The Medical Management of Compound Radiation Injury

A.K. Guskova, A.V. Barabanova
Institute of Biophysics, Ministry of Health, Moscow, Russian Federation

Using a term "compound radiation injury" (CpRI) we mean a case when an individual was exposed to ionising radiation totally, or subtotally, with very non-uniform distribution of dose within a body. In many cases it is a result of distant external gamma or gamma-neutron radiation with or without radioactive contamination on body surface (Slides 1-6). A term CpRI from our point of view, is better to use in case of combination of exposure to ionizing radiation with other physical or chemical factors.

Acute radiation disease (ARD) in case of CpRI is characterized with appearing at least two or three radiation syndromes. In most cases it is a sum of haematological syndrome and skin radiation injury. Some other organs/tissues can be involved as well. The frequency of such cases among all cases of RAD is close to 50% (slides 7,8).

Non-uniformity of distribution of dose within a body can be conditioned by several factors, among which short distance or close contact a source of radiation to a body is the most important. Another significant factor is an energy of radiation, its penetrating ability. Gamma.beta or gamma-neutron exposure, typical for reactor accident, leads to specific type o non-uniformity of dose distribution by depth with significant overexposure to skin and some underlying tissues.

For successful management of CpRI good knowledge of condition of exposure with all details is quite important. This can help in estimation of actual dose distribution, evaluation of local and total doses. All means must be used for this purpose: careful study of an accident circumstances, simulation of the accident with using different types of dosimeters, including multilayer skin dosimeters, calculations, biological dosimetry (chromosome aberration analysis of blood cells and bone marrow from different points of the body), electron spin resonance dosimetry of biological tissues and clothing (the last one sometimes can be especially useful).

The difference between local and mean total dose can reach 10-20 times, in some cases up to 100 times. Such type of exposure, as it was mentioned before, brings in development of several syndromes, among which skin injury, and especially, necrosis of skin is of great importance. This is a cause of more severe clinical course than in case of classical form of ARD.

So, first of all, the CpRI is characterized with more often skeptical complications and very severe pain syndrome. Its other features are more long period of high fever, significant decrease of mass of body, more early and deep anaemia, disproteinaemia, high tachycardia, neurological disorders. These symptoms from the syndrome of endogenic intoxication (SEI) In severe cases the SEI can be a cause of death, as it was in some Chernobyl patients, for example:

As it was shown in special study of clinical features of CpRI, the degree of SEI depends on the size of skin lesion, especially on the mass of skin in zone of necrosis, and less depends on the severity of bone marrow syndrome. (TRANSP). Late period of the CpRI is also much more severe. These patients need more long careful surveillance and treatment. Some of them are invalids. (Slides).

Planning of treatment in acute phase of the CpRI and in period of late effects should be based on early diagnostic and prognostic evaluations. Diagnosis of severity of haematological syndrome is based on generally accepted rules, in particular described by N. Wald (1955) G. Andrews (1961), H. Jammet (1964), A. Baranov (1980) and others. However, some corrections because of non-uniformity of exposure, are necessary. So, early leucocytosis can appear to be higher, and early lymphopenia deeper than in case of haematological syndrome only produced by the same mean total dose of exposure. The significance of evaluation of size of skin injury has already been mentioned. Prognostic evaluation of the severity of skin syndrome is more difficult task, since this is affected by many factors: type of radiation, its energy, size and localization of skin lesion and so on. However, in any case careful day-by-day observation of skin reaction with photo and/or video registration is very useful. In our practice we use also the registration of skin reaction as a function of time by means of arbitrary skin reaction scores elaborated for this purpose. (Transp).

Day by dat development of symptoms of injury, as well as the process of healing can be registered and presented in form of curve. Two examples shown on the figure demonstrate two different situations with different values of the rate of skin reaction (RSR), designated as index "J". The analysis of a number of such curves brought us to the conclusion that the RSR could serve as a prognostical criterion. This is because analysis has shown that there was some critical value of index "J" beyond which surgical intervention became a necessity. Moreover, it was found from retrospective analysis that some dependence pertained between this value of index "J" and the time of operation: the higher the RSR "J", the earlier the operation became essential. This means that estimation of the RSR in acute phase can help to predict the need of surgical treatment. Timely operation is essential to prevent the SEI and to avoid secondary changes in exposed and adjacent tissues.

However, observation and registration of skin reaction is not enough to make a choice of the type of operation (amputation, its level, necroecthomia with subsequent grafting, type of grafting and so on). The knowledge on the depth of the injury is very important. Special study performed by Drs T. Protasova and T. Davidovskaya showed that pathomorphological findings in skin exposed to radiation can serve as some sort of biological dosimetry and hence as a prognostic test. They recommend to consider three zones of character histological changes in exposed skin and underlying tissues. Each zone corresponds to some estimated dose. The first zone is a zone of Total Necrosis or zone of non-reparable changes, dose>30 Gy, the second zone - the zone of injury with possible reparation, the dose from 8Gy to 24 Gy; the third zone - the zone of relatively safe tissues - <8 Gy.

Pathological findings in these zones were described for different periods of time elapsed since exposure. The main recommendations of the authors were to: use the skin biopsy for diagnosis of the severity of injury and to perform operation, if necessary, in the periphery of the third zone or even better in zone of normal tissue. The best time for surgical intervention, from their point of view, is between the third week and third month since exposure. However, the point of view of clinicians is: operation should be performed as early as possible, or as soon as prognosis of severe skin injury with deep necrosis become clear. We have an experience of successful surgical treatment in latent period of haematological syndrome and even in period of cytopenia.

Thus:

i. the treatment of CpRi demands a participation of very qualified specialists (radioopathologist, haematologist, surgeon as minimum);

ii. the first medical aid and early management should include careful radiomonitoring of body surface with subsequent decontamination, if necessary;

iii. careful dosimetrical study with using of all possible means;

iv. careful observation and registration of skin reaction (better with using of arbitrary skin reaction scores for estimation of the RSR;

v. more earlier administration of antiinfectious means, including isolation in sterile room/block;

RERF EPIDEMIOLOGICAL STUDIES ON HEALTH EFFECTS OF EXPOSURE TO ATOMIC BOMB RADIATION

presented by Dr Yutaka Hasegawa, M.D., Ph.D.

