Biological Effects of Radiation

Health Physics

Fall 2004

UNITS for the purposes of this class ONLY

1 rad = 1 rem = 1 cGy = 1 cSv = 1 R

1 cGy = 10 mGy = 10 mSv

Biological Effects of radiation

- Molecular
- Cellular
- Deterministic
- Tissue and organ
- Acute whole body irradiation
- Stochastic
- Fetal and embryo

Molecular an cellular effects

- Linear Energy Transfer (LET)
  - Energy loss per unit length by a charged particle to a medium via local excitations and ionizations.
  - LET = dE/dL

Molecular and cellular effects

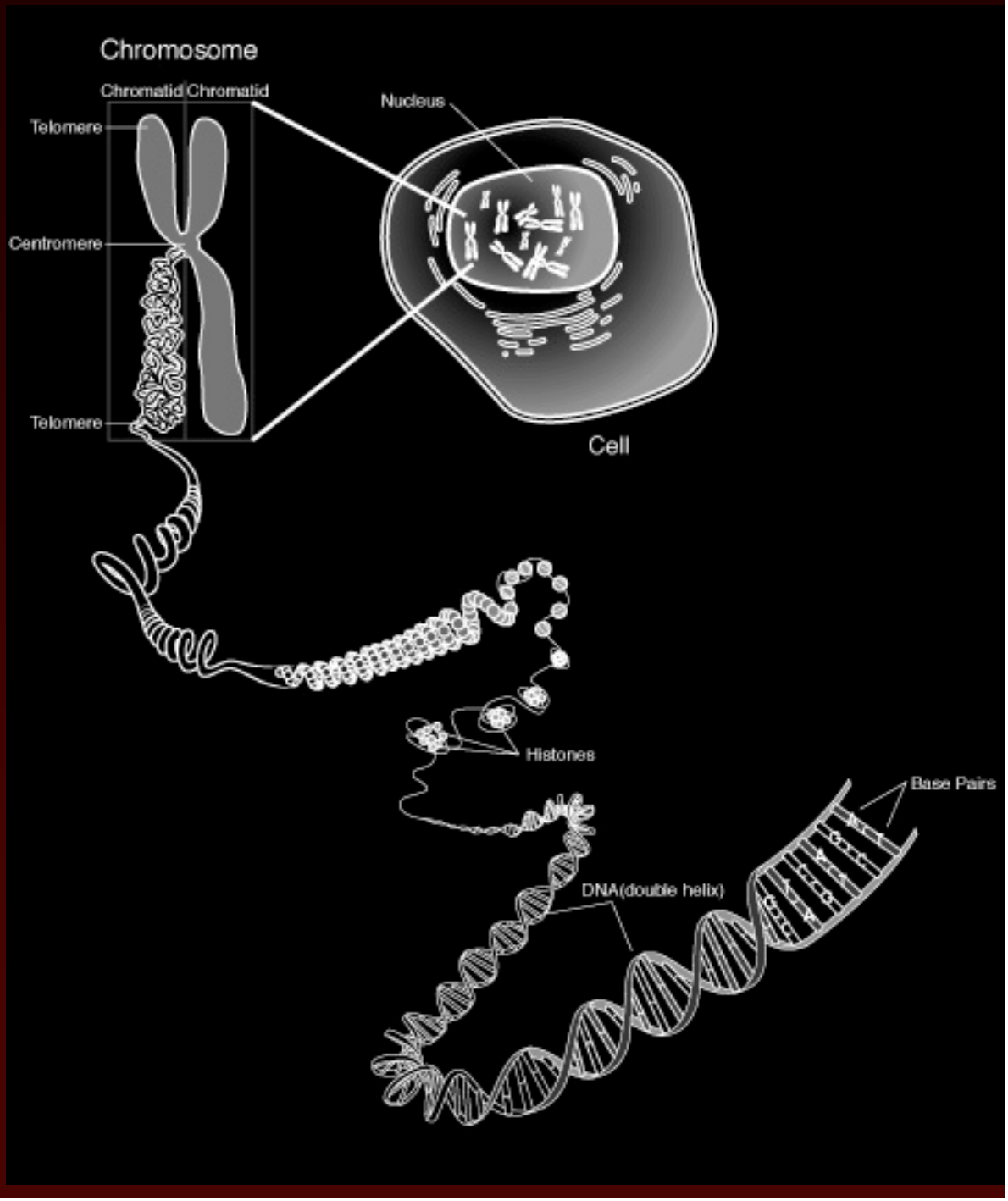
- TRACK averaged LET - same dL

- ENERGY averaged LET - same dE

Molecular and cellular effects

Radiation	LET (KeV/μm)
Cobalt 60	0.2
250 kV x-rays	2.0
150 MeV protons	0.5
2.5 MeV alpha	166
14 MeV neutron	12 (track)/100 (E)

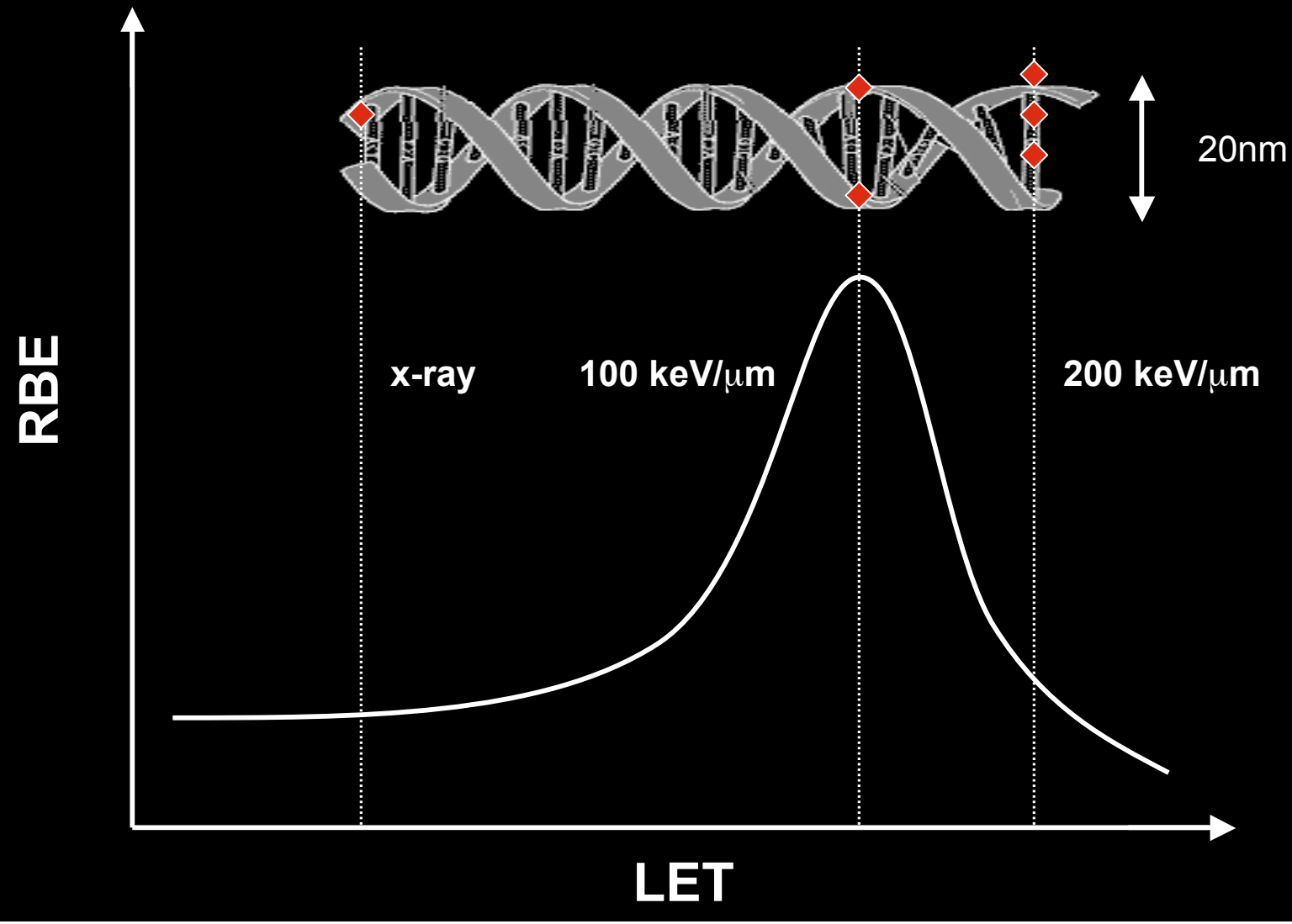
DNA, chromosomes and cells



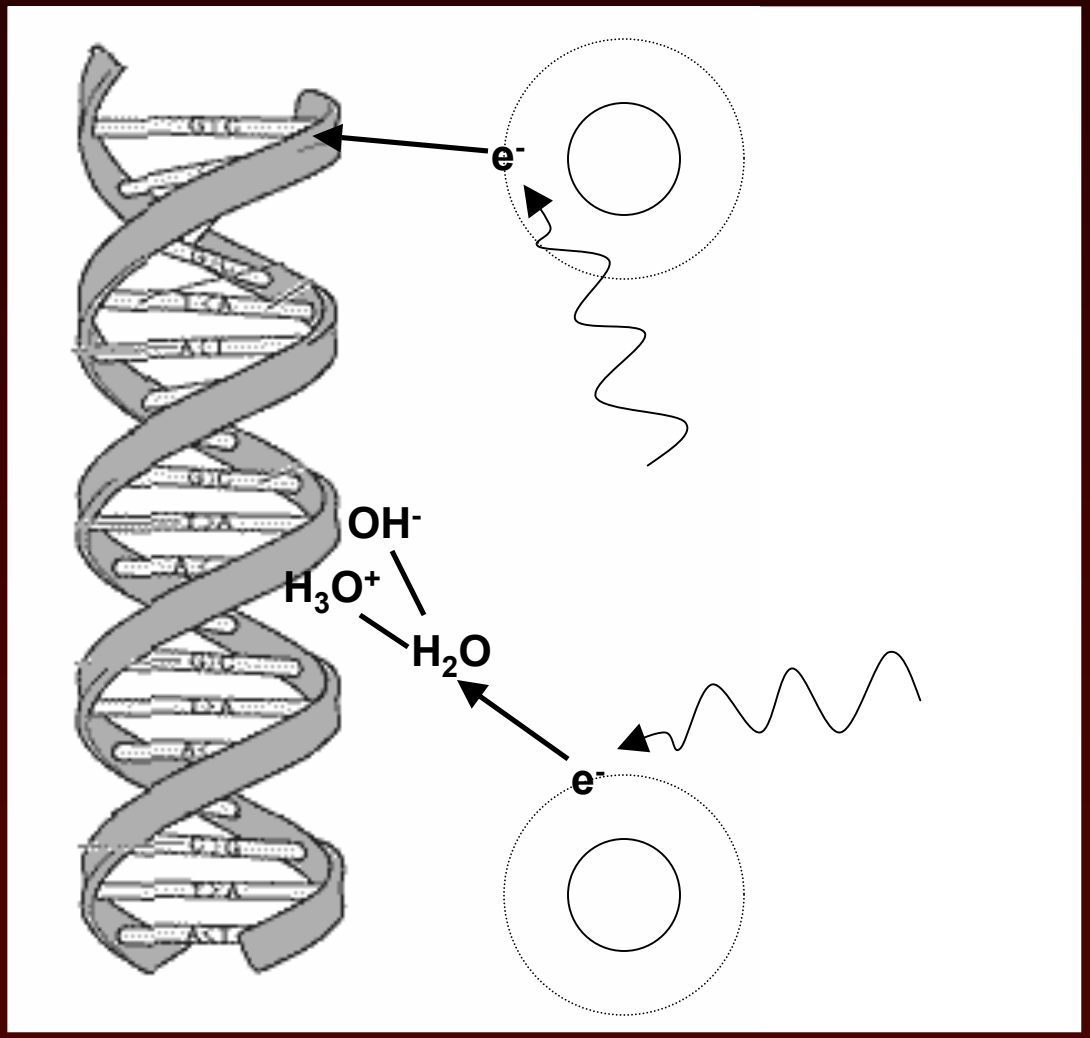
Cellular effects

- Nucleus:
  - Contains chromosomes and DNA
  - Radiosensitive: 1 Gy sufficient to kill cell
- Cytoplasm:
  - Contains other organs of cell
  - Radio-resistant : 10 Gy is required to kill cell

