Collection of Recorded Radiotherapy Seminars

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WHOLE BODY IRRADIATION

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WHOLE BODY IRRADIATION (WBI)

• WBI may be:
  – Accidental

  – Deliberate
    • Medical
      – Bone marrow transplant
    • Non-medical
ACCIDENTAL WBI

• Usually as a result of radiation disaster or accident
  – May also be due to medical accidents
    • Dislodged or stuck sources
• Results in WBI by photon and particles eg neutron, heavy ions.

Chernobyl
ACCIDENTAL WBI

• Radiation disasters
  – Chenobyl
  – Long Island New York

• Radiation accidents
  – “Stolen” radioactive sources
  – Malfunction industrial sources
ACCIDENTAL WBI

• Compared to medical irradiation
  – Dose is non-uniform
  – Dose level is not known
  – Dose may be due to mixed particle and non-particle radiation
  – Exposure time is not known
Acute Radiation Syndrome (ARS)

- Acute illness with course over hours to weeks.
- Stages
  - Prodromal symptoms
  - Latent period
  - Symptomatic illness
  - Recovery / sequelae
DOSE RANGES FOR ARS

• Sequelae of ARS is dependant on dose
  – < 100 cGy - asymptomatic
  – 100 - 200 cGy - minor symptoms
  – 250 – 500 cGy - haematopoietic syndrome
  – 800 – 3000 cGy - gastro-intestinal syndrome
  – > 2000 cGy - cerebro-vascular syndrome
Prodromal radiation syndrome

• Initial reaction to irradiation –
  – immediate response

• Characterized by
  – Nausea
  – Vomiting
  – Diarrhea

• Lasts from a few minutes to few days

• Happens at low doses but increases with dose
Prodromal radiation syndrome

• The symptoms vary according to dose:
  – Time of onset
    • Shorter with higher dose
  – Maximal severity
    • Worse with higher dose
  – Duration
    • Longer with higher dose

• Symptoms
  – Gastro-intestinal
    • Nausea, vomiting, diarrhea
  – Neuro-muscular
    • Malaise, apathy, sweating, headache
LOW DOSE WBI (<200 cGy)

- Nausea is common
  - mild
- Headache – uncommon
  - Very mild
- No diarrhea
Emesis as indicator of dose

Fig. 3. Average data: time to emesis; U.S. Radiation Accident Registry data.

Time to emesis is a function of dose, decreasing exponentially with increasing doses.
Latent Stage

- Characterized by apparent lack of signs
- Changes are occurring at the cellular level
- Patient has false sense of well being
- Lasts for a few days to a week or so
Illness Stage

• Time during which clinical illness is evident.
• Depending on the dose received
  – may last from a few minutes to several weeks
• Signs are referable to the type of syndrome being manifest.
  – Haematopoietic syndrome
  – Gastro-intestinal
  – Cerebro-vascular
• Ends in recovery or death
Haematopoietic syndrome

- Total Body Exposure (TBE) = 3 – 8 Gy
- May lead to death
  - LD$_{50}$ in man is approximately 4 Gy
    - Very young & very old are more sensitive to radiation
  - Due to radiation damage to haematopoietic system
  - Death in 30 – 60 days
- Susceptibility to radiation differs between species
  - Negative correlation with body weight.

Table 12.1 50% lethal dose (LD 50) in mammals.

<table>
<thead>
<tr>
<th>Species</th>
<th>LD 50 (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>1.55</td>
</tr>
<tr>
<td>Pig</td>
<td>1.95</td>
</tr>
<tr>
<td>Goat</td>
<td>2.30</td>
</tr>
<tr>
<td>Dog</td>
<td>2.65</td>
</tr>
<tr>
<td>Rabbit</td>
<td>8.40</td>
</tr>
<tr>
<td>Mouse</td>
<td>9.00</td>
</tr>
<tr>
<td>Rat</td>
<td>9.00</td>
</tr>
<tr>
<td>Hamster</td>
<td>9.00</td>
</tr>
<tr>
<td>Guinea-pig</td>
<td>2.55</td>
</tr>
<tr>
<td>Monkey (according to the species)</td>
<td>3.5-5</td>
</tr>
<tr>
<td>Man</td>
<td>4.5-5</td>
</tr>
</tbody>
</table>
Haematopoietic syndrome - Symptoms