1. Introduction

The Radiation Effects Research Foundation (RERF) is currently conducting 63 active research projects on the health effects of exposure to the atomic bomb radiation and almost all of the RERF studies are epidemiologically designed, that is, the effects are analyzed in relation to the exposure doses.

The major epidemiological studies of RERF are shown in Table 1 and main features of these and some other epidemiological studies are briefly described in the following sections.

Table 1. Major Epidemiological Studies

Studies	Number of Subjects	Year of Base Population	Year Commenced
Life Span Study (LSS)	120,000	1950	1958
Adult Health Study (AHS)	20,000	1950	1958
In Utero Study	2,800	1945–46	1956
Genetic Epidemiology Studies (F_1)			
Mortality	77,000	1946–	1960
Cytogenetics	33,000	1946–	1967
Biochemical Genetics	45,000	1946–	1975

2. Life Span Study (LSS)

This is one of the largest epidemiological studies in the world in terms of the size of the study population and the period during which the study population has been followed up.

About 120,000 subjects, including proximally and distally exposed A-bomb survivors living in Hiroshima or Nagasaki and nonexposed controls, were selected on the basis of data from the 1950 Japanese National Census. Whether the life span and causes of deaths of A-bomb survivors differ from those of unexposed individuals in the general Japanese population has been epidemiologically studied since 1958 with the help of information from vital-statistics surveys, tumor registries and other sources and in relation to the individual doses received by the exposed survivors. Individual dose estimates based on the Dosimetry System 1986 (DS86) are presently available for 95% of the exposed survivors.

The results of the LSS are explained in Section 8.

3. Adult Health Study (AHS)

This is a large clinical epidemiologic study in which about 20,000 subjects selected from the LSS sample have been followed through biennial health examinations since 1958.

General items in the AHS examination are physical examinations, ECG, chest X-ray, ultrasonography, blood tests (including biochemical), urinalysis, and stool tests. Using the data collected during these examinations, long-term follow-up studies on the prevalence and incidence rates of various diseases and changes in many physiological and biochemical endpoints have been conducted in relation to the exposure doses.

In the AHS, the medical history of each individual (morbidity, treatment, examination, etc.) and information on life-style (exercise, nutrition, smoking, etc.) are also collected. Therefore, when radiation effects are examined, an evaluation of the effects taking these factors into consideration is possible. In addition to the general examination, special tests, such as measurement of bone mineral content and gynecological examinations, are also conducted.

The results of the AHS obtained so far are given in Section 8.

4. In-utero Study

This epidemiological study on about 2,800 prenatally exposed A-bomb survivors has shown that the incidence of survivors with both small head circumference and severe mental retardation increased with increasing uterine absorbed dose. A strong influence of A-bomb radiation on the developing fetal brain was observed during the first 8–25 weeks of gestation. Approximately 80% of the mental retardation was caused by radiation exposure at 8–15 weeks of gestation, i.e., the most radiosensitive period of fetal brain development (Figure 1). The threshold appears to be in the range of 0.12 - 0.23 Gy.

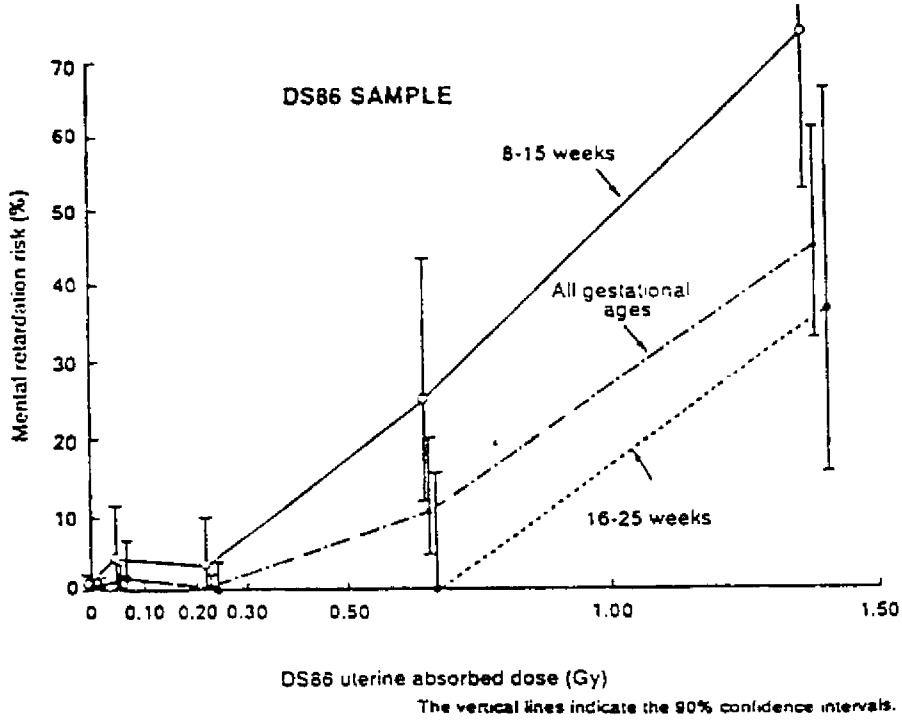


Figure 1. Mental retardation risk and uterine dose

5. Genetic Epidemiology Studies

The search for genetic effects in children (F_1) born to A-bomb survivors includes the following studies.

(1) *Untoward Pregnancy Outcome*: The Untoward Pregnancy Outcome Study was conducted during the period between 1948 and 1953, to search for the possible genetic effects of A-bomb radiation on over 70,000 pregnancy terminations in Hiroshima and Nagasaki. This study estimated the incidence of infants that were stillborn, exhibited major congenital malformation, or died within the first week of life.