Molecular and cellular effects



DNA radiation damage



DIRECT (33%)
e^- interacts directly with DNA

INDIRECT (67%)
e^- interacts with water creating radicals which interact chemically with DNA

Water radiolysis - free radicals

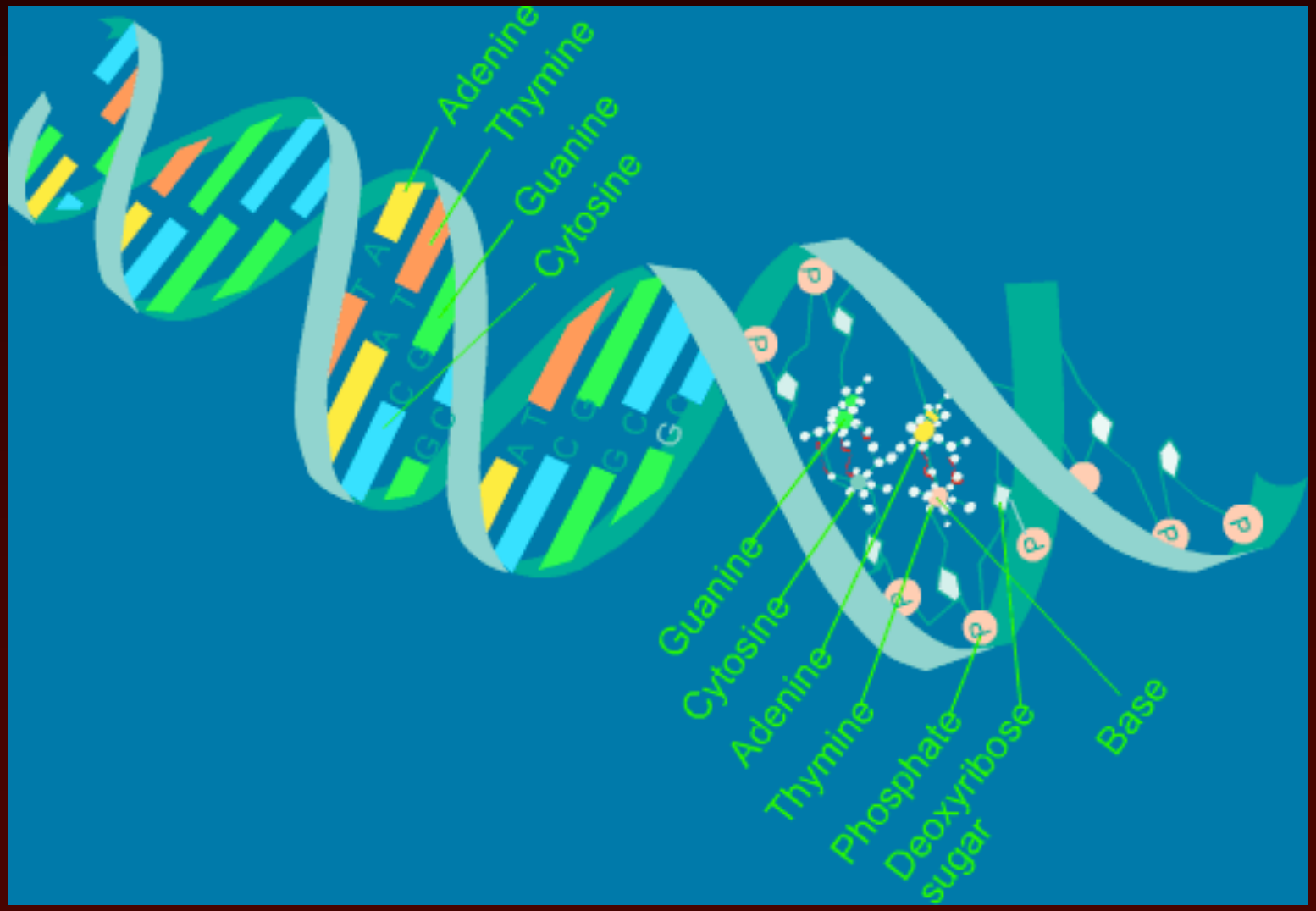
$$H_2O \rightarrow H_2O^+ + e^-$$

$$H_2O^+ + H_2O \rightarrow H_3O^+ + OH^-$$

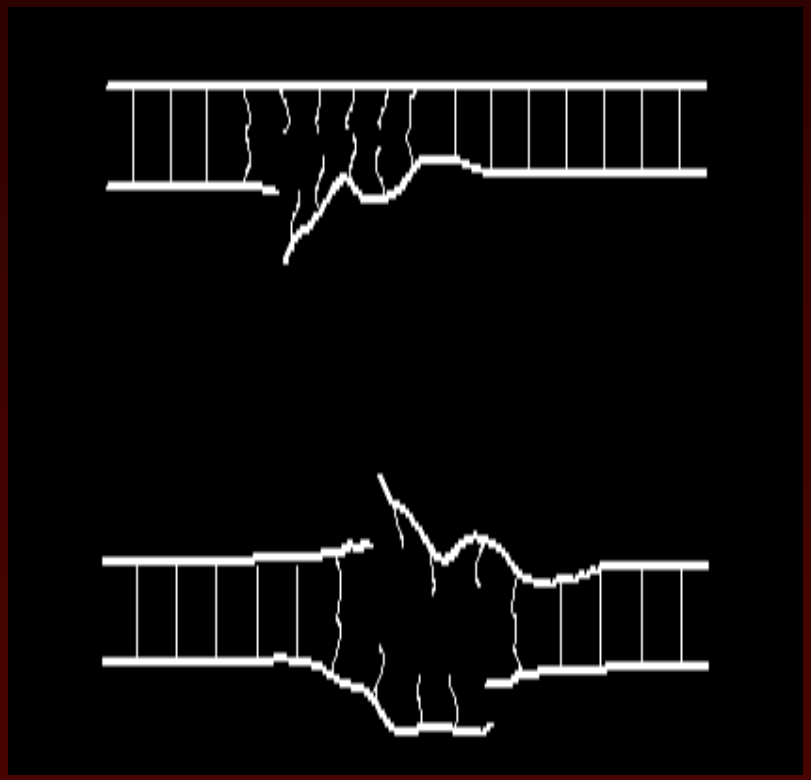
$$OH^- + R\text{-}H \rightarrow H_2O + R^-$$

