



IRSN

INSTITUT
DE RADIOPROTECTION
ET DE SÛRETÉ NUCLÉAIRE

IRSN summary of the UNSCEAR reports

// for 2003–2007

Version dated 15 september 2006

IRSN summary of the UNSCEAR reports

// for 2003-2007

First edition 15 september 2006

IRSN report 2006-74

ISRN IRSN 2006/74-ENG

IRSN

//short view

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IRSN employs more than 1,500 specialists, including engineers, researchers, doctors, agronomists, veterinarians and technicians, experts in nuclear safety and radiological protection and in the control of nuclear and sensitive materials

The Institute exercises specialist and research assignments in the following fields:

- nuclear safety;
- safety in transporting radioactive and fissile materials;
- protection of man and the environment against ionising radiation;
- protection and control of nuclear materials;
- physical protection of facilities and transport of radioactive and fissile materials.

Doctrine & synthèse

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Forward

The Institute for Radiological Protection and Nuclear Safety conducts research programmes and studies on nuclear and radiological risks; it is responsible for public service activities in the prevention of these risks and provides technical support to the competent public authorities in nuclear and radiological protection safety and security. In this respect, the Institute is called on to develop a position on a certain number of scientific and technical issues.

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Abstract

The present document provides a brief description of the nine reports discussed during the 54th session of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR)^[1]. This session was held in May 2006 and is part of a work cycle covering the period from 2003 to 2007.

Created in 1955, UNSCEAR periodically compiles reports which provide an exhaustive and international summary of scientific data on ionising radiation.

The reports discussed during the Committee's 54th session cover subjects as varied as sources of radiation, exposure of the public and workers, exposure due to radon, medical exposure, effects of radiation on humans and non-human biota, physiopathology of radiation effects, mechanisms and epidemiology of radiation-induced carcinogenesis, mechanisms of radiation effects, noncancer health effects, effects of radiation on the immune system, and non-targeted and delayed effects. These reports are practically all in final or near-final form, but some have not yet been completed.

[1]

UNSCEAR:
United Nations
Scientific Committee
on the Effects of
Atomic Radiation
www.unscear.org

Preface

Although this summary report is published in the IRSN's Doctrine and Summary Reports collection, it does not aim to define the Institute's positions but rather to present the main themes of the UNSCEAR reports for the period 2003–2007.

Another novel feature of this report is its publication before that of the UNSCEAR reports themselves. The objective is to help those in the radiological protection field stay informed of the latest findings of international authorities such as UNSCEAR. The IRSN's efforts have met with the approval of the UNSCEAR Secretariat.

The IRSN also fulfils its duties as a public advisory body open to society's various stakeholders by disseminating the information its experts gain through collaborative projects with international authorities.

Radiological protection standards are based on scientific understanding of the effects of radiation on humans and the environment. Given the complexity of this field and its relationships with disciplines as varied as medicine, biology, chemistry, physics and radioecology, it is essential that the international community regularly review new developments in the understanding of sources and risks. The mission of the United Nations Scientific Committee on the Effects of Atomic Radiation is to carry out such reviews and present its findings to the General Assembly of the United Nations. For the preparation of its reports, the Committee relies on consultants selected by its Scientific Secretariat. These reports are discussed by delegations from 21 nations during UNSCEAR's annual meetings. They are published at the end of a work cycle lasting roughly five years.

The current cycle (2003–2007) is not yet completed, but the nine reports discussed during UNSCEAR's 54th session in May 2006 provide a solid basis for a brief description of the major themes explored in the upcoming publications.

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1/

Introduction

Each subject is presented as a status report on the latest scientific developments. The reports had already undergone discussion and analysis during earlier sessions and some date back several years. The current versions are therefore extremely detailed, validated by the representatives of the various member nations of UNSCEAR. Five reports were presented in near-final form; publication is planned for 2006, or 2007 at the latest. They discuss: 1/ the effects of radon, 2/ epidemiological studies of radiation-induced cancer, 3/ noncancer health effects of radiation, 4/ effects of radiation on the immune system, and 5/ non-targeted and delayed effects of radiation. Four other reports were presented in draft form but are actually revised and improved versions of documents already presented or discussed during earlier sessions; they should be published within the next two years. They discuss: 1/ the effects of radiation on non-human biota (publication planned for 2008), 2/ radiation accidents (2007), 3/ sources of exposure for the public and workers (2007), and 4/ medical exposures (2008).

