



EFFECTS OF RADIATION ON NORMAL HUMAN TISSUE

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ABSTRACT When ionizing radiation passes through tissues result in damage to DNA mainly through the effects of free radicals. Damage to DNA results in immediate cell death or at next mitosis or result in permanent changes in genotype (mutation) which transmitted to future generation cells. Low dose radiation is more likely to cause changes in genotype since it will be below the level of cell death. Radiation exposure can be under following heads:

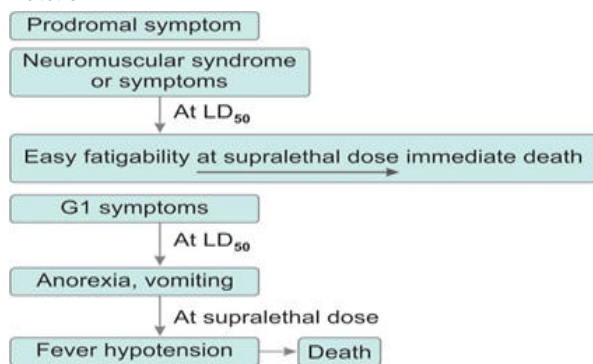
- Radiation Accident
- Atomic bomb explosion Severe
- Radiation Reaction Nuclear reactor
- Radiation devices -(X-rays) — Radiation Isotope
- Radiation as a part of treatment
- To whole body as irradiation called Magnafield irradiation
- HBI (Hemi Body irradiation)
- Human body exposure by radiation sources
- from background sources radioactive material Present in earth such as uranium/radium/thorium — Cosmic radiation – Dose se with height from surface.
- Human body itself contains radioactive elements like P40/C14/Sr90. They can be grouped under source of internal exposure.

KEYWORDS : Ionising radiation, Mutation**DISCUSSION-**

Acute Effects - Symptoms which appears early and last for limited period of time called as prodromal radiation syndrome, it may occur even at very low dose (exp. 5Gy within 5-15 min. of exposure).



Fig. 1: Severe Skin Reaction. Picture Shows Severe Radiation Reaction



Ld50 is the radiation dose that is equal to the dose that would be fatal to 50% of the population within specified period of time. Human prodromal 'syndrome vary with – Time of onset

- Maximum severity
- Duration
- Size of dose

Early Lethal Effects-

- Acute cerebrovascular syndrome
- Gastrointestinal syndrome
- Hemopoietic syndrome (Bone marrow toxicity)
- **Cerebrovascular syndrome-** occurs about 100 Gy Death occurs

24-48 hrs after exposure.

Cerebrovascular Syndrome**Symptoms**

Nausea Vomiting Diarrhoea Loss of coordination of muscular movement
Disorientation seizures, coma, death

Cause of Death

Increase leakage from small blood vessels of brain resulting INCREASE ICP, It has been found much higher doses are required to produce death if head alone irradiated rather than entire body thus radiation effects on the rest of the body, do have some effect as well.

Gastrointestinal Syndrome

- Nausea Vomiting Prolonged Diarrhoea Loss of Appetite appears sluggish and lethargic

Death Symptoms that appear and deaths that follow are attributed to depopulation of epithelial lining of Gastro Intestinal (GI) tract. Lining of GI tract compose of:

- Stem cell compartment
- Differentiating compartment
- Mature functioning cell
- Dividing cell confined to crypts which produces (stem cell).
- Continuous supply of new cells

- These cell moves up to villi differentiate and become functioning cells. Cell at the top of the fold of villi are slough off slowly but replaced by new cell which originate from mitosis in the crypts. Intestinal villi ,Mature functioning cell Stem cell

Radiation

Sterilizes a large proportion of dividing cell in the crypts thus as the surface of the villi slough off there are no replacement of cells from crypts, thus villi began to shorten and shrink (villus atrophy) on the worst stage of radiation enteritis villi are flat and completely free of cells. Most severe effects – noted in intestine, large intestine somewhat have better tolerance. Delay between time of radiation and onset of GI (radiation syndrome) depends upon life span (14 days) of mature functioning cells at the top of villi.

Hemopoietic Syndrome (Bone Marrow Toxicity)

At the dose of 3 to 8 Gy death occurs. At about 30 days after exposure and continue up to 60 days thus LD expressed for human as LD50₆₀.

Cause: Mitotically active cell (precursor cell) sterilized by radiation, thus supply of WBC, platelet, RBCs thereby diminished. Most marked effect fall on lymphocytes (half life 24 hr) than platelet (half life 7 days) than RBC (half life 120 days). Crisis occurs at which point of time when circulating cells in blood reaches a minimum level. It is only when mature circulating cells began to die off and supply of new cells is inadequate.

**Individual Variation
Do have role to play like**

Very young – Very Old, Old persons are more radiation sensitive than young adult. Female have greater degree tolerance than male.

LD50₃₀ at 5.3 Gy in rhesus monkey LD50₃₀ denotes death continue up to 30 days after exposure

Symptoms

3 weeks after exposure Onset of chills, fatigue, patchial hemorrhage, ulceration of mouth, epilation decrease Granulocyte counts causes fever, infection impairment of immune status, bleeding due to low platelet count Usually – anaemia due to haemorrhage (normally) not due to decrease RBC count (life span 120 days). Important cause of Death – that is infection can be controlled by antibiotic treatment mean lethal dose and **Bone marrow transplantation TBI** has been of interest from the point of view of bone marrow transplantation or in the case of rescue of patient receiving Chemotherapy or

Radiotherapy

- TBI (Total body irradiation)
- Radiolabelled antibodies

LD50₆₀ for human based on experiments at Hiroshima and Nagasaki. Lushbaugh claims best estimate is around 3.25 Gy for young adult without any medical intervention. Bone marrow rescue dose require for the person to recover – that is no. of transplanted bone marrow cells that are required for the person to recover from a supralethal dose. Larger the height, weight more hemopoietic toxicity occurs because there is inverse relation between body weight and hemopoietic stem cell concentration (that is number of hemopoietic stem cell). Human require 10 times more bone marrow cell per Kg body weight as mouse for successful bone marrow rescue. After supralethal dose because of lower concentration of hemopoietic stem cell.