Free radicals exist for less than 1 ms but can disrupt molecular bonds of DNA

DNA structure

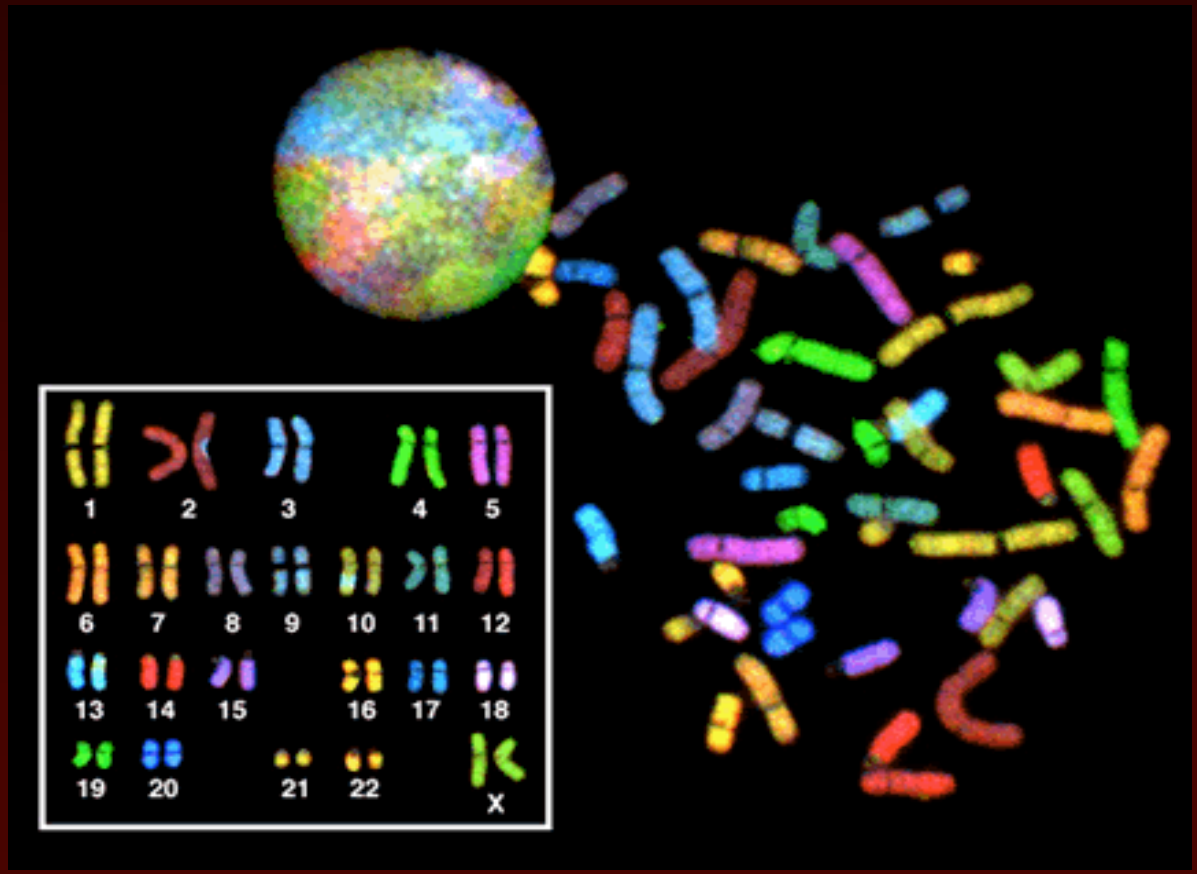


DNA strand breaks

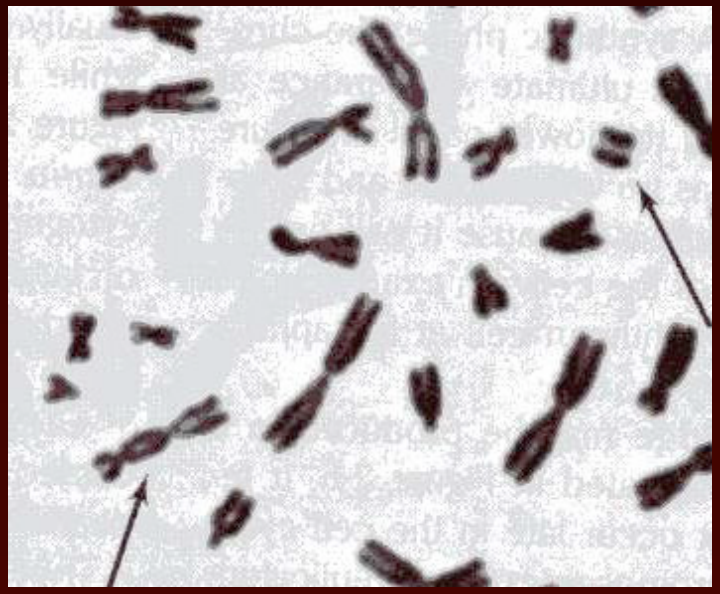


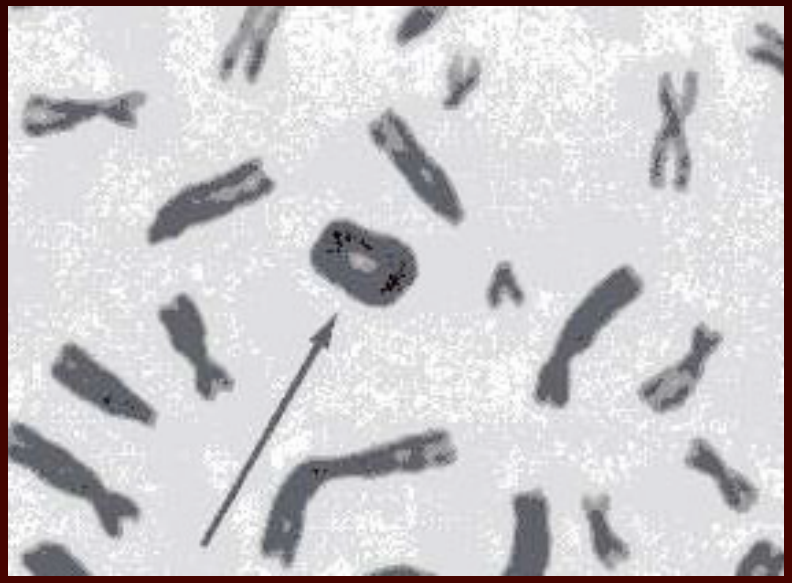
- Single strand break
  - repairable from mirror half of DNA
- Double strand break
  - less repairable
  - chromosome aberration
  - distant breaks repaired as if 2 single breaks

Chromosome aberrations



Chromosome aberrations





Damage to tissue or organs

- Radiation damage to cells can result in damage to tissue or organs
- Principal effect is atrophy (reduction in size)

Tissue radio-sensitivity

- High
  - Lymphoid, bone marrow, gonads
- Intermediate
  - Skin, GI, kidney
- Low
  - Brain, muscle, spine

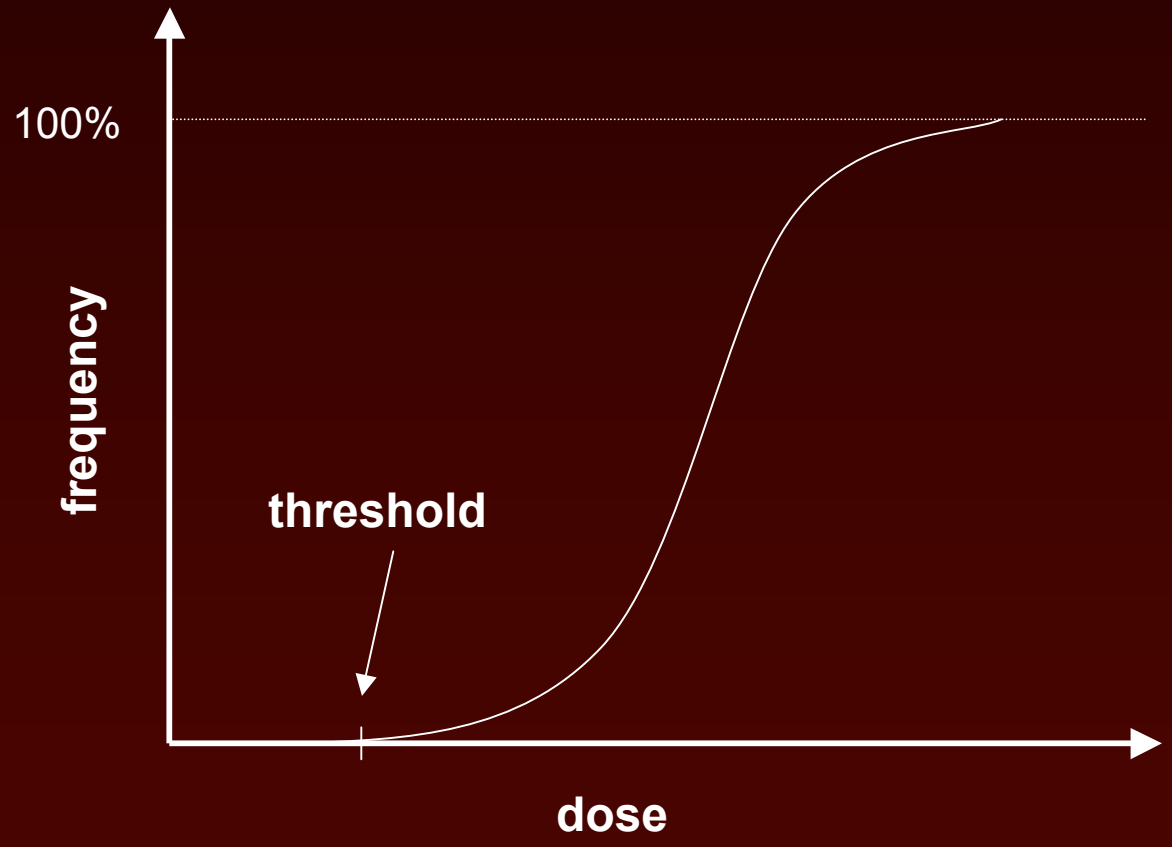
Whole body effects

- Early (deterministic)
  - Usually within weeks or months of exposure
  - High dose (>25 cGy)
- Late (stochastic)
  - Years after exposure
  - Low doses (<25 cGy)

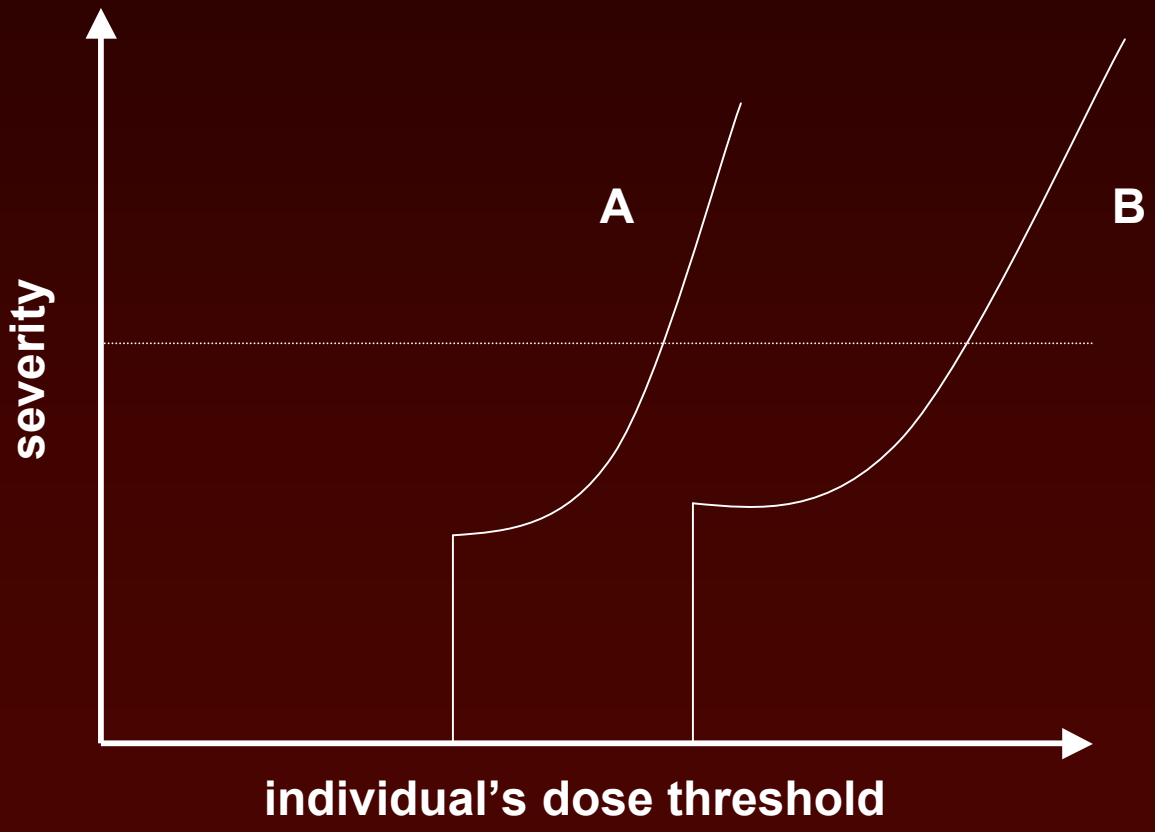
Deterministic effects

- Significant number of cells are injured or killed causing organ or tissue dysfunction
- Also called early or acute effects
- Dose threshold
- Severity proportional to dose

Deterministic effects



Deterministic effects



Deterministic effects

- Some deterministic effects are the result of a tissue dysfunction following irradiation, and are not directly attributed to cell death.
  - hormone dysfunction following pituitary irradiation
  - neurological or immunological effects following radiation

Whole body effects

Threshold dose	Effect
1 - 2 Gy	radiation sickness, malaise, nausea, fatigue, loss of appetite, vomiting
~ 4 Gy	death, $LD_{50/30}$

Skin effects

Threshold dose	Effect
3 - 4 Gy	Erythema, pigmentation, hair loss
10 - 15 Gy	Dry and moist desquamation
> 20 Gy	Ulceration and necrosis

Blood - bone marrow effects

Threshold dose	Effect
0.25 Gy	Decrease in lymphocytes
2 Gy	Decrease in lymphocytes and platelets over 4 weeks, then decrease in RBC, may result in anemia

Gastrointestinal effects

Threshold dose	Effect
6 Gy	Diarrhoea, disturbance of electrolyte and flid imbalance, possible ulceration of intestinal wall

Skeletal effects

Threshold dose	Effect
0.2 Gy	cessation of ossification, growth stunting in children, very high doses can lead to necrosis and breaks.