2/

Finalised reports

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Sources-to-effects assessment for radon in homes and workplaces¹

This voluminous report has been presented to the members of UNSCEAR on a regular basis for several years. The current format is identical to that of the 2004 version, with the same clear, logical approach. The document is exhaustive, constituting an encyclopaedia of studies on the effects of radon. However, the section on experimental studies is quite underdeveloped and refers to the American report NCRP 65 (2004)², also on radon risk. This gap can be explained by the report's objective, which is to assess the risk in humans, a difficult task to accomplish using animal models alone. The report reviews radon measurements and the related risks, as well as assessing study findings. It successively examines the studies carried out on 1/ miners exposed to radon risk in North America (United States, Canada, Newfoundland), Europe (France, the former Czechoslovakia, Sweden), China and Australia; and 2/ populations in the United States, Canada, Europe (Sweden, Finland, France, United Kingdom, Germany, Italy, Czech Republic, Austria) and China. The most detailed studies concern United States Colorado plateau uranium miners; Ontario, Saskatchewan and Port Radium Canadian uranium miners; the first Czech miners of pitchblende; Swedish iron miners; uranium miners in the former East Germany; French uranium miners; fluorspar miners in Newfoundland and Chinese uranium miners. French authors are duly cited: early specialists such as Jammet, Pradel, Chamaud and Zettwoog (IPSN/CEA/COGEMA) are cited 7 times and current experts are cited more than 20 times: Tirmarche, Laurier *et al.* (IRSN) 14 times and Monchaux *et al.* (CEA/DSV) 7 times. Regrettably, the report lacks a chapter on risk modelling, but there are considerable improvements compared with the previous version, especially with regard to the epidemiological studies on the consequences of residential radon exposure, which now include American and European case-control studies. This addition

¹

Report R.654:
Sources-to-effects assessment
for radon in homes and
workplaces

²

NCRP 65:
National Council on Radiation
protection and measurements.
Evaluation of occupational and
environmental radon risk.
NCRP SC 65, 2004

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facilitates comparison across the uranium miner studies and the population studies, which demonstrate a satisfactory level of consistency: the relative excess risk for developing lung cancer is estimated to be 0.16 per 100 Bq m⁻³ with an uncertainty factor of 3, higher or lower. This estimate is very close to the one given in the BEIR VI report¹, i.e. 0.15 per 100 Bq m⁻³. The contributions of Margot Tirmarche (IRSN) in this area were very warmly acknowledged by the consultant. As he rightly pointed out, there are unfortunately no studies on miners or the public that take the distribution of individual doses into account, a consideration which would have undoubtedly refined risk estimation. Smoking is a significant confounding risk, since 90% of the risk related to residential radon exposure is linked to smoking. Because the experts were divided as to whether smoking has a multiplicative effect or a sub-multiplicative effect on the risk of radon-induced lung cancer, the report does not take a position on this issue.

This report was presented in its final form, notwithstanding a few minor additions and corrections suggested during the session. A general conclusion will also be added. It should be published before the end of 2006.

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Epidemiological studies of radiation and cancer²

This thick report – including detailed tables and figures as well as technical appendices on methodology, risk measurement and modelling – complements UNSCEAR's previous reports. It presents the findings of studies not previously analysed or summarised; it allows risk factors to be assessed for individual organs and tissues. Compared with the previous document published in 2004, this report is exhaustive, providing readers with numerous data sources and results. Amongst the populations particularly vulnerable to the risk of radiation-induced cancer but not included in previous versions, the following merit particular attention:

- **Workers at the Mayak nuclear complex**, including several people who incorporated plutonium, usually in moderate quantities. Cancer mortality was studied in a cohort of 21,500 workers, including 26% women. The cohort workers were employed at the complex between 1948 and 1972, with a cumulative average dose of 0.8 Sv. This population has received high-quality follow-up since 1977. Amongst the 7,067 deaths observed, 1,730 were due to solid cancers and 77 to leukaemia. Plutonium was found in the organs of



BEIR VI:
Committee on the Biological effects of Ionizing Radiation. The health effects of exposure to indoor radon. National Academy of Sciences (USA), National Research Council. National Academy Press, Washington, 1999