(2) *Mortality Study*: This study looks for any shortening of the life span of the F_1 generation compared with the nonexposed and attempts to find the predominant diseases regarded as causes of death. It is a long-term investigation directed at about 54,000 subjects born between May 1946 and December 1958. Later, approximately 23,000 people born in or after January 1959 were added.

(3) *Cytogenetics*: The frequency of chromosome mutations induced in parental germ cells was assayed by measuring the frequency of children with chromosome abnormalities. A study on a total of 16,000 participants, 8,000 proximally exposed and 8,000 distally exposed, has been completed.

(4) *Biochemical Genetics*: A total of 23,700 F_1 subjects, including 11,400 whose parents were proximally exposed and 12,300 whose parents were distally exposed (or nonexposed), are electrophoretically examined for the presence of radiation-induced mutations of enzymes and proteins in the blood.

(5) *Cancer Mortality*: The Mortality Study has been further extended to analyze and compare the death rates from malignant tumors of the children of the exposed with the rates of their control parents to see if there is any increase in the cancer mortality attributable to parental A-bomb exposure.

None of the above studies have shown a statistically significant relationship between the parental exposure to atomic bomb radiation and the effects that have been studied on the children.

6. Epidemiological Study on Somatic Chromosome Aberrations

Ionizing radiation is well known to produce chromosome aberrations in living cells. The yield of such chromosome aberrations is proportional to the radiation dose. Thus, the frequency of chromosome aberrations in human blood lymphocytes provides a reliable indication of the degree of radiation exposure in vivo.

Cytogenetic data on 1,200 survivors in Hiroshima and Nagasaki have shown that lymphocytes with radiation-induced chromosome aberrations induced in 1945 have persisted for many decades in the peripheral blood of A-bomb survivors. The rates of cells with such chromosome aberrations increase with increasing radiation doses in both cities (Figure 2).

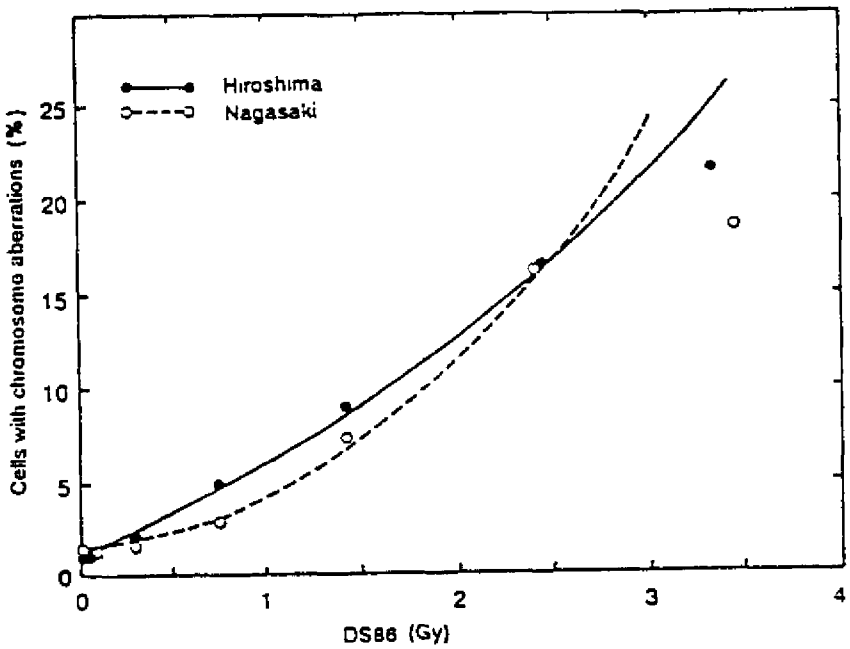


Figure 2. A graph illustrating dose-response relationships for chromosome aberration frequencies plotted against dose estimates assigned to individual A-bomb survivors

7. Epidemiological Studies on Immune Competence and Somatic Cell Mutation Frequencies

(1) *Studies on Immune Competence*

Trends in the immune competence of A-bomb survivors are studied to determine whether there is any immunologic disorder or acceleration of immunologic aging phenomena among the A-bomb survivors and, if there is, its relationship with the development of radiation-induced disease. Further studies are being performed on the effects of A-bomb radiation on the development and maturation of immune-competent cells according to age at the time of the bombings and radiation dose.

(2) *Somatic Cell Mutation Frequencies*

The frequency of the genes of mutant cells in the lymphocytes and erythrocytes of A-bomb survivors is determined, and the DNA of these mutant cells is analyzed in relation to the radiation dose to investigate continuing radiation effects and their relationship to the incidence of malignant tumors. Possible applications to biological dosimetry for A-bomb survivors and other radiation-exposed people are being considered.

The results of these studies are given in Section 8.

8. Summary of Results of ABCC/RERF Epidemiological Studies

The results of ABCC/RERF epidemiological studies are summarized in Table 2.

The diseases, abnormalities and changes mentioned in the left column of this table have been found to have a statistically significant association with exposure to atomic bomb radiation. Those in the middle column are related to exposure to atomic bomb radiation with a borderline statistical significance. No association with atomic bomb radiation has so far been found with respect to the diseases and changes in the right column.

As indicated in the footnote of the table, no effects with statistical significance have yet been found among the children of A-bomb survivors in relation to parental exposure to atomic bomb radiation.

A list of the references of the relevant studies is attached to the Table 2.

ACKNOWLEDGEMENTS

The author is grateful to Dr I. Shigematsu, RERF Chairman, for his kind advice and to the RERF research scientists who made their valuable data available for this paper.