Thyroid effects

Threshold dose	Effect
100 Gy	reduction in thyroid function

Eye effects

Threshold dose	Effect
2 Gy	Cataracts, require latent period (months to years) depending on amount of radiation, fractionation, LET

Immune system effects

Threshold dose	Effect
4.5 Gy	inhibition of immunological functions

Reproductive system effects

Threshold dose	Effect
0.15 - 0.3 Gy	Reduced sperm count
3.5 - 6 Gy	Permanent sterility (males)
2.5 - 4 Gy	Permanent sterility (females)

Acute whole body irradiation

- Death within days to weeks
- Prodromal syndrome - early symptoms
- CNS, GI, bone-marrow failiures
- $LD_{50/30}$ ~ 4 Gy

Prodromal syndrome

- Symptoms (at ~ 4 Gy):
  - Anorexia, nausea, vomiting, fatigability
  - Varies in time of onset, severity, and duration
- Immediate diarrhea, fever, hypotension indicate a supra-lethal dose

Cerebrovascular syndrome

- Total body dose in excess of 100 Gy
- Severe nausea and vomiting (minutes)
- Disorientation, loss of coordination, respiratory distress, convulsions, coma, death
- Death results in a matter of hours

Gastrointestinal syndrome

- Total body dose in excess of 10 Gy
- Symptoms include nausea, vomiting, and prolonged diarrhea
- Dehydration, weight loss, emaciation, complete exhaustion, death
- Death results in 3 - 10 days, due to depopulation of epithelial lining of GI tract

Hematopoietic syndrome

- Whole body dose 2.5 - 10 Gy
- Left untreated results in death within 60 days
- Production of RBC, WBC, and platelets is suppressed
- Effects are not seen till weeks after exposure

Hematopoietic syndrome

- Latent for 3 weeks then chills, fatigue, petechial hemorrhaging of the skin, ulcerations in mouth, suppressed immune system.
- Patient is susceptible to infections, dies as a result.
- Patients may be treated with BMT, antibiotics, platelet infusions

Bone marrow transplants

- Total body irradiation (TBI) may be used to prepare the patient for BMT
- Dose 10 - 12 Gy over 4 days
- 3 reasons
  - suppress immune system (prepare for transplant)
  - kill leukemic cells
  - Destroy bone marrow
- Patient treated with antibiotics, BMT, and careful nursing

Survivors of acute exposures

- About 70 people in US have been occupationally exposed to doses up to 3 Gy in the last 50 years.
- No additional cancers, shortened life-spans, or degenerative diseases have been observed.
- In fact the highest non-lethal dose only increases the chance of cancer by 24%.

Summary: general

Level of Biological Organization	Important Radiation Effects
Molecular	Damage to enzymes, DNA etc. and interference to biological pathways
Subcellular	Damage to cell membranes, nucleus, chromosomes etc.
Cellular	Inhibition of cell division, cell death, transformation to a malignant state
Tissue, Organ	Disruption to central nervous system, bone marrow, intestinal tract. Induction of cancer
Whole Animal	Death; 'radiation life shortening'
Populations	Changes in the genetic characteristics of individual members

Summary: effects organs

Radiation Effects Following Acute Exposures In Rads To Target Organs		
Exposure Health Effect	**Organ**	**Absorbed dose in Rad**
Temporary Sterility	Testes	15
Nausea	Whole Body	35
Depression of Blood Cell Forming Process	Bone Marrow	50
Reversible Skin Effects (e.g., early reddening)	Skin	200
Permanent Sterility	Ovaries	250-600
Vomiting	Gastrointestinal Tract	300
Temporary Hair Loss	Skin	300-500
Permanent Sterility	Testes	350
Skin Erythema	Skin	500-600

Summary: whole body

Biological Effects of Short Term Radiation on Humans	
Dose (Rad)	**Effect**
0-20	No detectable effects
20-100	Measurable transient blood changes. Temporary decrease in white blood cell count.
100-200	Acute radiation sickness - nausea, vomiting, longer-term decrease in white blood cells.
200-300	Vomiting, diarrhea, loss of appetite, listlessness, death in some cases.
300-600	Vomiting, diarrhea, hemorrhaging, deaths occurring in 50% of cases at 350 rad or above without medical treatment.
Above 600	Eventual death in almost all cases

Stochastic effects

- Stochastic means random
- Also known as late effects
- Years after exposure
- Low doses (<25 cGy), sometimes high doses

Stochastic effects

- The probability of a stochastic effect increases with dose
- The severity of the effect is not dose related
- Cancer induction

Stochastic effects

- Stochastic effects are predicted for populations not individuals
- Applied for low dose, low dose-rate irradiations
  - Dose < 2 Gy, rate < 10 cGy/hr

Stochastic effects

- Somatic cells
  - May cause cancer induction
- Germinal cells
  - May cause hereditary effects in progeny of irradiated individual

Radiation carcinogenesis

- Radiation is a weak carcinogen
- Most damaged cells either repair themselves or die
- Cancer induction following radiation is a stochastic effect

Radiation carcinogenesis

- Latency is the amount of time required for the cell to grow to macroscopically sized tumor
- Median latency is 8 years for leukemias and 16 to 24 years for solid tumors
- Minimum latent periods are 2 years for leukemias and 5 to 10 years for solid tumors

Radiation carcinogenesis

- There are 4 steps in the development of cancer cells:
  - Initiation (initial changes to normal cells)
  - Promotion (further changes over a long time)
  - Conversion (cell becomes malignant)
  - Progression (cell division and multiplication)

Sources of data

- Japanese A-bomb survivors
- Patients exposed for medical treatment or diagnosis
- Occupationally exposed workers
- Animal and in vitro studies

Japanese A-bomb survivors

- On going follow-up study of 76,000 survivors of Hiroshima and Nagasaki
- Primary source of data for somatic stochastic effects
- Individuals of both sexes
- Wide range of approximately whole body doses

Japanese A-bomb survivors

- High doses and dose rates
- Dosimetry is approximate
- 60% of cohort is still alive, data must be projected to a full lifespan
- Data must be transferred to other populations (eg. Japanese to Western)

Medically exposed

- Patients with *Ankylosing Spondilitis* treated with X-rays to relieve pain (UK)
  - 14,000 patients (1935-1954)
  - Dose ~ 2 Gy
  - Looking for leukemia and other cancers
  - By 1992 increase in relative risk to 1.30

Medically exposed

- Female patients treated for post partum mastitis (NY)
  - 45,000 (1940 - 195?)
  - 2 - 3 Gy
  - 601 cancers
  - 115 additional breast cancer cases

Medically exposed

- Cervix cancer patients
  - 150,000 women treated at 20 centers world wide
  - 4,188 developed a second primary cancer
  - Many organs studied

Medically exposed

- Canadian fluoroscopy study
  - Breast cancer in patients given multiple fluoroscopies during management of TB (NS, MA) (1930-1952)
  - 31,000 women
  - Some patients received breast dose up to 2 Gy
  - Relative risk 1.36 (> 10 cGy), 1.11 (< 10 cGy)

Medically exposed: problems

- Not a complete lifespan study
- Patients received high doses in a few high dose rate fractions
- Not whole body doses
- Patients' medical conditions may bias results
- Socio-economic and ethnic make up of cohorts bias data

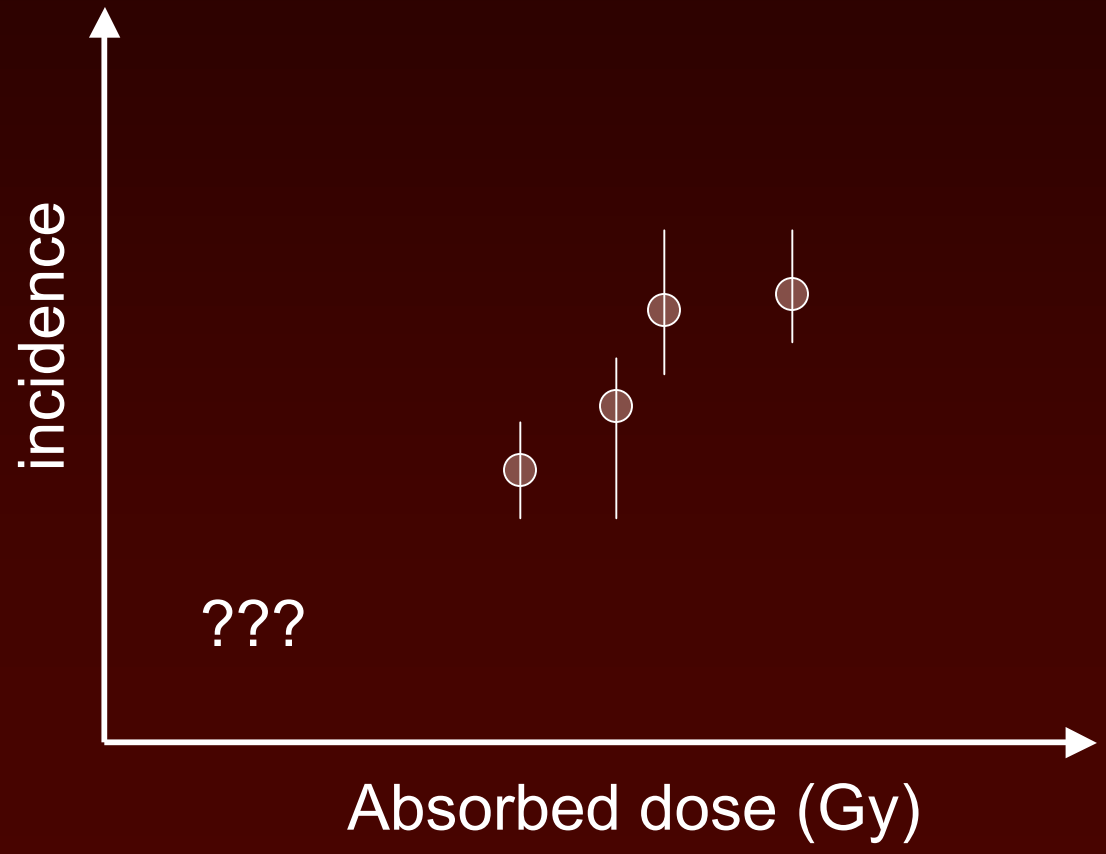
Study	Endpoint	Cancer	Cases	Patients
A-bomb	Mortality	ALL	5,936	76,000
AS (UK)	Incidence	ALL (no colon)	402	14,000
TB (NS)	Mortality	Breast	482	31,000
TB (MA)	Mortality	Breast	74	31,000
PPM (NY)	Incidence	Breast	115	45,000

BEIR V, 1990

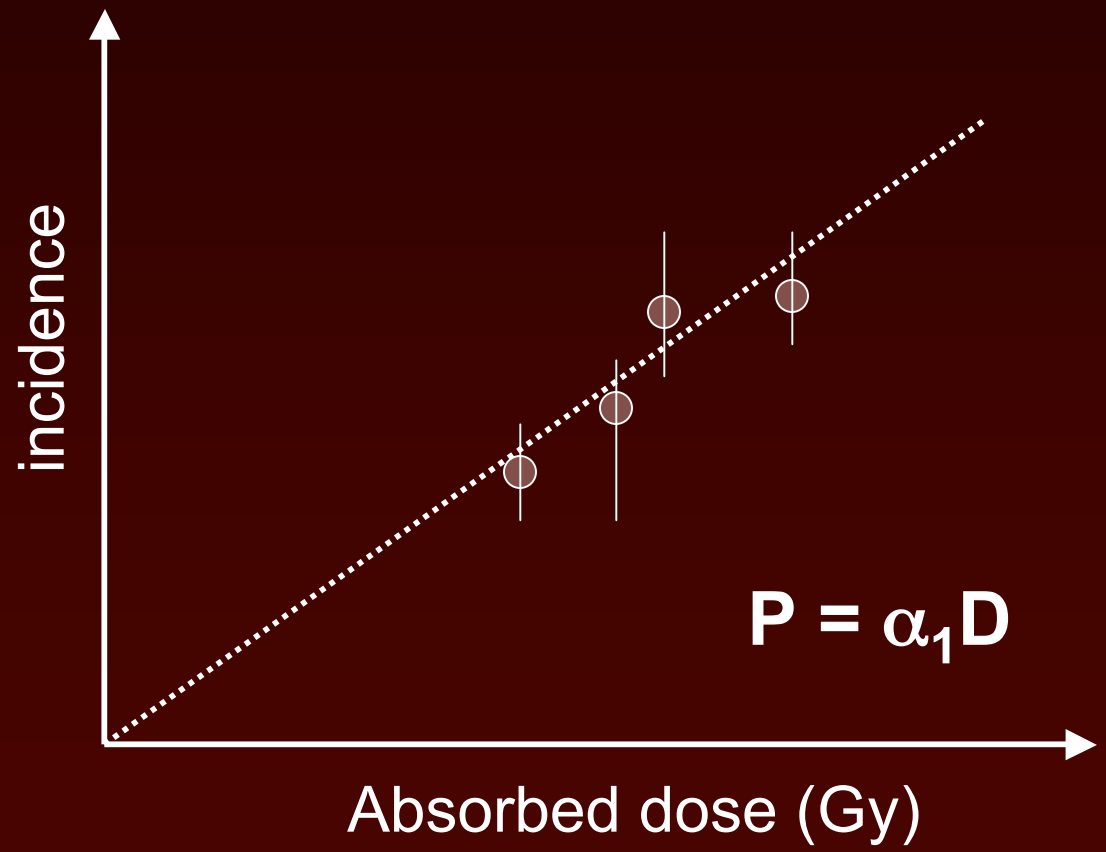
Occupational exposures

- Uranium miners (lung)
- Radiologists (skin, leukemia)
- Radium dial painters (bone)
- Radiation accidents (all)