Report R.658:
Epidemiological studies of radiation and cancer

668 people who had died from cancer. Lung and stomach cancer are the predominant causes of death. Excess relative risk is 0.30 Gy^{-1} for the lung, liver and skeleton. The dose-effect relationship is slightly concave at higher doses, expressing an inversely proportional risk factor at these doses. The level of risk observed in this study is markedly lower than that observed for the Japanese survivors of Hiroshima and Nagasaki. This finding may be due to dose uncertainty, plutonium contamination of the lungs (sufficient in some cases to produce fibrosis) or to the fact that the most exposed individuals were autopsied more frequently (and thus received more reliable diagnoses). Moreover, neither the age at initial exposure nor the time elapsed after exposure appears to be risk-modifying factors, even though risk has been shown to decrease with age.

- **Populations living along the Techa River (Southern Urals),** exposed to huge quantities of radioactive effluents which the former Soviet Union carelessly dumped in the river during the nuclear weapons race. Scientists began assessing internal exposure in 1951 using autopsy sample measurements. In 1959 they began using whole body countings as well as *in vivo* measurements on teeth. Approximately half of these populations were assessed for individual strontium-90 body burdens (using yttrium-90 measurements). However this is an ecological study, based on measurements of the average internal and external exposures for all residents of a given village. There is also a great deal of dose uncertainty and most importantly, a very high degree of variation in dose distributions (at least two orders of magnitude). Consequently, the results of this study should be interpreted with caution. For example, excess relative risk for solid cancers varies with untypical parameters, such as age at initial exposure and attained age. This is contrary to the findings for Hiroshima and Nagasaki survivors.

- **Populations living around the Semipalatinsk test site (Kazakhstan).** Ten villages were exposed to fallout from 122 atmospheric explosions conducted between 1949 and 1962. The study followed individuals born before 1961. The findings are not consistent with other studies considered as reliable: relative excess risk for these populations is 0.81 Sv^{-1} for all solid cancers, 0.95 Sv^{-1} for stomach cancer and 1.76 Sv^{-1} for lung cancer. Risk is shown to increase with age at exposure, which is contrary to study findings for Hiroshima and Nagasaki survivors. The question remains as to whether this untypical relationship results from ecological bias, or whether it points to the difference between the acute exposure of

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Japanese survivors and the prolonged exposure around Soviet test sites.

- **Cohorts of workers employed in the civil nuclear industry** (*International worker study*), which bring together 407,391 subjects of all different nationalities and backgrounds. Amongst them, 190,000 were excluded from the study for various reasons: they had not been employed in one or several installations for a year or more, their doses had not been recorded or they had received internal or neutron exposure. The cohort accumulated 5.2 million person-years. The average individual dose was 19.4 mSv. The distribution of cumulative doses indicates that 90% of subjects received less than 50 mSv and less than 1% of subjects received more than 500 mSv. Amongst the deaths recorded for all cohorts, 6,519 were due to cancers and 196 were due to leukaemia. According to the main study, conducted by the International Agency for Research on Cancer (IARC) ¹, relative excess risk is 0.97 Sv^{-1} for solid cancers and 1.93 Sv^{-1} for leukaemia. The risk estimate for solid cancers is 8 times higher than that published in the Japanese Life Span Study (LSS) ², even after reduction by a factor of 2 to account for low doses and low dose rates. Lung cancer (1.86 Sv^{-1}) has a strong impact on the rate of solid cancers. The risk of cancer – excluding leukaemia, lung cancer and pleural cancer – is only 0.59 Sv^{-1} . However, because cancers attributable to smoking represent an relative excess risk of 0.21 Sv^{-1} , the risk for noncancer radiation-induced respiratory disease is 1.16 Sv^{-1} , whereas the risk for chronic obstructive bronchitis and emphysema is 2.12 Sv^{-1} . The conclusion is that the confounding factors arising from smoking, when taken together, may partially, but not totally, explains the increased risk of mortality for all cancers, except leukaemia. If the cohorts are considered separately, we see that the Canadian worker study has a strong impact on relative excess risk for solid cancers. Although this study accounts for only 400 cancer cases overall (6.1%) and the average individual dose is comparable to that of all cohorts taken together (19.5 mSv versus 19.4 mSv), excluding it from the overall study reduces the risk to 0.58 Sv^{-1} . Moreover, the risk for lung cancer is abnormally high in the Canadian study, i.e. 3.1 Sv^{-1} , as is the number of deaths from such diverse causes as parasitic and infectious diseases (4.9 Sv^{-1}), cardiovascular diseases (2.3 Sv^{-1}) and accidents (8.8 Sv^{-1}). These surprising figures are most likely the result of several unidentified biases in the study. These biases taint much of the overall study, which involves 15 countries.