Table 2. **Summary of results of ABCC/RERF epidemiological studies for late health-related effects of radiation**

Association with Atomic Bomb Radiation	STRONG Statistically significant results in one or more studies. Questions about potential biases are largely resolved. Risk clearly related to amount of exposure.	WEAK Borderline statistical significance or inconsistent results. More studies may be needed.	NONE No statistically significant effect observed. This may reflect a true lack of effect or result from inadequate sample size.
A-Bomb Survivors (except in-utero Survivors)			
Malignant Tumors	Leukemia (except chronic lymphoid leukemia and adult T-cell leukemia), Breast (women); Thyroid; Colon; Stomach; Lung; Ovary	Esophagus; Salivary glands; Liver; Skin; Urinary bladder; Nervous system; Multiple myeloma; Malignant lymphoma	Chronic lymphoid leukemia; Adult T-cell leukemia; Pancreas; Gallbladder; Rectum; Uterus; Bone
Noncancer Diseases and Conditions	Radiation cataract; Hyperparathyroidism; Delays in growth and development (exposed at young ages)	Cardiovascular mortality and total non-cardiovascular mortality at high doses (>1.5 Gy); Thyroid diseases; Chronic hepatitis and liver cirrhosis; Myoma uteri; Earlier onset of menopause	Infertility; Glaucoma; Autoimmune diseases; Generalized premature aging; Senile cataracts
Immune Competence	Decrease in T-cell- mediated responses, Changes in humoral immune response	Susceptibility to viral infections; increased autoantibodies	Changes in natural immune responses
Chromosomal Aberrations	Lymphocytes		
Somatic Mutations	Erythrocytes	Lymphocytes	
In-utero Survivors			
Malignant Tumors		Total solid tumors	Leukemia
Noncancer Diseases and Conditions	Microcephaly; Mental retardation; Delays in growth and development; Lower IQ and poorer school performance		Noncancer mortality
Chromosomal Aberrations		Lymphocytes	

Notes: For the children of A-bomb survivors (F_1), no effects with statistical significance (including borderline statistical significance) have yet been found in relation to exposure to atomic-bomb radiation. The lack of statistically significant relationships with atomic-bomb radiation has been confirmed for the following effects: solid tumors, leukemia, stillbirth, major congenital anomalies, early mortality, chromosomal abnormalities, and protein variants.

LIST OF REFERENCES FOR TABLE 2

1. Diseases/conditions under "strong" category

A-Bomb Survivors (except In-Utero Survivors)	Reference
. Leukemia (except chronic lymphoid leukemia and adult T-cell leukemia)	TR 5-88, TR 24-92
. Breast cancer (women)	TR 5-92, TR 5-88
. Thyroid cancer	TR 5-91, TR 5-92
Colon cancer	TR 5-92, TR 15-92, TR 5-88
. Stomach cancer	TR 5-92, TR 5-88
. Lung cancer	TR 5-92, TR 5-88
. Ovary cancer	TR 5-92, TR 5-88
Radiation cataract	TR 4-89, Otake M. and Schull W.J. (1991) J. Rad. Res. Vol. 32 suppl 283-293, TR 11-92
. Hyperparathyroidism	TR 8-90
. Delays in growth and development (exposed at young ages)	ABCC TR 35-71, TR 19-84
. Decrease in T-cell mediated responses	TR 23-81, TR 19-87
. Changes in humoral immune response	TR 4-92
. Chromosomal aberrations: lymphocytes	TR 12-77, TR 7-88
. Somatic mutations: erythrocytes	TR 9-88
In-Utero Survivors	
. Microcephaly	TR 6-92
. Mental retardation	TR 16-87
. Delays in growth and development	TR 19-92
. Lower IQ	TR 3-88
. Poorer school performance	TR 2-88

(Notes) TR stands for an RERF (or ABCC) technical report. The detailed information on each TR will be found in the attachment to this list of references.

2. Diseases/conditions under "weak" category

A-Bomb Survivors (except In-Utero Survivors)	Reference
. Esophagus cancer	TR 5-92, TR 5-88
. Salivary glands cancer	TR 5-92, TR 5-88
. Liver cancer	TR 5-92
. Skin cancer (except melanoma)	TR 5-92
Urinary bladder cancer	TR 5-92
. Nervous system cancer (except brain tumor)	TR 5-92
. Multiple myeloma	TR 24-92
. Malignant lymphoma	TR 24-92
. Cardiovascular mortality	TR 2-91
. Total non-cancer/cardiovascular mortality at high doses	TR 2-91
. Thyroid diseases	TR 1-92
. Chronic hepatitis	TR 1-92
. Liver cirrhosis	TR 1-92
. Myoma uteri	TR 1-92
. Earlier onset of menopause	Soda M , et al (1993) RERF Update, Vol.5, Issue 2, 3-4
. Susceptibility to viral infections	TR 13-80, TR 14-92
. Increased autoantibodies	TR 4-92
Somatic mutations: lymphocytes	TR 13-87

In-Utero Survivors	
. Total solid tumors	TR 4-88
. Chromosomal aberrations: lymphocytes	ABCC TR 7-68 (a new TR in preparation)

3. Diseases/conditions under "none" category

A-Bomb survivors (except In-Utero Survivors)	Reference
. Chronic lymphoid leukemia	TR 13-81
. Adult T-cell leukemia	TR 24-92
. Pancreas cancer	TR 5-92, TR 5-88
. Gallbladder cancer	TR 5-92, TR 5-88
. Rectum cancer	TR 5-92, TR 5-88
. Uterus cancer	TR 5-92, TR 5-88
Bone cancer	TR 5-88
. Infertility	TR 2-75
. Glaucoma	TR 1-92
. Autoimmune diseases	TR 4-92
. Generalized premature aging	TR 11-78
. Senile cataracts	TR 1-92
. Changes in natural immune responses	TR 12-88
In-Utero Survivors	
. Leukemia	TR 4-88
. Non-cancer mortality	TR 4-88
F_1	
. No effects of A-bomb radiation with statistical significance (including borderline statistical significance)	Neel, J.V. and Schull, W.J. ed. (1991) The Children of Atomic Bomb Survivors: A Genetic Study, National Academy Press, Washington, D C.
. Solid tumors	TR 4-90
. Leukemia	TR 11-81, TR 4-90
. Stillbirth	TR 13-89
. Major congenital anomalies	TR 13-89
. Early mortality	TR 1-91
. Chromosomal abnormalities	TR 21-88
. Protein variants	TR 10-87, Neel, J V. et al (1988) Am. J. Hum. Genet. 42: 663-676