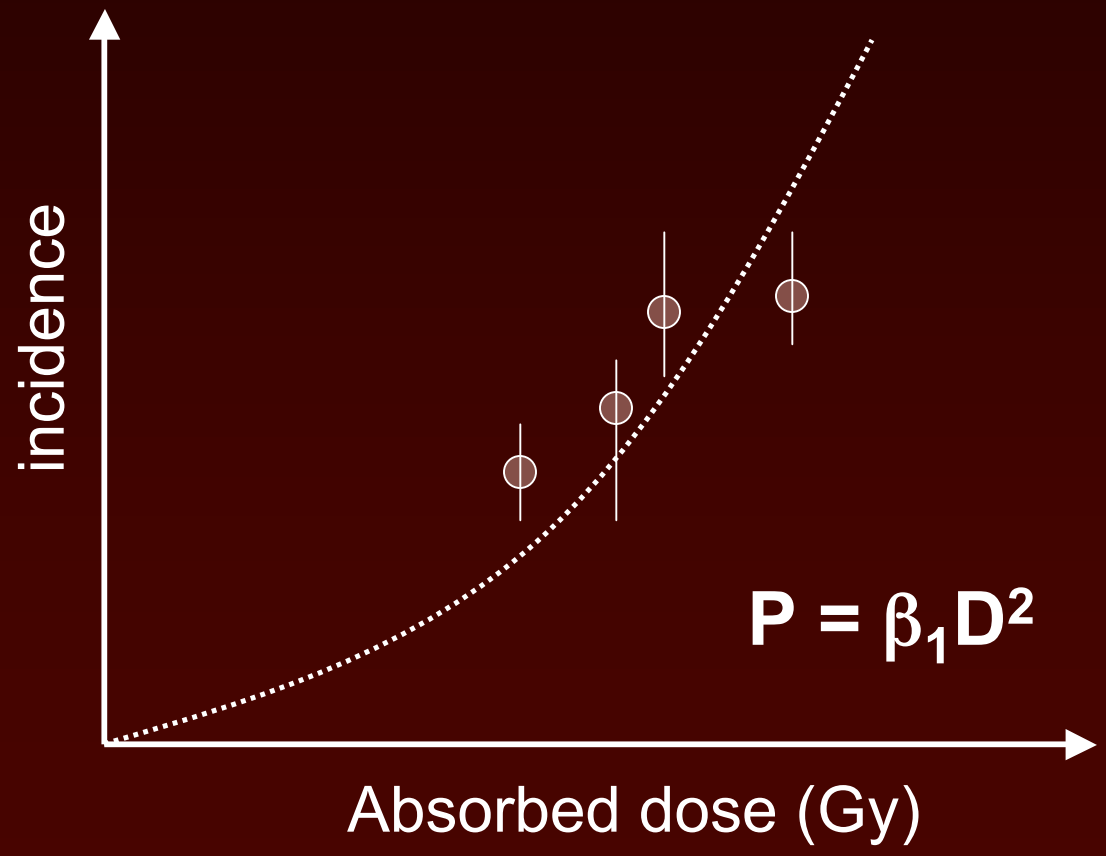
Dose response - stochastic



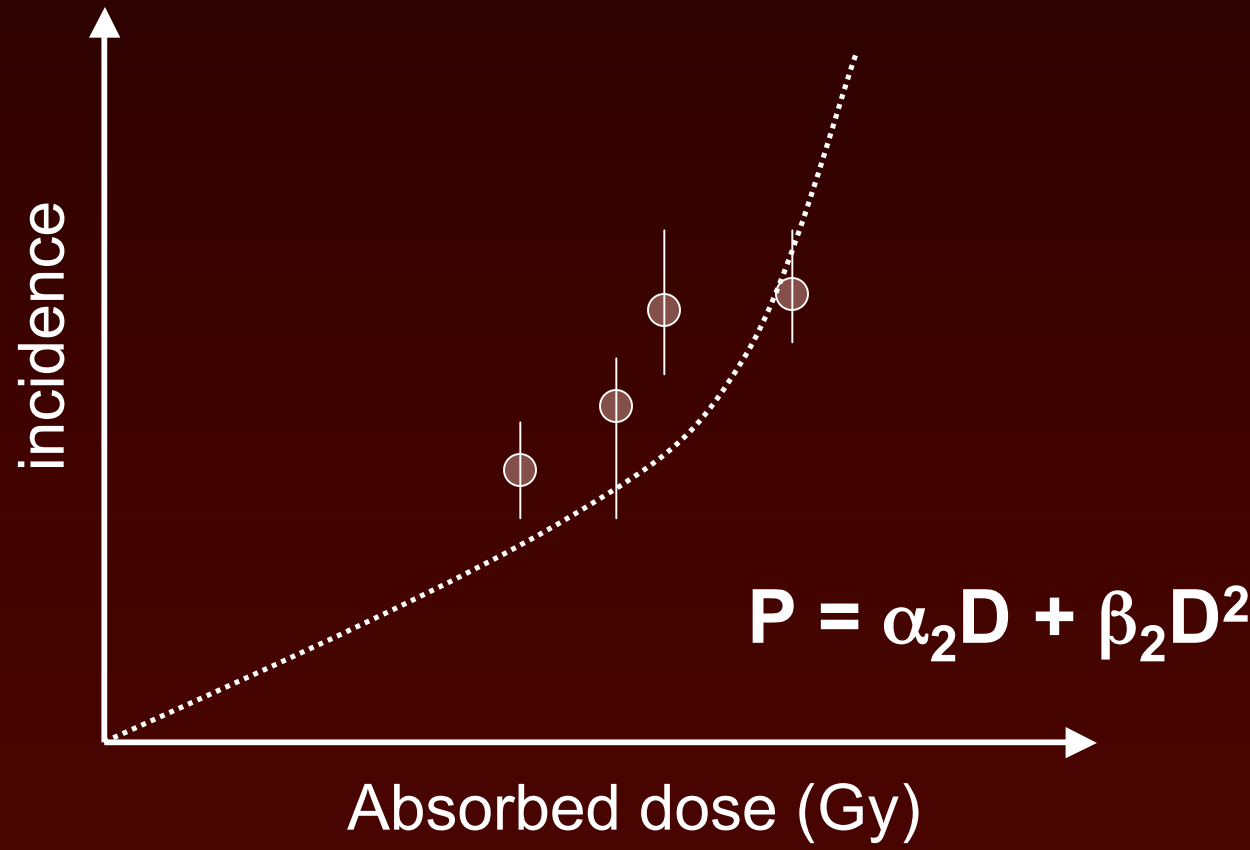
Linear model



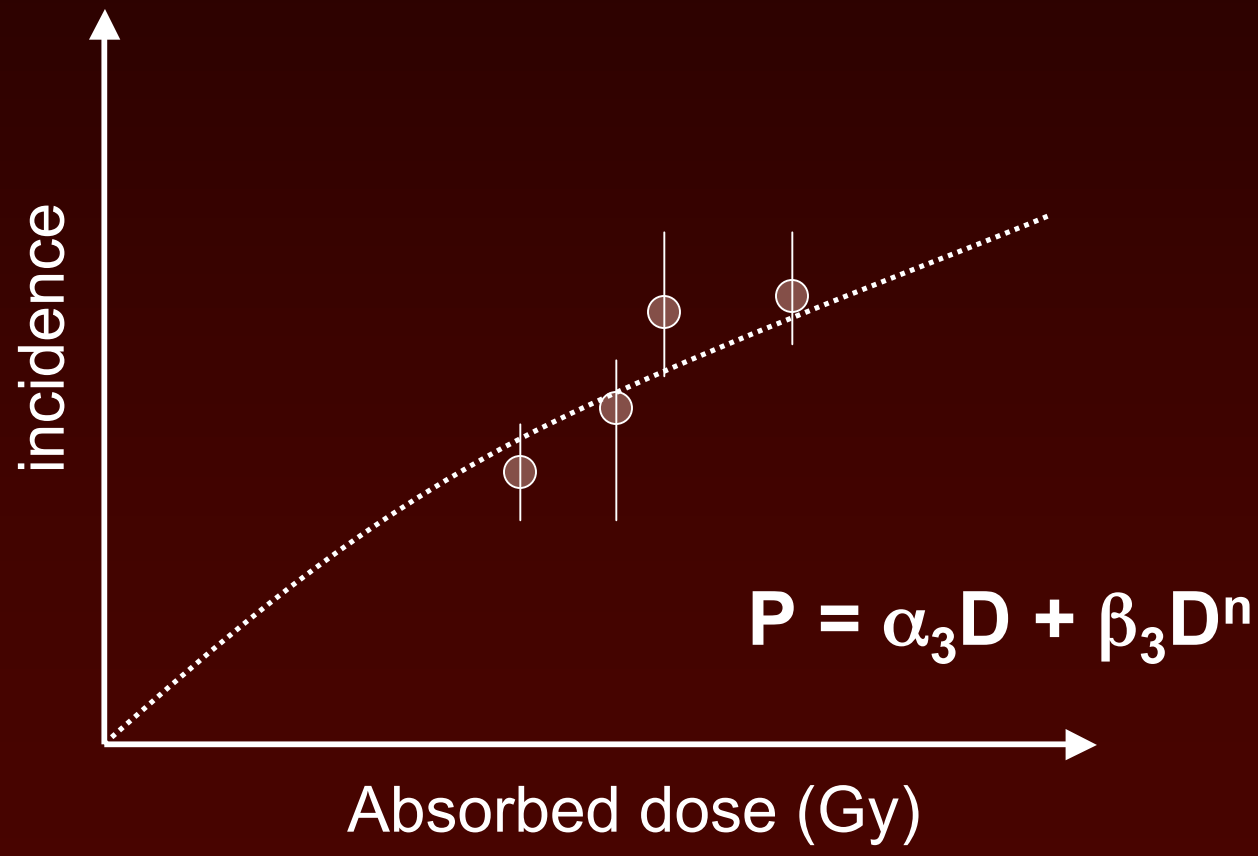
Quadratic model



Linear - Quadratic model



Fractional power model



DDREF

- Dose rate effectiveness factor
- Fewer cancers induced if dose is given over a longer period of time at a low dose rate as opposed to an acute exposure.
- For doses < 2 Gy and rates < 0.1 Gy/hr
- ICRP 60 recommends DDREF = 2 (double the risk for acute exposures)