- **American radiology technicians**, a population of 146,000 people, including 107,000 women; their cases were documented



IARC:

International Agency for Research on Cancer: IARC Study Group on cancer risk among nuclear industry workers. Direct estimates of cancer mortality due to low doses of ionising radiation: an international study. *Lancet* Vol 344 -October 15, 1994, 1039-1043



D.L. Preston, Y. Shimizu, D. A. Pierce, A. Suyama and K. Mabuchi. Studies of mortality of atomic bomb survivors. Report 13: Solid cancer and non cancer diseases mortality: 1950-1997. *Radiation Research*, 160, 381-407, 2003

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between 1926 and 1982. In 1997, amongst the 12,624 deaths in a cohort of 90,305 subjects, cancer was the cause of death in 2,651 cases. Dose reconstruction is underway but not yet available. The results of the study are still fragmentary but suggest that the number of years spent working with radiation is not associated with an increased risk of cancer. There does seem to be a trend towards excess mortality in general and excess breast cancer in particular. However there are serious doubts concerning the study's core data, and therefore its robustness. This is due to confusion between job entry dates and birth dates, dose uncertainty, the lack of correction for geographic factors, etc.

- **Chinese radiologists and technicians;** their cases were documented between 1950 and 1995. This population included 27,011 people scattered across 24 Chinese provinces. There are no dose data prior to 1985, but with retrospective assessment using biological methods, the cumulative average individual dose is estimated to be 758 mGy for those who worked before 1960, 279 mGy for those who worked between 1960 and 1969, and 83 mGy for those who worked between 1970 and 1980. An excess is observed for solid cancers taken together, with a relative risk of 1.19, and for leukaemia, with a relative risk of 2.17. Excesses are also observed for breast cancer (relative risk of 1.34), skin cancer excluding melanoma (4.05), oesophageal cancer (2.65), liver cancer (1.20), lung cancer (1.20) and bladder cancer (1.84). The age at exposure seems to be determinant for lung and thyroid cancers. However, these results must be interpreted with caution because the calculations were not carried out in a very rigorous manner, especially those for the control group.

- **Aircraft personnel** are exposed to relatively significant doses which were frequently as high as 6 mSv per year, but lifetime doses do not exceed 80 mSv. There is a substantial neutron component (25% to 50 %). Three studies are of particular interest; the first includes the personnel of several European airlines and the other two focus on pilots. The parameters differ for each study: time spent working, time-of-flight at high altitudes and exposure level. In the first two studies, an excess of melanomas is observed in male pilots, whereas this excess is not observed for women in the first study (the second study only involves men). This specific excess risk was not observed in the third study. There is a slight trend across the three studies towards an excess relative risk for all cancers. This risk increases with dose; for doses above 25 mSv, the relative risk is 0.74. Dose uncertainty is due to the fact that the level of solar exposure is not accounted for in the melanoma figures. As no

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correlation was found between increased risk and time spent working, there is considerable doubt surrounding the aetiology of skin diseases attributed to radiation.

- **The studies of specific risk factors** are particularly detailed and focus on over 20 organs and tissues: salivary glands, oesophagus, stomach, small intestine, colon, rectum, liver, pancreas, lungs, bone and connective tissue, skin, breast, uterus, ovary, prostate, bladder, kidney, brain and central nervous tissue, thyroid gland, lymphatic system (for non-Hodgkin's lymphoma and Hodgkin's disease) and bone marrow (for multiple myeloma and leukaemia). Eight of these organs were not considered in the UNSCEAR report presented in 2000¹. The current findings suggest that it is impossible to define a single value for either overall risk or specific risks, mainly because of the variability in the methods used to project risk. In general, risk uncertainty for a given organ or cancer is greater than that for total cancer. As of this writing, the following points seem firmly established:

1/ For each of the solid cancers, relative excess risk and excess absolute risk are proportional to a product of powers of time since exposure and attained age;

2/ Relative excess risk for leukaemia is also proportional to a product of powers of age at exposure and attained age, whereas absolute excess risk is proportional to a power of time since exposure;