Species	Per Body	Unit	Rescue dose	Relative hemopoietic stem cell concentration
	Average Body Wt.	LD50 Gy	$\times 10^{-8}$	
Mouse	0.05 Kg	7 Gy	2	10
Dog	12 Kg	3.7 Gy	17.5	1.1

Delay between the time of irradiation and the onset of subsequent radiation syndrome is dictated by the normal life span of the mature functioning cell.

Acute Radiation Induce Toxicity Profile

Result from total body exposure to about 100 Gy result in death between 30-50 hrs. The cause of cerebrovascular syndrome is due to permeability of small blood vessels in brain.

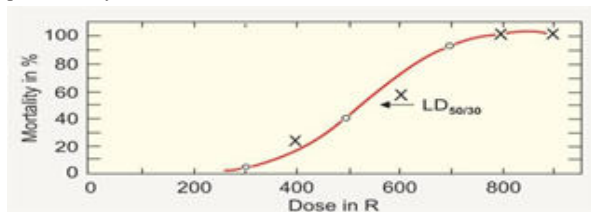


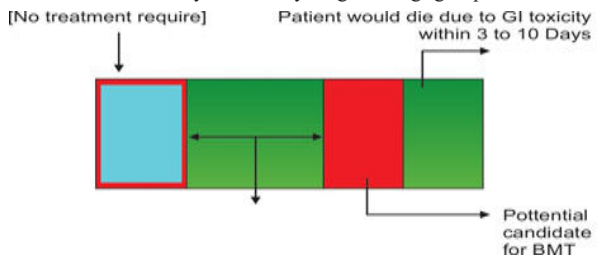
Fig.2: Radiation Effect

GIT syndrome do occur from TBI to about 10 Gy dose, death occur in 9 days in human population due to depopulation of epithelial lining of GI tract. hemopoietic syndrome – It results from total body exposure to 3 to 8 Gy since radiation sterilizes some or all mitotically active precursor cell symptoms occur after 3

week. LD50 for human is about 3-4 Gy for youth, adults without medical intervention dose will be little less to very young or very old. The dose window over which bone marrow transplantation is useful is very narrow 8 to 10 Gy.

Management of Acute Radiation Exposure at the Dose Close to LD50–

- Patient should be taken out from the place of exposure and isolated in a barrier (nursing room)
- Blood Count : should be done 6 hrly interval upto 72 hrs, since TLC may fall to less than 1000 cell/mm³ within 24 hrs.
- To know the amount of dose count should be sent before 24 hrs of exposure because peripheral lymphocytes (in which chromosomal abberation occurs provide clue that how much dose patient has been exposed) disappear from peripheral blood before 24 hrs so we can do cytogenetic study.
- LFT, KFT, electrolytes should be done.
- Blood culture in order to start appropriate antibiotic.
- ECG to be done.
- Patient should be given antiseptic bath (with diluted savlon)
- A part from IV antibiotic, oral antifungal to be given (exp. fluconazole, ketoconazole) to combat fungal infection in upper aerodigestive tract.
- For gut sterilization oral antibiotic (cotrimoxazole) should be given.
- IV fluid and electrolytes according to need should be given.
- Colony stimulating factor (GM-CSF) can be given subcutaneously to promote haemopoiesis.
- Blood component can be given (fresh blood, packed cell, fresh platelets)
- In blood component – we should prefer (platelet, packed cell, RBC) because whole blood itself causes bone marrow suppression.
- In bone marrow failure cases BMT can be done with appropriate HLA matched donor/ autologous BMT window period within which BMT is use for is 8 to 10Gy up to pose of 8Gy most persons would survive with proper antibiotic and careful nursing.
- Above 10 Gy most of the patient dies due to radiation induced GI syndrome and dose up to 2Gy no T/t is required.
- Overall Ld50 for human is 3-4 Gy for young adult without medical intervention it may be less for young & old age group.



Bone marrow toxicity occurs but only supportive care is the treatment

Bone Marrow Transplantation (BMT)

- Allogenic BMT (taking other marrow done by matching with HLA typing (human leucocyte antigen)
- Autologous – Patient’s own marrow taken for BMT : HLA typing test is required.
- In allogenic bone marrow transplantation, marrow injected intravenously into recipient who is suitably undergone conditioning.
- What is conditioning therapy before allogenic BMT requir – High dose of cyclophosphamide — Give total body irradiation

Why Just to abate recipient hemopoietic and immunological tissue now, injected cell home to bone marrow and produces erythrocytes/ granulocytes/ platelets in about 3-4 weeks period is important. We should give antibiotic / antifungal in the patient. Best result from BMT seen in young age. Old age BMT results are not so good.

Complication Due to BMT

- Complication occurs in 30% cases of BMT more in allogenic type.
- GVHD (Graft versus Host Disease)
- Interstitial Pneumonitis
- Graft versus hostel Reaction occurs: Mainly because of donor T

lymphocytes and its cytotoxic activity due to lymphocyte sensitization to new host. It can attack liver, skin, GUT, decrease immune status leads to infection. Treatment is antibiotic/antifungal, cyclosporine, Steroids, Methotrexate. Intestinal pneumonitis for this immunological injury occurs to lung treatment is steroid.

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