Nominal probability coefficients for stochastic detriment ICRP 60

ICRP 60	Workforce	Public
Fatal cancer	0.04 / Sv	0.05 / Sv
Non-fatal cancer	0.008 / Sv	0.01 / Sv
Hereditary effects	0.008 / Sv	0.013 / Sv
Total	**0.056 / Sv**	**0.073 / Sv**

Hereditary effects

- Exposure of a population can cause adverse health effects in descendants due to mutations induced in germ cells
- Radiation only increases mutation rate
- Information on mutation rates comes almost entirely from animal studies (ex. Mega-mouse project)

Hereditary effects

- Doubling dose is the dose required to double the normal spontaneous rate.
- Estimated from mouse data the doubling dose for humans is ~ 1 Gy.
- From the A-bomb survivors and their children the doubling dose is estimated at ~ 2 Gy.
- No hereditary effects from radiation exposures have been observed in humans

Childhood cancer after irradiation in-utero

- Low dose irradiation in-utero (last trimester) causes increased risk of childhood malignancies
- An OBS x-ray exam dose ~ 10 mGy
- relative risk of childhood cancer is increased by 40%
- Absolute risk is still about 0.06 / Sv

Fetal and embryo exposures

- Counseling of pregnant patients:
  - Diagnostic radiology tests
  - Nuclear medicine exams
  - Radiation therapy

Risks of pre-natal irradiation

- When risks are properly explained pregnancy is usually continued
- Risk must be evaluated relative to other pregnancy risks
- Therapeutic abortion should not be recommended for doses < 50 mGy (5 cGy)

Expected effects of a 10 mSv dose per 10,000 conceptions

Effect	Natural frequency	Additional cases after 10 mSv
Spontaneous abortion	1,500	none
Congenital abnormalities	300	None
Mental retardation	50	None
Childhood cancer	70	3 - 5
Lifetime cancer	2500	15
Genetic defects	2500	2

Stewart and Kneale, 1970

Factors to consider

- Stage of pregnancy
- Menstrual history
- Previous pregnancy history
- History congenital defects
- Age of parent
- Type of radiation test
- Calculation of embryonic dose
- Status of pregnancy (wanted or unwanted)

Estimated fetal dose from diagnostic exams

Examination	Dose (mGy)
Upper extremity	0.01
Lower extremity	0.01
Skull	0.04
Chest (film)	0.04
Chest (fluoro)	0.70
Cholecystography	2.0
Abdomen	2.9
IV pyleography	4.0
Upper GI series	5.6
Barium enema	8.0

Estimation of risk to human embryo

Embryo age (days)	Minimum lethal dose	LD50	Dose for Permanent growth retardation	Dose for Increased mental retardation	Dose for anatomy malformed	Dose for Cancer or hereditary effects
1-5	100	<1000	No effect			UNK
18-28	250-1000	1400	200-500	20-50*	200	UNK
36-50	500	2000	250-500	50	500	UNK
50-150	>500	> 1000	250-500	50	N/A	UNK
No term	>1000	Mother	>500	100	N/A	UNK

all doses in cGy

Large dose fetal irradiation

Gestation week	Effect of 2.5 Gy dose to human embryo
2 - 3	No severe abnormalities Increase in spontaneous abortions
4 - 11	Severe abnormalities of many organs
11 - 16	Eye, skeletal, genital malformations Stunted growth and mental retardation
16 - 20	Mild microcephaly and mental retardation Growth stunting
30+	No gross malformations Some functional impairment possible

Dekaban, 1968

Diagnostic exposure

- 29 year old woman
- 6 months pregnant
- Dental x-ray - dose 0.01 mGy
- Child born with slight hand deformity
- Mother wanted to sue!
- No evidence of radiation risk
- In fact risk of malformation is 3%

Therapy exposure

- Hodgkin's disease
- 31 year old woman
- 6 months pregnant
- Received 32 Gy in 4 weeks to thorax
- Fetal dose estimated at 250 mGy
- Child born OK

Nuclear medicine

- 31 year old woman
- I-131 scan 100 uCi
- Concerns for thyroid dose to fetus
  - Thyroid not sufficiently developed to uptake
- Whole body dose to fetus 0.1mGy
- Radiologist refused to to the procedure

Biological Effects of radiation

- Molecular
  - Direct, indirect, free radicals, chromosome aberrations
- Cellular
  - Cell dies, or repairs itself, or slowly get converted to cancer
- Tissue and organ
  - Atrophy, eventual organ failure for high exposures

Biological Effects of radiation

- Deterministic
  - Early, high dose, threshold, severity increases with dose
- Acute whole body irradiation
  - CVS, GIS, HPS
- Stochastic
  - Late effects, usually low dose, somatic (cancer induction), risk estimate for population, no threshold, no severity dependence on dose, also hereditary

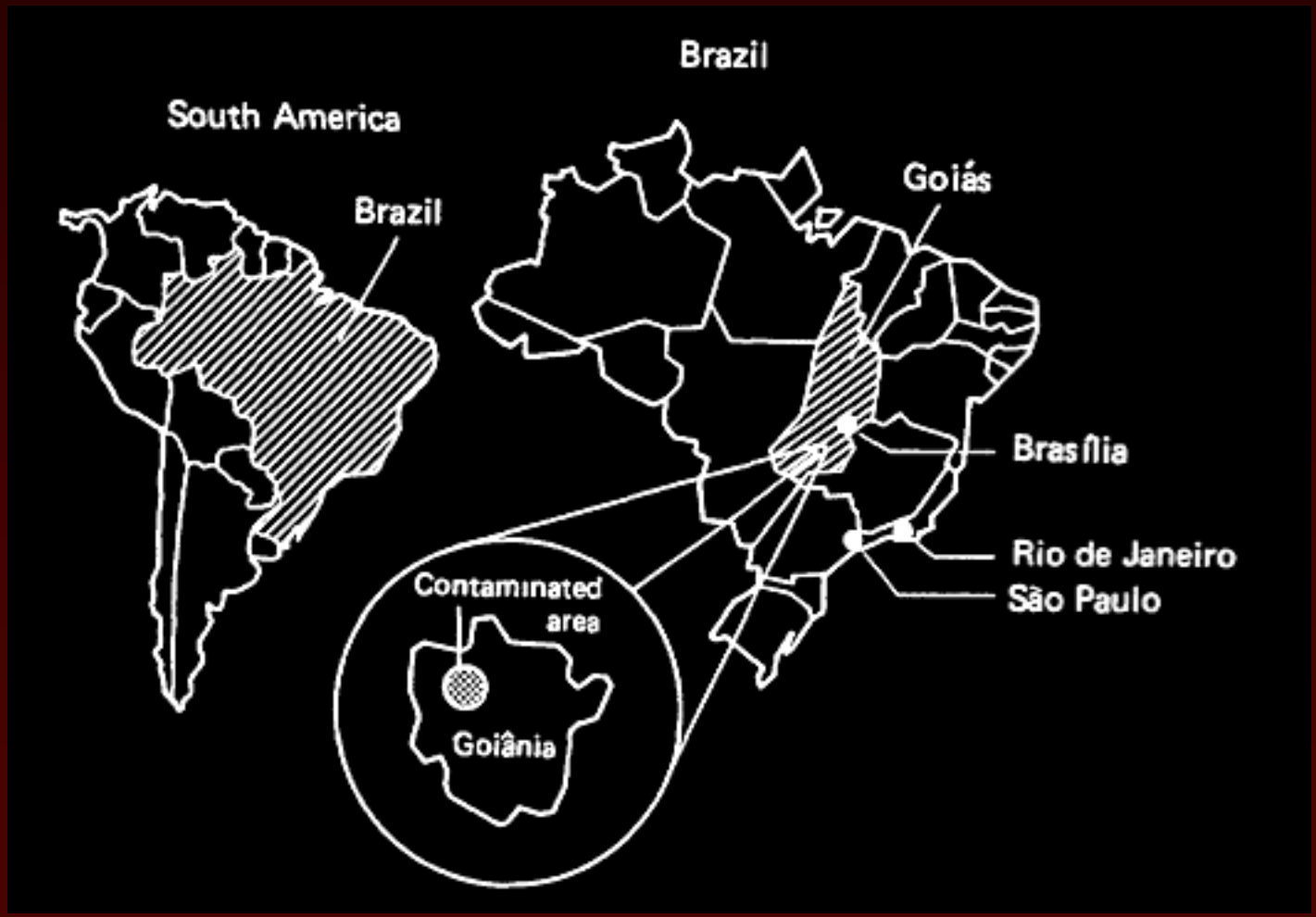
Biological Effects of radiation

- Fetal and embryo
  - Doses below ~50 mSv are reasonable
  - Above this risks for deformities, mental impairment, death increase
  - Most sensitive time is middle of first trimester
  - When dealing with patients other risks of pregnancies must be put into perspective