3/ When these risk models are applied to any of the core study populations (in China, Japan, Puerto Rico, United States, United Kingdom), the lifetime risk (an average of values for both sexes) is estimated to be between 4.3% and 7.2% for a dose of 1 Sv; these values may vary depending on the population and the models used ;

4/ These estimates are slightly lower than those previously reported by UNSCEAR and other organisations. This reduced risk can be explained by the new dosimetry for the Japanese A-bomb survivors and by the use of new models ;

5/ These risk estimates involve an uncertainty factor of 2, higher or lower; they may be 50% lower in the case of prolonged exposure, which is also marred by an uncertainty factor of 2, higher or lower ;

6/ The cancer risk is markedly greater for children – as much as 2 or 3 times higher – compared with the risk for a mixed-age population ;

7/ The study of cancers in the Japanese A-bomb survivors produced findings consistent with a linear (or linear-quadratic) dose-effect relationship. Consequently, the linear extrapolation of



UNSCEAR 2000: United Nations Scientific Committee on the Effects of Atomic Radiation. Report to the General Assembly with Scientific Annexes. Vol. II: Effects, Annex I: Epidemiological evaluation of radiation-induced cancer, United Nations, New York, 2000

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the risk value at 1 Sv (acute dose) can be used to obtain an initial estimate of low-dose risk ;

8/ Finally, for site-specific cancers the findings presented in 2000 remain unchanged or differ only slightly.

The results not reported in earlier reports involve specific systems, organs and diseases:

1/ The potential for developing cancer varies widely for the different organs of the digestive system. Further studies are needed to clarify the possible relationships between radiation-induced liver cancer and other diseases, such as viral infections (hepatitis C) and cirrhosis;

2/ The pancreas seems relatively resistant to radiation-induced cancer ;

3/ The lung is very sensitive to radiation, as shown by: studies of the Japanese survivors of Hiroshima and Nagasaki, patients exposed for medical reasons, populations around the Mayak site, etc. Relative excess risk appears to be higher for women and does not decrease with age. There are no studies demonstrating the carcinogenicity of radiation at low doses and low dose-rates. Radiation's cancer-inducing ability has an additive effect on that of smoking; in some cases the effect is multiplicative or even greater ;

4/ The breast is a very sensitive organ for which there are aggravating factors, such as predisposition to cancer linked to genetic or reproductive parameters ;

5/ The uterus and the kidney are relatively resistant to radiation; uterine cancer is only reported at doses of several tens of Gy or higher ;

6/ The thyroid gland is amongst those organs which are particularly sensitive to radiation; for children the relative excess risk persists throughout life, but there are studies suggesting it may decrease 20 years after exposure.

2/3

Epidemiological evaluation of cardiovascular disease and other noncancer diseases following radiation exposure¹

The main criticism of the 2004 version was that its title (*Epidemiological evaluation and dose response of diseases other than cancer*) gave the impression that it described a number of



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of cardiovascular disease
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diseases following radiation
exposure

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noncancer radiation-induced diseases affecting various organs and tissues. In fact, the report only addressed cardiovascular diseases caused by radiation exposure and made no mention of other systems and organs known or believed to be targeted by noncancer radiation-induced diseases, such as the digestive and respiratory systems, the lens of the eye and the thyroid gland. Although the document has been considerably substantiated since 2004, the same criticism applies to the 2006 report. The Committee therefore decided to change the title to reflect the focus on cardiovascular diseases. The reasons for overlooking the other systems and organs are well founded: 1/ because these other diseases are only rarely fatal, unlike cardiovascular diseases, the data lack robustness and are difficult to use; 2/ there is a substantial number of diseases for a given system or organ; 3/ the number of biases and confounding factors for each disease is particularly high; and 4/ numerous other risk factors, not to mention socio-economic factors, are harder to define than for the cardiovascular system. However, these arguments are not valid for cataracts and noncancer thyroid diseases. There are now reliable data on these conditions, particularly for the workers and populations affected by the Chernobyl accident. These data were analysed in the UNSCEAR Chernobyl report and therefore are not reviewed in the report under discussion. Although this report may give the false impression that cardiovascular diseases predominate amongst noncancer radiation-induced affections, the document is very satisfactory, in terms of both form and content. It explains the selection criteria for the cohorts and discusses the healthy worker effect, the quality of mortality data (overestimation of noncancer diseases due to errors in determining cause of death), confounding factors due to the multiple causes of cardiovascular diseases, and considerable variations based on lifestyle, location and socio-economic status. The report mentions the biases apparent in certain publications. These biases are due to the fact that epidemiological studies on the effects of doses below the threshold values for deterministic effects have so far focused primarily on radiation-induced malignant diseases. The current report leaves out the chapter on the Hiroshima and Nagasaki survivors – a noteworthy improvement compared with the 2004 report. As a result, diseases are categorised by type and not by cohort origins; therefore the diseases observed in the Japanese survivors are now considered together with those of the other cohorts.