- Nausea / vomiting is prominent
  - Moderate to severe
- “Latent period”
  - Patient is asymptomatic
  - Progressive depletion of haematopoietic cell due to death of stem cells in bone marrow
  - Leads to pancytopenia
- Death often due to infection 2 - 4 weeks post-exposure
Gastro-intestinal syndrome

- TBE > 10 Gy
- Death within 3 – 10 days
- Symptoms
  - Nausea / vomiting
    - severe
  - Diarrhea
    - Early onset, hours after exposure
  - Dehydration
  - Loss of appetite & weight
  - Lethargy,
  - Headache
    - moderate
GASTRO-INTESTINAL SYNDROME

Crypts of Lieberkuhn

Stem cells in intestinal crypts
GI syndrome - Pathology

• Depopulation of GI tract
  – Stem cells are sterilised and therefore normal epithelium replacement is absent
  – Leads to progressive shortening of villi, mucosal ulceration & oedema
  – Denuded GI tract leads to intestinal obstruction & invasion of gut bacteria
    • Bacteria toxins found in blood
    • Loss of integrity of “tight junctions”
CEREBRO-VASCULAR SYNDROMES

• Total body exposure (TBE) > 100 Gy
  – Lower limit is 20 – 40 Gy
• Death in hours – days
  – Manifested by altered consciousness and vascular instability
• Symptoms
  – Nausea & vomiting
  – Diarrhea
  – Confusion & coma
  – Seizures
CEREBRO-VASCULAR SYNDROME

• Mechanism of death is uncertain
  – Maybe be related to cerebral oedema and hypoxia

Soft tissue oedema post-irradiation
## Summary of ARS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Dose—Gy</th>
<th>Average Survival Time</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodromal</td>
<td>1</td>
<td>—</td>
<td>Nausea, vomiting, diarrhea, fatigue, leukopenia</td>
</tr>
<tr>
<td>Latent</td>
<td>1–100</td>
<td>—</td>
<td>None</td>
</tr>
<tr>
<td>Hematopoietic</td>
<td>1–10</td>
<td>6 to 8wk (doses over 2Gy)</td>
<td>Nausea; vomiting; diarrhea; pancytopenia; hemorrhage; infection</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>6–10</td>
<td>3–10 days</td>
<td>Severe nausea, vomiting, diarrhea, fever, fatigue, loss of appetite, lethargy, anemia, pancytopenia, hemorrhage, infection, electrolytic imbalance, and emaciation</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>&gt;20</td>
<td>Several hours to 2 or 3 days</td>
<td>Same as GI syndrome plus nervousness, confusion, ataxia, loss of vision, a burning sensation of the skin, disorientation, shock, stupor, edema, loss of equilibrium, respiratory distress, vasculitis, coma</td>
</tr>
</tbody>
</table>
ACCIDENTAL WBI

• Radiation accidents
  – “Stolen” radioactive sources
    • Samut Prakarn, Thailand
      – Stolen disused cobalt source
  – Malfunction industrial sources
    • Yanango
      – Detached HDR (industrial) source
    • Soreg
      – Malfunction industrial sources
        » 12.6 PBq (KCi)
YANANGO INCIDENT

• Detached industrial HDR source found and taken home by worker
• Held in hand and put in back pocket
• Clothes discarded in pile at home
• Wife sat on clothes to feed child
• Patient developed pain and blister at buttock
CLINICAL CONSEQUENCE

Blister then ulceration of buttock
PROGRESSION

Skin necrosis
Color Photo C- 16. Accident at Yanango: Perineal area with fibrosis and urethral fistula (February 2001).
### Skin effects with radiation exposure