The Radiological Accident in Goiânia

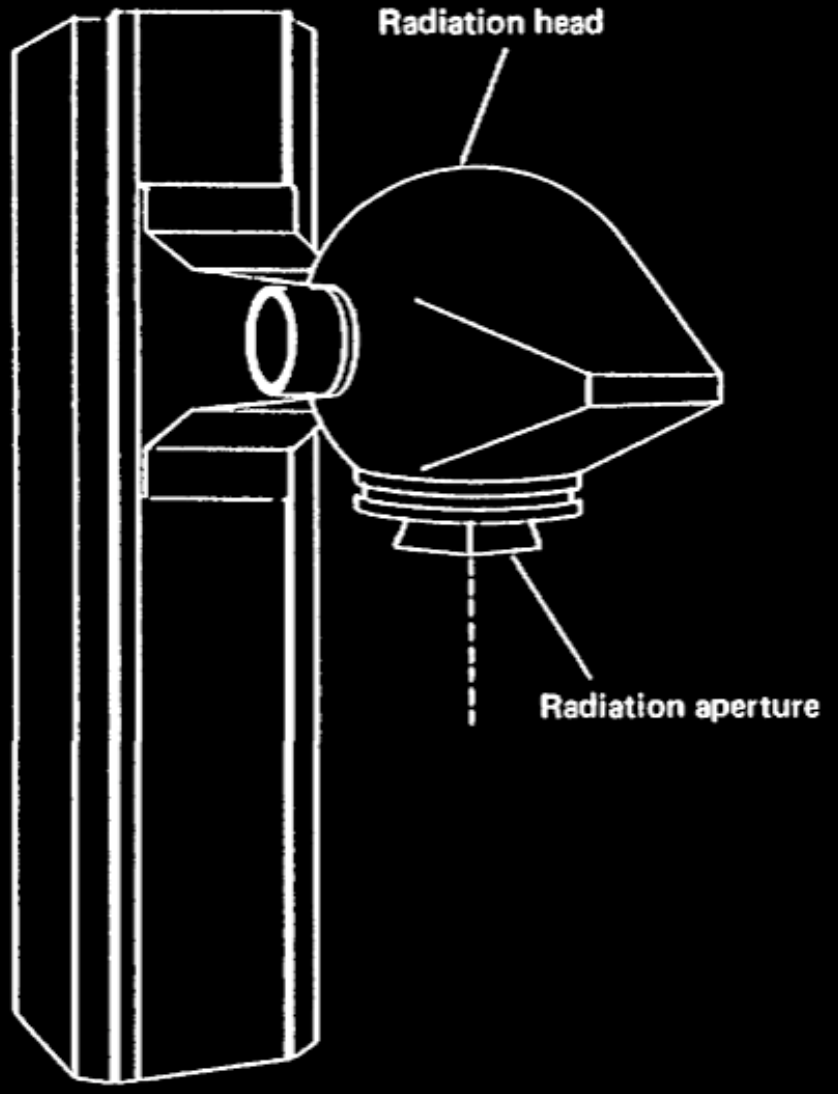
INTERNATIONAL ATOMIC ENERGY AGENCY, VIENNA, 1988

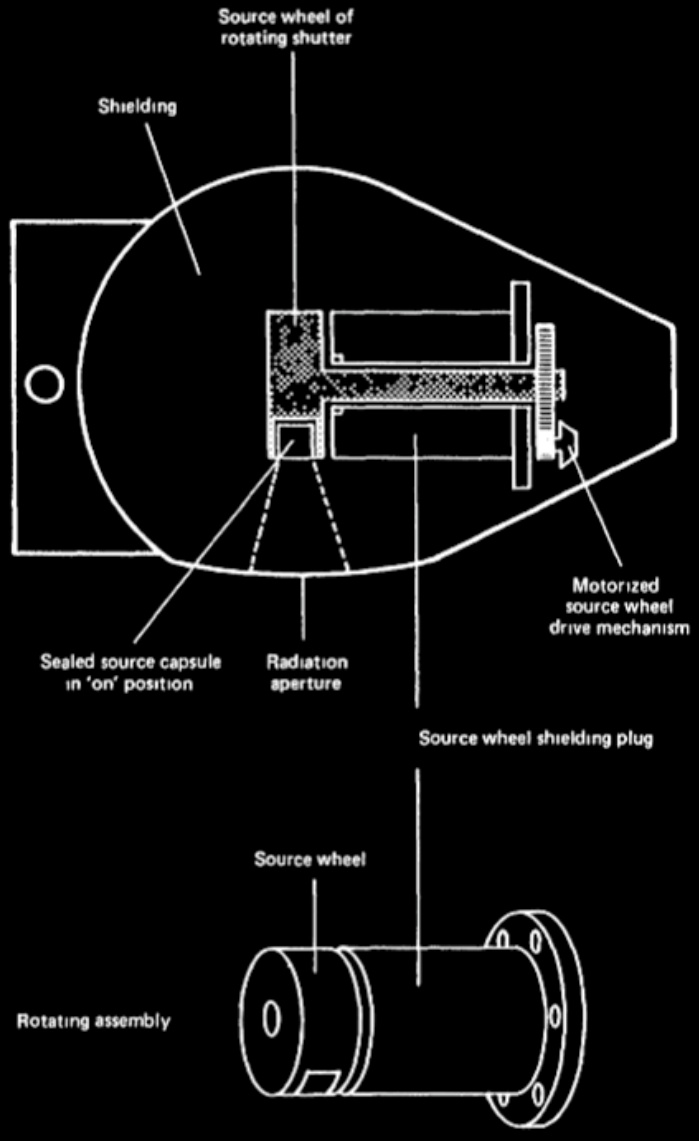
Accident summary

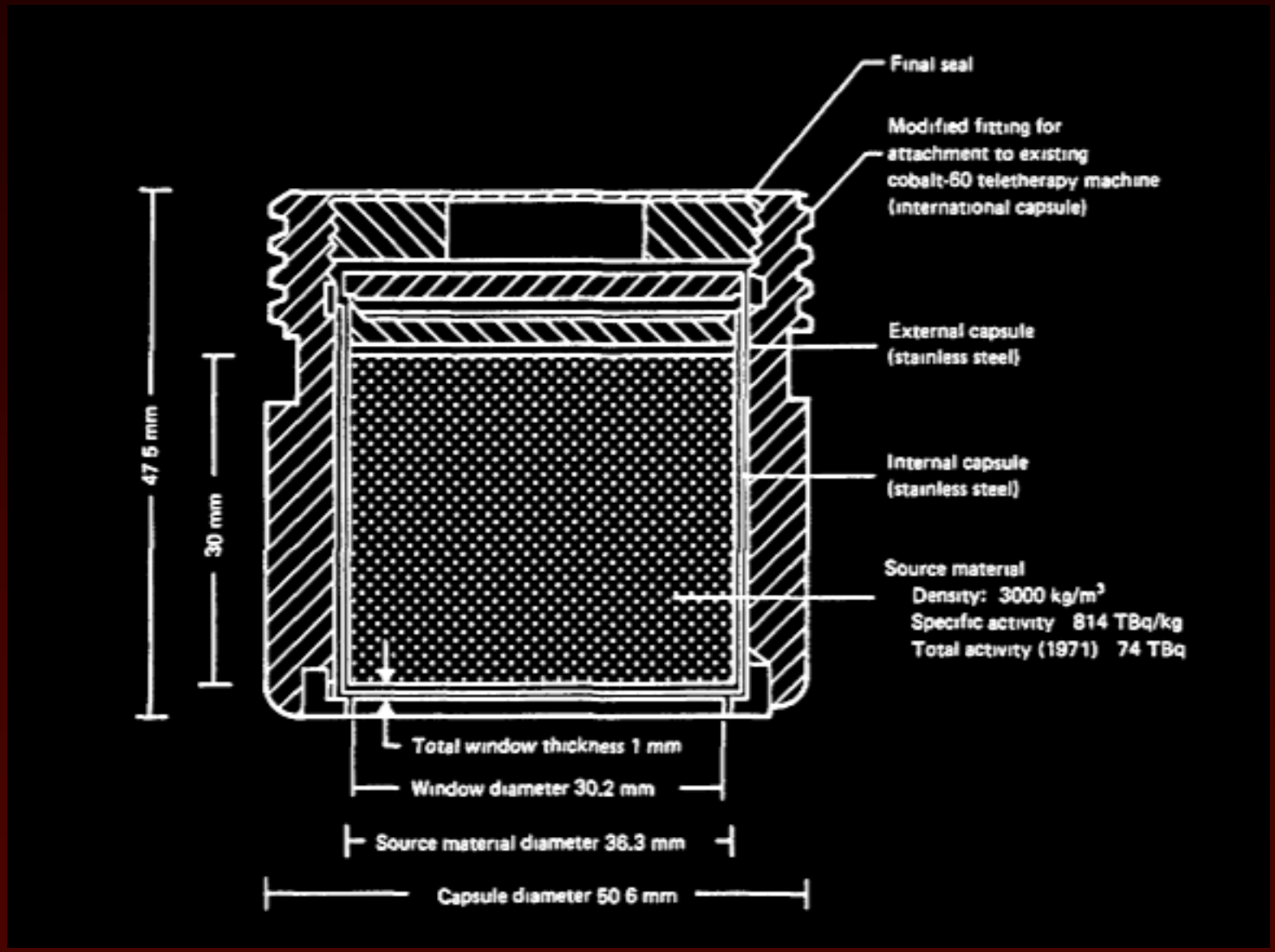


Accident description

- 1985 radiotherapy clinic abandoned
- Cs-137 treatment unit and source left behind
- 2 scavengers removed source assembly
- 2 other guys removed source from assembly
- Capsule was ruptured
- CsI - salt highly soluble, very readily dispersible


Radiation head
Radiation aperture


Source wheel of rotating shutter
Shielding
Motorized source wheel drive mechanism
Sealed source capsule in 'on' position
Radiation aperture
Source wheel shielding plug
Source wheel
Rotating assembly


Final seal
Modified fitting for attachment to existing cobalt-60 teletherapy machine (international capsule)
External capsule (stainless steel)
Internal capsule (stainless steel)
Source material
Density: 3000 kg/m³
Specific activity 814 TBq/kg
Total activity (1971) 74 TBq
47.5 mm
30 mm
Total window thickness 1 mm
Window diameter 30.2 mm
Source material diameter 36.3 mm
Capsule diameter 50.6 mm

Accident description

- CsI powder glowed and was shown and handled by many people including children
- Individuals presented with GI symptoms after a few days
- Initially exposed individuals went to hospital with symptoms and were first told it was food poisoning, then some kind of tropical disease

Accident description

- One of the wives suspected the powder, took it by bus to a medical clinic
- MD at clinic suspected radiation and called a medical physicist
- Physicist arrived with survey meters and “discovered” the accident

TABLE I. BASIC DATA ON CAESIUM-137

Basic data on caesium-137

Gamma emissions		0.66 MeV (84%)
Beta emissions	Maximum energies	0.51 MeV (95%)
		1 17 MeV (5%)
	Mean energy	0.187 MeV
Half-life		30 years
Specific gamma ray constant	8.9×10^{-2} mGy·h^{-1} at 1 m per GBq	
	(0.33 rad·h^{-1} at 1 m per Ci)	

Data on the caesium source of the IGR clinic (September 1987)

Radioactivity	50.9 TBq (1375 Ci)
Dose rate at 1 m	4.56 Gy·h^{-1} (456 rad·h^{-1})

Human exposure

- 6 people received doses between 4.5 and 7 Gy (4 died)
- 112,000 individuals were monitored
- 249 were “contaminated”
- 20 people were hospitalized
- 14 sent to Rio de Janeiro
- 6 remained in Goiania

Environmental effects

- Severe contamination
- Several “foci” of contamination were found with dose rates up to **2 Sv/h-m**
- 85 homes were found to be contaminated
- 42 were decontaminated, 7 demolished
- Soil, plants, fruit were OK @ > 50m