The report's conclusions are particularly relevant to radiological protection. Noncancer radiation-induced diseases affecting the cardiovascular, respiratory and digestive systems have until now

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been considered part of the family of deterministic effects, with relatively high dose thresholds (4–5 Gy depending on the disease and the affected organ), but it now appears that these diseases can be induced by lower doses. This point is underscored by the Life Span Study (Japanese A-bomb survivors) in particular. It points to the need for new studies on populations exposed to relatively low doses. The challenge is that many of the existing studies (almost 50%) cannot be applied to noncancer effects. Most of the data for these effects come from cohorts of patients irradiated for medical reasons (treatment of benign diseases or diagnostic radiology examinations); cardiovascular disease was the predominant complaint amongst these patients. For example, the risk of coronary heart disease increases when the heart is exposed to a dose of 1.6–3.9 Gy. Given that the findings of mortality studies are consistent with those of morbidity studies, noncancer effects are all the more credible. The biological mechanisms that cause such diseases remain unknown. The report suggests mechanisms involving primary damage to the microvessels of the pericardium and myocardium, atheromatous lesions of monoclonal origin, and inflammation, but is unable to provide convincing evidence. In conclusion, the report stresses the need for further studies, in the fields of epidemiology and biological mechanisms.

The report was deemed to be in near-final form and should thus be published rapidly. It will contain no animal data, because it focuses exclusively on epidemiological studies. The authors must now add the final conclusion, which will highlight the following points:

1/ Previously the risk of cardiovascular disease was linked to doses above 40 Gy (irradiations of the mediastinum for Hodgkin's disease), but there are now data to suggest risk at lower doses, around 30–35 Gy for adults and 15–25 Gy for children. For even smaller doses (patients irradiated for ankylosing spondylitis with an average dose to the pericardium of 2.5 Gy) the number of cardiovascular deaths is higher than for patients with the same disease but no exposure. However, it is impossible to draw solid conclusions because of the low excess risk ;

2/ Risk varies with age at exposure and the time elapsed since the event, but it may persist for three or four decades. Risk data from patient studies are consistent with follow-up results for the survivors of Hiroshima and Nagasaki ;

3/ It would be interesting to study the cohorts of health professionals exposed in the early 20th century. Unfortunately, the lack of dosimetric data would make any definitive conclusions impossible. The same is true for cohorts of industrial workers, but

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for these populations it is the existence of several unidentified confounding factors that weakens the studies ;

4/ For diseases other those affecting the cardiovascular system, there are data from the follow-up studies of Hiroshima and Nagasaki survivors suggesting a causal relationship with doses of 1–2 Gy or lower. However, this conclusion is less robust than for cardiovascular diseases because of the limited data, the wide range of diseases, the various aetiologies and pathological mechanisms, and the multitude of confounding factors ;

5/ The Committee underscores the fact that the report's conclusions may have socio-economic consequences; in many countries it has become an established practice to seek compensation for cancers and other diseases attributed to radiation exposure, and there are numerous claims of this sort.

2/4

Effects of ionising radiation on the immune system¹

This report is a follow-up to the 2004 report, in which numerous sections required further development. It offers a very technical review aimed at specialists, despite a clear effort to make it accessible to readers with a limited understanding of the immune system. This study is particularly interesting because the primary function of the immune system is to protect against infections and cancer through a system which recognises antigens. Response quality depends on four parameters: memory, specificity, diversity and the ability to discriminate. The report reviews the components and parameters that play a role in the immune response. The main cells involved are lymphocytes – B cells and T cells – which mature in the bone marrow and the thymus. B cells govern the humoral response whereas T cells play a central role in cellular responses. Transported by the circulatory system, mature lymphocytes cluster in the lymph nodes, the spleen and the other tissues of the lymphatic system. As for the skin, its ability to block and defend against pathogenic agents can be either innate or acquired. Finally, immunosenescence is a complex phenomenon resulting from the dysregulation of the immune system rather than an overall decline. According to the studies, both high sub-lethal doses and low doses of radiation appear to significantly reduce immune capacity across all parameters of the immune response. This response depends on the total dose, but dose rate has little or no impact. This suggests that response to high dose rates may be used to predict the effects