#### Table 5. Radiation dermatitis.

<table>
<thead>
<tr>
<th>Radiation</th>
<th>Dose</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>6–20 Sv</td>
<td>Erythema only</td>
</tr>
<tr>
<td></td>
<td>20–40 Sv</td>
<td>Skin breakdown in 2 wk</td>
</tr>
<tr>
<td></td>
<td>&gt; 3000 Sv</td>
<td>Immediate skin blistering</td>
</tr>
<tr>
<td>Chronic</td>
<td>&gt; 20 Sv</td>
<td>Dermatitis, with cancer risk</td>
</tr>
</tbody>
</table>
SAMUT PRAKHAN

• Disused Cobalt teletherapy source taken to junk yard for scrap metal
• Manipulated by workers
  – Used acetylene torch to open source housing
An Accident with $^{60}\text{Co}$

- Problem - 3 improperly stored tele-therapy units
- 1 unit was dismantled (100kg cylinder removed, 10” diameter x 20” long)
- cylinder was cut open releasing source
FIG. 20. Wet desquamation 30 cm long in the popliteal area of the right knee of P3 five weeks after severe local exposure.
Epilation and skin lesion of P6/NP
Reconstruction of event

• Find source strength (if any)
  – Last calibration, age of source etc

• Reconstruct incidence, estimating
  – Position of patient
  – Distance from source
  – Duration of exposure
  – Exposure of source to environment
Incidence in Belarus

Assumed position of the operator during exposure (time ~ 1.5 minutes)
ESTIMATING DOSE

• Onset and severity of early symptoms
• Blood counts
  – Lymphocytes
  – Leucocytes
• Chromosomal aberrations
  – Half life of lymphocytes with aberrations is 3 years
  – Number of aberration (dicentrics) can be compared to calibration curve
  – Reliable for doses > 1Gy, unreliable < 20cGy
Guide for the management of radiation injuries based on early symptoms

<table>
<thead>
<tr>
<th>Clinical signs</th>
<th>Corresponding dose (Gy)</th>
<th>Decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBE &amp; LE</td>
<td>WBE &amp; LE</td>
<td></td>
</tr>
<tr>
<td>No vomiting</td>
<td>&lt;1</td>
<td>Outpatient with five week surveillance period (blood, skin)</td>
</tr>
<tr>
<td>No early erythema</td>
<td>&lt;10</td>
<td></td>
</tr>
<tr>
<td>Vomiting 2-3 h after exposure</td>
<td>1-2</td>
<td>Surveillance in a general hospital (or outpatient for 3 weeks followed by hospitalization if necessary)</td>
</tr>
<tr>
<td>Early erythema or abnormal sensation 12-24 h after exposure</td>
<td>8-15</td>
<td></td>
</tr>
<tr>
<td>Vomiting 1-2 h after exposure</td>
<td>2-4</td>
<td>Hospitalization in an haematological or surgical (burns) department</td>
</tr>
<tr>
<td>Early erythema or abnormal sensation 8-15 h after exposure</td>
<td>15-30</td>
<td></td>
</tr>
<tr>
<td>Vomiting earlier than 1 h after exposure and/or other severe symptoms e.g. hypotension</td>
<td>&gt;4</td>
<td>Hospitalization in a well equipped haematological or surgical department with transfer to a specialized centre for radiopathology</td>
</tr>
<tr>
<td>Early erythema within the first 3-6 h (or less) after exposure of skin and/or mucosa with oedema</td>
<td>&gt;30</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Consequences

• Initial (0-7 days) - Latent period
  – When operator sees source in upper position, he noted a metallic taste in mouth and a feeling of heat on his face.
  – About 6 minutes post-exposure, experiences nausea and vomiting, recurring over next 6 hours.
  – Within 15 minutes, single case of diarrhea.
  – Low psychological state
Clinical Consequences (cont)

• Clinical (8-39 days) - ARS
  – Fever
  – Blood changes
  – Mucositis and oral herpes
  – Intestinal bleeding
  – Skin injuries appearing on day 11
    • erythema, edema, wet desquamation
  – Severe pain in feet
  – Infection starts
ESTIMATING DOSE (2)

• Changes in blood profile within 24 hours
  – Lymphocytes most sensitive
    • 50% drop in 24 hours indicates significant radiation exposure
    • Rate of fall and absolute nadir counts may indicate dose
  – Leucocytes and platelets less sensitive
LYMPHOCYTE FALL WITH RADIATION
LYMPHOCYTE DROP

Fig. 4. Decrease in absolute lymphocyte count 0 to 2 days after a neutron–gamma mixed-field accident with a gamma-equivalent dose of approximately 3.5 Gy. REAC/TS Case No. 1935.