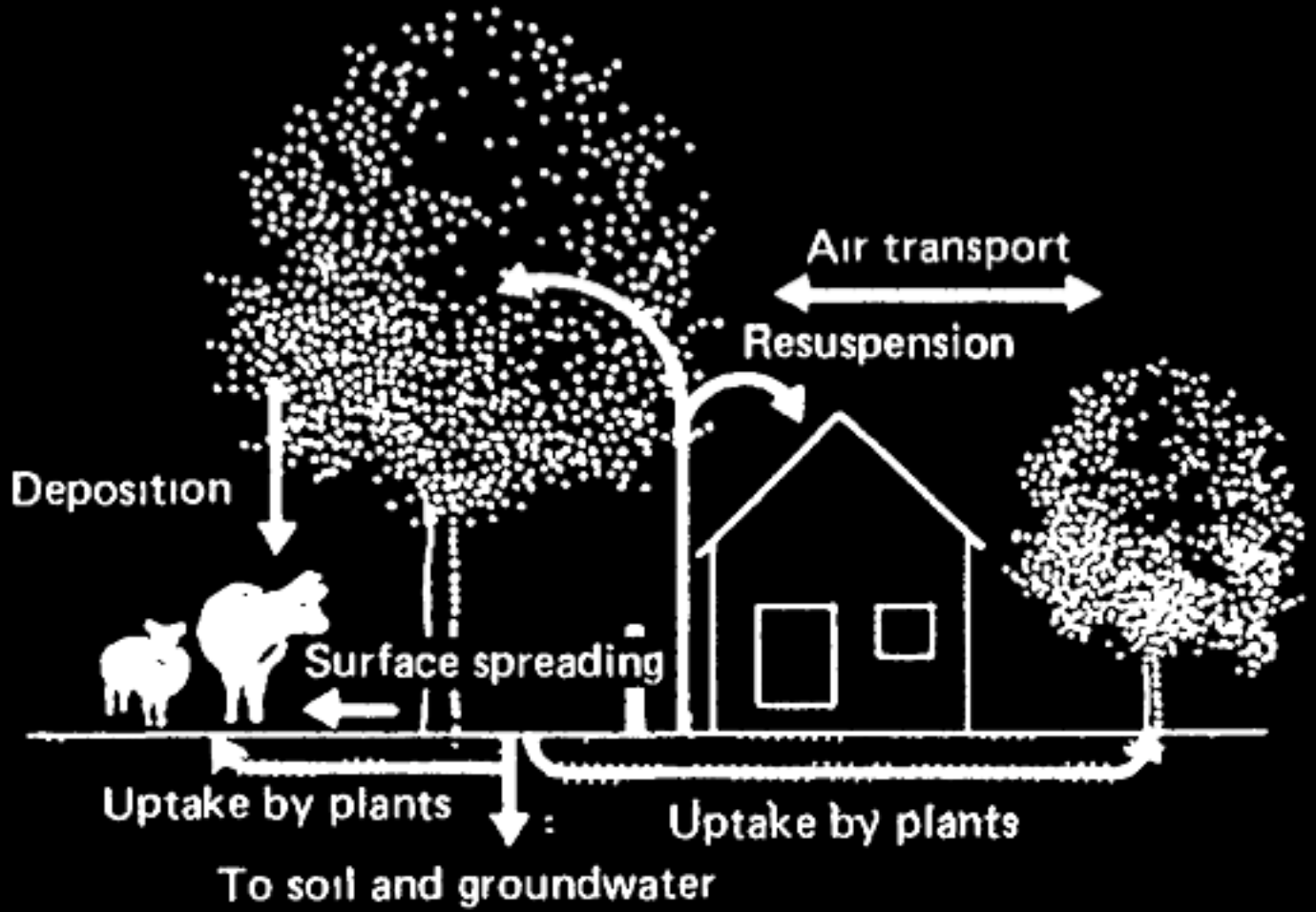


FIG 17 Contamination pathways for caesium.

Medical response

- Managing critical period of acute radiation syndrome (bone marrow depression)
- Treating local radiation injury
- Decorporation of Cs-137
- Psychology, support

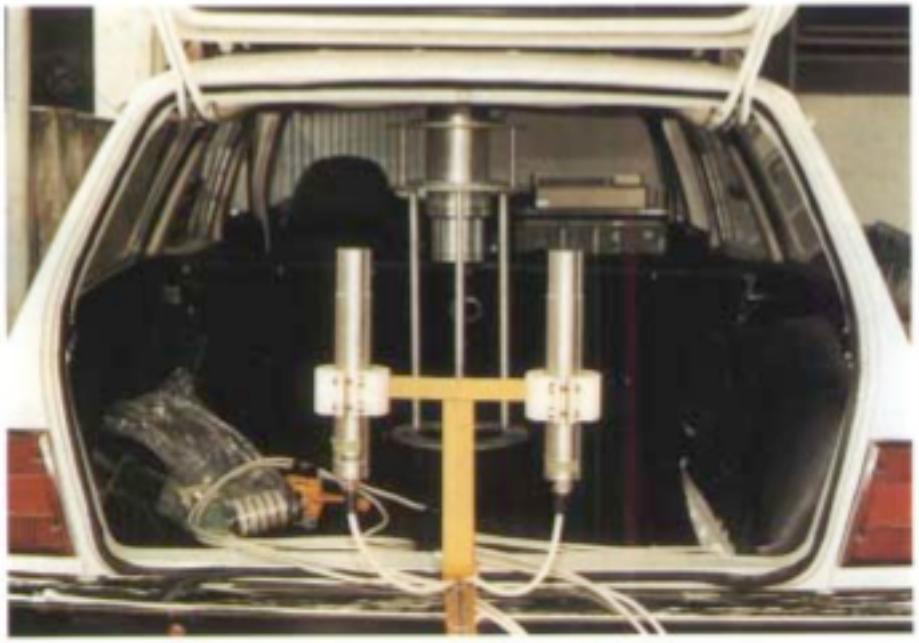
Medical response

- Prussian blue used very sccesfully to decontaminate patients
- Cytogenic analysis useful in estimating doses received
- Facilities generally adequate for care of patients (transfusions etc.)

1. The derelict radiotherapy clinic in Goiânia from which the caesium source was taken.

2. The derelict radiotherapy clinic in Goiânia from which the caesium source was taken.

5. Monitoring people for contamination at the Olympic stadium.



6. Mobile radiation monitoring Nal and GM detectors mounted on a car

7. *Preparing to demolish the house of E.F.2 and S.F.1. near Junkyard I.*

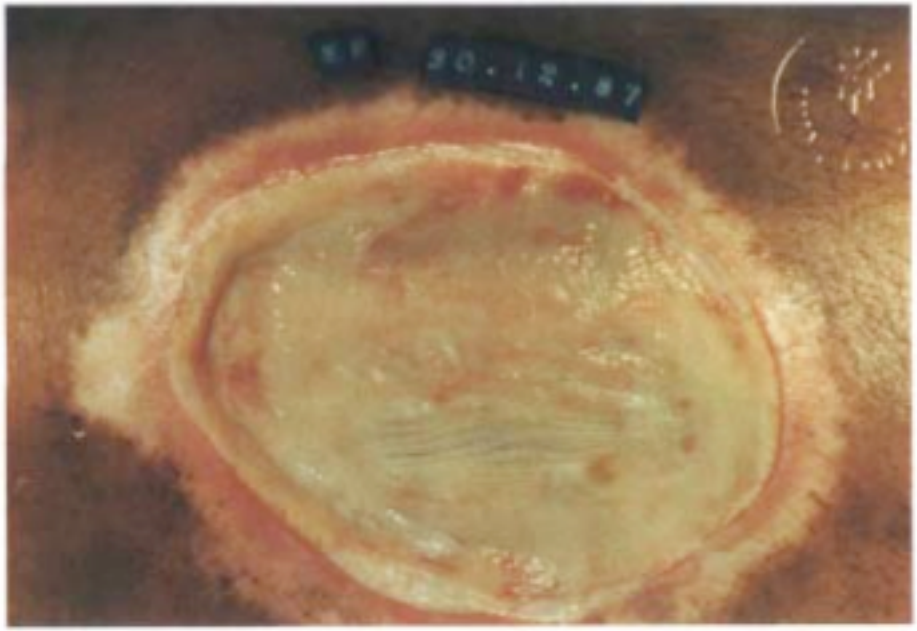
11. *Clearing the site at Junkyard II on 6th Street.*

17. *Decontaminating a vehicle. About 50 contaminated vehicles were found.*

23. *Boxes and drums of waste stacked and covered at the temporary storage site.*

27. *Waste containers at the temporary storage site.*

25. *A radiation induced lesion on the thigh about 25 days after irradiation.*



29. *Bulla completely broken down and injury extended to index and middle fingers.*

5.4.1. Case 1: M.F.1: 38-year-old woman; died 23 October 1987

The external examination showed: Orbital haematomas; severe alopecia; mucosal pallor; and haemorrhages in the neck, thorax, conjunctivae, arms, legs and skin.

The internal examination showed: Diffuse haemorrhages in all organs, most severe in the lungs and heart. The blood was fluid and dark. Haemorrhagic plaques were found throughout the skeletal muscles. There was cerebral oedema. The leptomeninges showed multiple foci of haemorrhage. The cerebrospinal fluid was xanthochromic. Multiple areas of haemorrhage were present in the serosae of intestines and stomach. The lumina of these organs contained large amounts of haemorrhagic faecal material. There were diffuse oedema and petechiae throughout the intestinal and gastric mucosae. The liver was enlarged and soft.

Gross impression: Widely disseminated haemorrhagic diathesis (the acute radiation syndrome). Cerebral oedema and petechial haemorrhages (possibly secondary to septic toxaemia).

5.4.2. Case 2: L.F.2: 6-year-old girl; died 23 October 1987

The external examination showed: Severe oedema in the face, neck and superior third of the thorax; mucosal pallor. Multiple spots of alopecia. Multiple areas of petechiae throughout the skin, mucosae and conjunctivae. Multiple areas of epidermal dry desquamation with areas of hyperpigmentation. Areas of dermal ulceration, especially in the abdomen, periumbilical area and legs. Large area of necrosis in the palm of the left hand, also affecting the fingers. There were dark spots on the soles of the feet.

The internal examination showed: Multiple areas of haemorrhage in plaques and spots through the entire skeletal musculature. The internal organs were heavily congested with haemorrhagic areas. The lungs and heart were the organs most affected by the diffuse haemorrhage. The lumina of the stomach and intestines contained haemorrhagic material with involvement of the mucosae. The renal pelves were haemorrhagic. Ecchymoses and petechial haemorrhages were also found in the serosae and in the cerebral and medullary leptomeninges. The spinal fluid was clear.

Gross impression: Disseminated haemorrhagic diathesis (secondary to the acute radiation syndrome). Haemorrhagic pneumonia and haemorrhagic nephritis, myocardial myomalacia.

5.4.3. Case 3: I.S.: 22-year-old man; died 27 October 1987

The external examination showed: Mucosal pallor Haemorrhages in the conjunctivae and mucosae, as well as petechiae in the skin. Multiple depigmented dermal areas of desquamation Foci of necrosis and localized inflammation. These lesions were more severe on the internal surfaces of the thighs, scrotum and penis, and in the gluteal and inguinal regions. There were areas of epidermal desquamation and necrosis on the palms of the hands

The internal examination showed. Haemorrhagic ecchymoses and petechiae of the serosae, most severe in the pericardium The lungs were firm, haemorrhagic and poorly aerated Their cut surface showed slightly elevated yellowish areas. There were fibrinous adhesions in the interlobular spaces. The right ventricle of the heart was enlarged Haemorrhagic petechiae and ecchymoses were found in the interventricular and subendocardial myocardium. The gastric and intestinal mucosae showed petechial haemorrhages. There was generalized hyperplasia of the lymph nodes There was hyperaemia of the leptomeninges.

Gross impression· Bilateral haemorrhagic bronchopneumonia (secondary to total body irradiation) Fibrous pleuritis, right ventricular hypertrophy. Lymph node hyperplasia

5.4.4. Case 4: A.S.: 18-year-old man; died 28 October 1987

The external examination showed: Diffuse mucosal pallor Generalized and severe alopecia. Multiple areas of hyperchromasia in the epidermis with desquamating lesions, but with no inflammatory foci. There was an area of desquamation with necrosis in the palm of the left hand.

The internal examination showed Diffuse congestion of all organs. The lungs were enlarged, showing haemorrhagic areas, particularly in the inferior lobes, where the cut surfaces had small elevated areas The heart was enlarged, mainly owing to the enlargement of the right ventricle. Haemorrhagic subendocardial and subpericardial petechiae were found The stomach and intestines showed mucosal petechial haemorrhages The skeletal muscles contained several haemorrhagic ecchymoses but less severe than those in the first two cases. The liver, spleen, kidneys, pancreas and adrenal glands showed petechial haemorrhages.

Gross impression. Bilateral haemorrhagic bronchopneumonia. Generalized systemic and cardiac haemorrhagic diathesis (secondary to the acute radiation syndrome) Right ventricular hypertrophy.