List of TRs

ABCC TR 7-68 : Bloom AD, et al. (1968) Cytogenetics of children exposed in utero, Hiroshima and Nagasaki
(Lancet 2:10-2, 1968)

35-71: Belsky JL and Blot WJ (1971) Stature of adults exposed in childhood to the atomic bombs, Hiroshima and Nagasaki
(Am J Public Health 65:489-94, 1975)

RERF TR 2-75 : Blot WJ, et al. (1975) Frequency of marriage and live birth among survivors prenatally exposed to the atomic bomb
(Am J Epidemiol 102:128-36, 1975)

12-77: Awa AA, et al. (1977) Relationship between dose and chromosome aberrations in atomic bomb survivors, Hiroshima and Nagasaki
(J Radiat Res (Tokyo) 19:126-40, 1978)

11-78: Belsky JL, et al. (1978) Aging studies in atomic bomb survivors

13-80: Kato H, et al. (1980) The relationship of HB surface antigen and antibody to atomic bomb radiation in the Adult Health Study sample, 1975-77
(Am J Epidemiol 117:610-20, 1983)

11-81: Ishimaru T, et al. (1981) Leukemia incidence among individuals exposed in utero, children of atomic bomb survivors, and their controls: Hiroshima and Nagasaki, 1945-79

13-81 Ichimaru M, et al. (1981) Incidence of leukemia in a fixed cohort of atomic bomb survivors and controls, Hiroshima and Nagasaki, October 1950 - December 1978

23-81: Yamakido M, et al. (1981) T and B cells and PHA response of peripheral lymphocytes among atomic bomb survivors
(Radiat Res 93:572-80, 1983)

19-84: Ishimaru T, et al. (1984) Relationship of height, body weight, head circumference, and chest circumference at age 18, to gamma and neutron doses among in utero exposed children, Hiroshima and Nagasaki

10-87: Neel JV, et al. (1987) Search for mutations altering protein charge and/or function in children of atomic bomb survivors: Final report
(Am J Hum Genet 42:663-76, 1988)

RERF TR 13-87: Eto R, et al. (1987) An autopsy study of histopathologic changes in the urinary bladder transitional epithelium of atomic bomb survivors, 1960-83
(Hiroshima J Med Sci 37:11-5, 1988)

16-87: Otake M, et al. (1987) Severe mental retardation among the prenatally exposed survivors of the atomic bombing of Hiroshima and Nagasaki: A comparison of T65DR and DS86 dosimetry systems. (Congenital Anomalies 29:309-20, 1989)

19-87: Akiyama M, et al. (1987) Age- and dose-related alteration of in vitro mixed lymphocyte culture response of blood lymphocytes from A-bomb survivors (Radiat Res 117.26-34, 1989)

2-88 : Otake M, et al. (1988) Effect on school performance of prenatal exposure to ionizing radiation in Hiroshima: A comparison of the T65DR and DS86 dosimetry systems. (Congenital Anomalies 29:309-20, 1989)

3-88 : Schull WJ, et al. (1988) Effect on intelligence test score of prenatal exposure to ionizing radiation in Hiroshima and Nagasaki: A comparison of the T65DR and DS86 dosimetry systems
(Congenital Anomalies 29:309-20, 1989)

4-88 . Yoshimoto Y, et al. (1988) Risk of cancer among in utero children exposed to A-bomb radiation, 1950-84
(Lancet 2:665-9, 1988)

5-88 : Shimizu Y, et al. (1988) Life Span Study Report 11 Part 2 Cancer mortality in the years 1950-85 based on the recently revised doses (DS86)
(Radiat Res 121:120-41, 1990)

7-88 : Preston DL, et al. (1988) Comparison of the dose-response relationships for chromosome aberration frequencies between the T65D and DS86 dosimetries

9-88 · Kyoizumi S, et al. (1988) Detection of somatic mutations at the glycophorin-A locus in erythrocytes of atomic bomb survivors using a single beam flow sorter (Cancer Res 49:581-8, 1989)

12-88: Akiyama M, et al (1988) Immunological responses of A-bomb survivors (Radiat Res 116:343-55, 1988)

RERF TR 21-88: Awa AA, et al. (1988) Cytogenetic study of the offspring of atomic bomb survivors, Hiroshima and Nagasaki

4-89 : Otake M and Schull WJ (1989) Radiation-related posterior lenticular opacities in Hiroshima and Nagasaki atomic bomb survivors based on T65DR and DS86 dosimetry systems
(Radiat Res 121:3-13, 1990)

13-89: Otake M, et al. (1989) Congenital malformations, stillbirths, and early mortality among the children of atomic bomb survivors· A reanalysis
(Radiat Res 122:1-11, 1990)

4-90 : Yoshimoto Y, et al. (1990) Frequency of malignant tumors during the first two decades of life in the offspring (F_1) of atomic bomb survivors
(Am J Hum Genet 46:1041-52, 1990)

8-90 : Fujiwara S, et al. (1990) Hyperparathyroidism among atomic bomb survivors in Hiroshima, 1986-88
(J Radiat Res (Tokyo) 32S:245-8, 1991)

1-91 : Yoshimoto Y, et al. (1991) Mortality among the offspring (F_1) of atomic bomb survivors, 1946-85
(J Radiat Res (Tokyo) 32:327-51, 1991)

2-91 : Shimizu Y, et al. (1991) Life Span Study Report 11. Part 3. Noncancer mortality, 1950-85, based on the revised doses (DS86)
(Radiat Res 130:249-66, 1992)

5-91 : Akiba S, et al. (1991) Thyroid cancer incidence among atomic bomb survivors, 1958-79

1-92 : Wong FL, et al. (1992) Adult Health Study Report 7. Non-cancer disease incidence in the atomic bomb survivors, 1958-1986 (Cycles 1-14)
(Radiat Res 135:418-30, 1993)

