time for the bone marrow to regenerate

Treatment of Radiation Accident Victims



Can also give bone marrow transplants:

- Results appear controversial, appears to be a very narrow therapeutic window, between 8-10 Gy

BMT after Chernobyl Accident

- ✱ Following Chernobyl accident, 202 persons were admitted to Clinical Hospital 6 in Moscow within 4 days of explosion
- ✱ 105 received an estimated total-body dose of $\geq 1-2$ Gy
- ✱ 33 initially considered to have received a dose of ≥ 6 Gy and were potential candidates
- ✱ 8 subsequently excluded when cytogenetic analyses indicated probable doses of < 6 Gy (7 recovered, 1 died from skin burns)

BMT after Chernobyl Accident

- ✱ 10 persons who received dose ≥ 6 Gy excluded due to extensive nonhematologic damage, mainly burns
- ✱ Remaining 15: 1 received a fetal liver rather than BMT, 1 refused, 13 received BMT 4-16 days after the accident

BMT after Chernobyl Accident

- ✱ Only 2/13 (doses of 5.8 and 9.0 Gy) survived, began regenerating their own bone marrow on day 28
- ✱ 5 died mainly from burns, although 3 had GI damage and 1 radiation pneumonitis
- ✱ 3 died mainly from radiation pneumonitis
- ✱ 2 died from graft-versus-host disease
- ✱ 1 died from acute renal failure and adult respiratory distress syndrome.

Growth Factor Stimulation of Bone Marrow Proliferation

- ✱ Post-irradiation stimulation of cell proliferation in the bone marrow predicted to be advantageous > 40 years ago by Lajtha (1960)
- ✱ Recent animal experiments using hematopoietic growth factors and the clinical experience from the treatment of accidental radiation exposure in Goiania, Brazil (1987) are supportive of this farsighted prediction

Goiania Accident

September 13 1987, Goiania, Central Brazil

- ✱ Approx 250 people exposed to a ^{137}Cs source from an abandoned RT unit
- ✱ 14 individuals showed bone marrow depression, 8 developed acute radiation syndrome

Goiania Accident

- ✱ 8/14 received GM-CSF iv
- ✱ None received BMT
- ✱ GM-CSF treatment not started until 23-48 days after initial and 19-37 days after final exposure
- ✱ 4 died from hemorrhage and infection