- Rate of fall can be predicted with certain dose ranges
Using metaphase spread, the number of chromosomal abnormalities can be counted

- Dose can be estimated from plot
## Summary of dose estimation

<table>
<thead>
<tr>
<th>Class of biomarker</th>
<th>Assay</th>
<th>Time window</th>
<th>Operating dose window (Gy, acute photon-equivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodromal signs and symptoms</td>
<td>Onset of vomiting</td>
<td>&lt; 12 hours</td>
<td>2–20</td>
</tr>
<tr>
<td>Hematological</td>
<td>Depletion of peripheral blood lymphocytes</td>
<td>&lt; 1.5 weeks</td>
<td>2–8</td>
</tr>
<tr>
<td>Cytological</td>
<td>Lymphocyte-metaphase spread dicentric</td>
<td>&lt; several months*</td>
<td>0.2–5</td>
</tr>
<tr>
<td></td>
<td>Lymphocyte-prefmature chromosome condensation</td>
<td>&lt; several months*</td>
<td>0.2–20</td>
</tr>
</tbody>
</table>

*Generally, blood is sampled 24 hours after radiation exposure for cytological chromosome aberration analysis of dose.*
TREATMENT

• Symptomatic & supportive
  – Replace blood and platelets
    • Prophylactic transfusion delays recovery of bone marrow
    • GCSF, ?thrombopoietin
  – Infections
    • Antibiotics
    • Barrier nursing
  – Supportive care
    • Fluids, nutrition (TPN)
  – ? Bone marrow transplant
P5/LS

WBC / Cu.mm

Days after exposure

*Died

G-CSF

GM-CSF

Days after exposure

17/2/00 24/2/00 2/3/00 9/3/00 16/3/00 18/3/00

17 24 31 38 45 47
MEDICAL EXPOSURE
LARGE FIELD IRRADIATION

• Conventional radiotherapy utilises precise field sizes adequate to cover tumour and draining node

• Large field irradiation may be used in certain circumstances to cover metastatic or disseminated tumour
  – Total body radiation and hemi-body radiation are well accepted practices in cancer management.
MEDICAL IRRADIATION

- Total body irradiation (TBI) often used as part of conditioning regime for bone marrow transplantation
  - Doses used exceeds LD$_{50}$
    - Rescued by donor bone marrow
- Short and long term consequence to irradiated organs are a concern
  - Mortality and morbidity is dependent on dose fractionation
ORGANS AT RISK

• Short term
  – Liver
  – Bone marrow

• Long term
  – Lungs
  – Kidneys
  – Lens
  – Fetus
  – Gonads
TBI

• Dose / fractionation
  – Single fraction
    • Rarely used now
  – Fractionated
    • Usually 12 - 14 Gy in 8 fractions
TBI SIDE-EFFECTS

• Acute parotitis
  – 1\textsuperscript{st} day, subsides by 3\textsuperscript{rd} day

• Veno-occlusive disease of liver
  – Hepatomegaly, ascites, jaundice, weight gain

• Interstitial pneumonitis
  – 50% risk with single fraction
  – Occurs 2 - 6 months post RT

• Kidneys
  – Most patient develop impaired renal function post TBI
TBI SIDE-EFFECTS (2)

- **Gonads**
  - All patients develop primary gonadal failure after TBI

- **Cataracts**
  - Occurs with dose > 5 Gy
  - > 30% with fractionated doses >12 Gy

- **Carcinogenesis**
  - In conjunction with chemotherapy, risk of 2\textsuperscript{nd} cancer is 20% at 10 years
Summary

• Whole body irradiation results in specific syndromes depending on the dose received
• Acute radiation syndrome has 4 stages namely, prodromal, latent, illness and recovery/sequelae stage
• In accidental radiation exposure, the dose may be estimated by symptoms, blood and cytogenetic parameters
• Treatment is mainly symptomatic and supportive
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