4-92 : Fujiwara S, et al. (1992) Autoantibodies and immunoglobulins in A-bomb survivors
(Radiat Res 137:89-95, 1994)

5-92 : Thompson DE, et al. (1992) Cancer incidence in atomic bomb survivors. Part II: Solid tumors, 1958-1987
(Radiat Res 137:S17-S67, 1994)

RERF TR 6-92 : Otake M and Schull WJ (1992) Radiation-related small head sizes among prenatally exposed A-bomb survivors
(Int J Radiat Biol 63:255-70, 1993)

11-92: Schull WJ and Otake M (1992) Radiation cataracts among Hiroshima A-bomb survivors, 1949-1964

14-92. Akiyama M, et al (1992) Study on the titers of anti-Epstein-Barr virus antibodies in the sera of atomic bomb survivors
(Radiat Res 133:297-302, 1993)

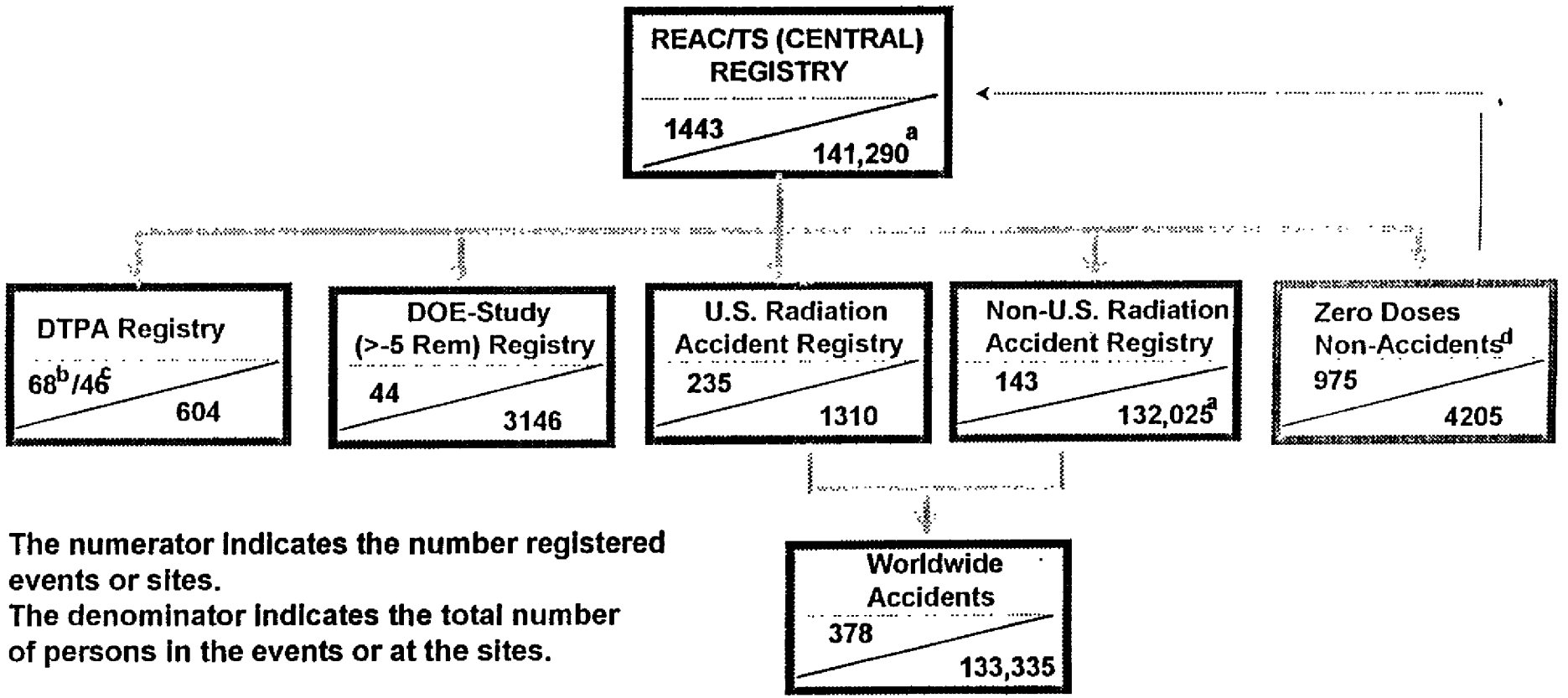
15-92: Nakatsuka H, et al. (1992) Colorectal cancer incidence and radiation dose among atomic bomb survivors, 1950-80
(J Radiat Res (Tokyo) 33:342-61, 1992)

19-92: Otake M, et al. (1992) A longitudinal study of growth and development of stature among the prenatally exposed atomic bomb survivors
(Radiat Res 134:94-101, 1993)

24-92: Preston DL, et al. (1992) Cancer incidence in atomic bomb survivors. Part III: Leukemia, lymphoma and multiple myeloma, 1950-1987
(Radiat Res 137:S68-S97, 1994)

USA Registries: Presented by: Dr R. Ricks, RESC/TS, NRC

STATUS OF REAC/TS REGISTRIES SEPTEMBER 1994



The numerator indicates the number registered events or sites.
The denominator indicates the total number of persons in the events or at the sites.

a - Includes Chernobyl - 116,500; Brazil - 249; Mexico II - 4,000; Kyshtym - 10,180; Spain - 27
b - Includes 22 former DTPA co-investigator sites
c - Co-investigators reporting
d - Worldwide

Source: Radiation Emergency Assistance Center/ Training Site Radiation Accident Registries

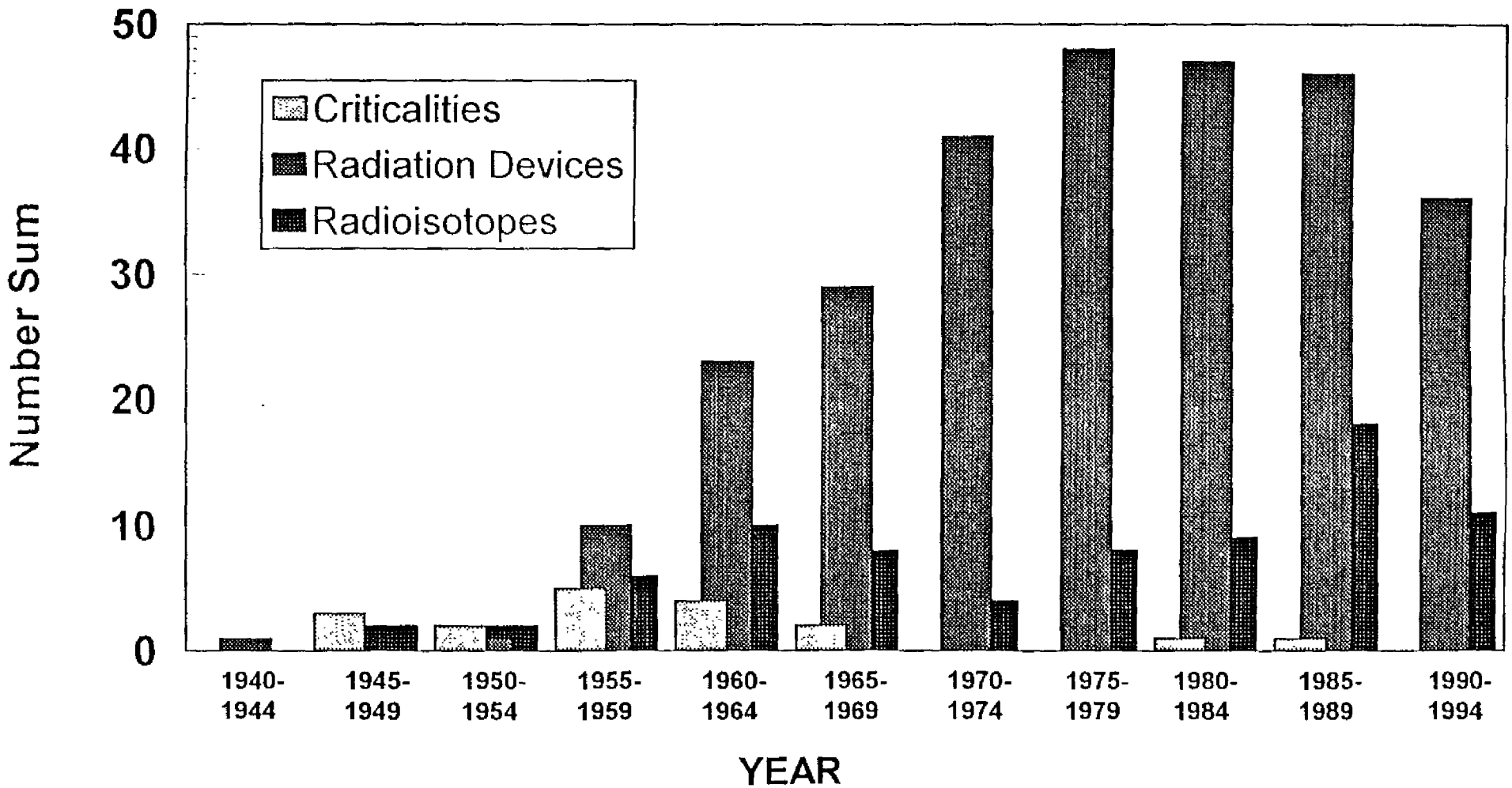
ORISE-MSD-REAC/TS

Where Do Radiation Accidents Occur?

1. Irradiation Facilities
2. Nuclear Reactors
3. Isotope Production Facilities
4. Materials Testing (sealed sources)
5. Materials Testing (x-ray devices)
6. X-ray and Radiotherapy Devices (medicine, research)
7. Unsealed Radionuclides (medicine, research)
8. Transportation
9. ???

Source: DOE - REAC/TS Radiation Accident Registry

FREQUENCY DISTRIBUTION OF MAJOR RADIATION ACCIDENTS (BY DEVICE) WORLDWIDE: 1940 - SEPTEMBER 1994



MAJOR RADIATION ACCIDENTS WORLDWIDE (1944-September 1994): "CLASSIFICATION BY DEVICE"

"Criticalities"		**18**
Critical assemblies	**6**	
Reactors	**7**	
Chemical operations	**5**	
Radiation devices		**282**
Sealed sources	**191**	
X-ray devices	**70**	
Accelerators	**20**	
Radar generators	**1**	
Radioisotopes		**78**
Transuranics	**26**	
Tritium	**1**	
Fission products	**10**	
Radium spills	**2**	
Diagnosis and therapy	**27**	
Other	**12**	
TOTAL		**378**

Source: **Radiation Emergency Assistance Centre/Training Site**
Radiation Accident Registries **ORISE-MSD-REAC/TS**

MAJOR RADIATION ACCIDENTS: HUMAN EXPERIENCE 1944-SEPTEMBER 1994*

Location	No. of Accidents	No. of Persons Involved	Significant Exposures**	Fatalities
U.S.	235	1310	780	30
Non-U.S.	143	132,025	2098	73
TOTAL	378	133,335	2878	103

* Source: DOS/REAC/TS Radiation Accident Registries

** DOE/NRC dose criteria

MAJOR RADIATION ACCIDENTS: WORLDWIDE
TYPES OF EXPOSURES: 1944-SEPTEMBER 1994

Type	Number of Accidents	Individuals >=Dose Criteria	Fatalaties (U.S.)	
TBI	66	173	23	(2)
LOCAL	199	442	17	(12)
TBI + LOCAL	52	71	14	(4)
INTERNAL	59	88	8	(8)
TBI + LOC + INT	5	212	22	(-)
TBI + INT	3	1,142	11	(-)
INT + LOC	1	1	(-)	(-)
NON-RAD	4	(-)	8	(4)
RAD Rx	(-)	749	(-)	
TOTAL		2,878	103	(30)

a - DOE/NRC Accident Dose Criteria
Source: REAC/TS Registries

ORIS-MSD-REAC/TS

MAJOR RADIATION ACCIDENTS WORLDWIDE (1944-SEPTEMBER 1994): ACUTE, ASSOCIATED, AND NON-RADIATION DEATHS

United States		Other	
New Mexico	3	Algeria	2
Ohio	10	Argentina	1
Oklahoma	1	Brazil	4
Pennsylvania	1	Bulgaria	1
Rhode Island	1	Belarus	1
Texas	9	China (PR)	6
Wisconsin	1	El Salvador	1
		Israel	1
	26	Italy	1
		Marshlall Islands	1
		Mexico	5
Non-radiation deaths		Morocco	8
Canada	1	Norway	1
Idaho	3	Spain	3
USSR	3	USSR	30
Washington	1	United Kingdom	2
		Yugoslavia	1
TOTAL	8		
			69

ORISE-MSD-REAC/TS

WORLDWIDE FATALITIES
1944 TO SEPTEMBER 1994

Country	Number of Accidents with Fatalities	Number Fatalities
Algeria	1	2
Argentina	1	1
Brazil	1	4
Bulgaria	1	1
Belarus	1	1
Canada	1	1
China	1	6
El Salvador	3	1
Israel	1	1
Italy	1	1
Marshall Islands	1	1
Mexico	1	5
Morocco	1	8
Norway	1	1
Spain	1	3
United Kingdom	1	2
United States	13	30
USSR	3	33
Yugoslavia	1	1
TOTAL	35	103

Source: Radiation Emergency Assistance Centre/Training Site Radiation Accident Registrie

ORISE-MSD-REAC/TS

COMMON CAUSES OF RADIATION ACCIDENTS

- Lost or mishandled sources
- Interlock bypass
- Failure to use survey instruments
- Inadequate training/written procedures
- Failure to use criticality control
- Inadequate radiation protection programmes
- Calibration/programming errors
- Inadequate supervision/quality control
- Medical misadministration
- Human factors

Brief Summary of Some Individual Presentations

- Dr Baranov presented a review of the Ulm/Moscow database programme. The University of Ulm and the Moscow Institute of Biophysics agreed to develop the databases for radiation exposure case histories in 1990. The December 1992 report was approved by the 4th REMPAN meeting and published in 1993 with the blessing of WHO.

  Dr Baranov illustrated the use of the database proformas with data from one of the Chernobyl patients. There are now some 102 case histories in the database, inlcuding 77 from Chernobyl, with 158 in pre-computer case reports and another 5 on paper awaiting data entry. There are many more cases waiting to be recorded.

  It is hoped to begin work on an "expert system" based on the database in January 1995.

- Dr Kindler gave a comprehensive explanation of how the database was designed and how it can be used. He showed how the original data is converted to a paper pre-computer report (converting to standard terminology), SI units, etc.) using the published proformas and how this is then computerised and, finally, translated through a software package into the computer database (a relational database using ORACLE).

  A prototype "expert system" is udner development. The acute-phase database can assist in decision making in patient management, for example, by providing similar case histories for comparison.

  A new classification of severity of radiation injury is being developed, based on granulocyte concentration. A codex for the use of the database is also being developed, with a meeting scheduled in Ulm in 1995 to discuss legal issues and access protocols, etc.

- Dr Iyer presented a case history of an Indian railway workers who picked up an iridium-192 source of 4.5Ci and put it in his pocket for about 2½ hours. Dr Iyer explained how the radiation dose was estimated through reconstruction of events and through the use of TLDs in an exposed phantom. The dose to the right thigh was estimated at 11.500 rads. The patient was eventually discharged after skin grafts to both thighs.

- Dr Turai presented a preliminary report on an accident which had occurred very recently (October 1994) in Estonia. Two cylindrical sources throught to be from a sterilisation plant and of about 90Ci of ^{137}Cs (or ^{60}Co) were found by a 25-year-old worker and placed in his trouser pocket. This man died, probably from kidney failure, on 2 November 94 from a dose which was later estimated to be 1830Gy to the thigh and 4Gy whole body dose. Five other people were exposed to doses of up to 30Gy to the extremities from handling sources. The source was not found until 17/18 November after a 13-year-old boy reported his injuries to hospital.

- Dr Makio gave an outline of the Hiroshima International Council for Health Care of the Radiation-Exposed (HICARE). This was established in 1991 and has so far received 391 scientists for training based on the expertise which has accumulated on the health effetcs of A-bomb survivirs. HICARE has the capacity for about 100 trainees per year in a range of courses including radiation dosimetry, assessment of biological effects, epidemiological and statistical methods, and clinical laboratory and nursing techniques.

- Dr Ye presented a review of the Chinese data bank and consulting system for the medical management of acute radiation syndrome patients. The data bank has information on 630 cases worldwide, including 54 deaths. Dr Ye described a case study from 1 1992 accident in Shanghai and gave a real-time demonstration of the software.

- Dr reiffers described a French registry of clinical data on patients who have received total body irradaiiton. (There is also a bone-marriw transplant register in Milwaukee, USA). There are 28 centres doing allogenic and syngenic transplants (about 70% for leukaemia) and 73 carrying out autologous ytransplants (about 43% for non-Hodgkins lymphoma, 17% or myeloma and 30% for breast cancer). Total body irradaition is used to prepare patients in about 80% of the former category, but only 30% of the latter; in most cases the doses are fractioned. The total number of transplants is running at about 2000 per year.

- Dr Laugier continued the discussion, describing the use of the aregister (BENEDICT) to record patient and tratment data. He also gave a real-time demonstration of the software.

- Dr Cosset gace a description of the collection of radiopathology patient data in France. The data covers the period 1951-194 and includes 952 patient histories. About 59% of the cases arose from accidents, about 35% from radiotherapy and complications and some 6% are describved as "radiophobia". Of the 560 accident cases, 144 received treatment. There are 51 cases of major sequlae, including amputations and 3 deaths The incidence of radiotherapy cases appears to be rising with time much faster than the accident cases.