Report R.661:
Effects of ionising radiation on
the immune system

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of low dose rates, across a wide range of doses and dose rates. Lymphoid cells and tissues are particularly sensitive to high LET¹, radiation, even at relatively low doses; the negative effects persist long after absorption.

Exposure of experimental animals to prolonged low dose radiation results in adaptation of the haematopoietic system, which is normally very sensitive to radiation but under these conditions develops a relative resistance to it. This modification affects progenitor cells, and recovery may be incomplete. There is a great deal of evidence that this type of exposure activates immune functions: under the same exposure conditions, inhibition of malignant tumour growth, of metastasis and of carcinogenesis in general have been observed. Furthermore the adaptive response is a phenomenon observed in numerous systems and appears linked to the reduced apoptosis (programmed cell death) observed in the haematopoietic system following exposure to high doses.

The short-term effects observed in the Japanese A-bomb survivors mainly involved acute bone marrow exhaustion related to cell death and proportional in severity to the dose received. Such effects are reversible within several months. The most noteworthy consequences are quantitative and functional abnormalities in T and B cells in subjects exposed to doses above 1 Gy. However, there appears to be no quantitative or functional effect on natural immunity as there is on adaptive immunity.

Abnormalities of all sorts were detected in members of the general population exposed to radiation as a result of the Chernobyl accident, but they are difficult to interpret because of the many confounding factors. The data vary as a function of studied population, dose, dose distribution over time, type of exposure (external and/or internal) and time elapsed since exposure. Short- and long-term effects were found in children living in the particularly contaminated zones around the site. They involved functional modifications of T and B cells, as well as changes in the biosynthesis of the immunoglobulins in serum and saliva. Some of these phenomena were dose-dependent. The immune system is implicated in the pathogenesis of thyroid diseases observed in some victims; the combination of radiation and antigenic phenomena apparently provoked an autoimmune response. Stress-related hormonal reactions, respiratory diseases and chronic infections may have also contributed to the various immunological disorders observed in the populations affected by the accident. Among the workers who helped clean up the site (the liquidators), responses were most pronounced amongst those exposed to the highest doses

1

LET:

Linear energy transfer, which measures the density of ionisation along the path of a charged particle with a given energy; it is expressed as the average energy transferred to the local surroundings by the particle, divided by the distance travelled.

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(firemen and rescue workers involved during the accident received doses of 0.5-9 Gy; those involved in the first days after the accident received doses of 0.1–0.5 Gy).

The findings in populations as diverse as the Japanese A-bomb survivors, the persons affected by the Chernobyl accident and villagers along the Techa River show that the negative effects on the immune system persist more than 50 years after exposure. The proliferation of radiation-induced cellular mutations can cause clonal expansion, affecting haematopoietic stem cells, specific progenitor cells and mature T cells in particular. It appears that clonal expansion, which is not especially dangerous, emerges a few years after exposure and most likely signals an attempt to repair the damage to the immune system. Epidemiological studies appear to suggest that radiation-induced modifications of immune capacity may increase the risk of developing those diseases observed in older people. Therefore radiation may accelerate immunosenescence, like natural aging, by disrupting the homeostasis of T cells. Apoptosis is essential to maintaining normal cellular homeostasis in the immune system. The bystander effect, the adaptive response and genomic instability have been shown to play a role in the immune response to radiation. However, their potential health consequences have been neither explained nor demonstrated. Nonetheless, lowered immune defences can increase the risk of cancer by affecting reactions which target malignant cells. Moreover, individual genetic susceptibility to radiation, which has been demonstrated, is often associated with functional damage to the immune system.

The main conclusions of the report are as follows:

1/ The immune system is undoubtedly one of the body's most complex systems, involving numerous cells in the various organs and tissues where stem cells mature. Immune cells communicate with help from cytokines – soluble molecules which stimulate cellular proliferation and differentiation.

2/ The data examined in the report suggest that radiation exposure often results in immunosuppression, particularly after high doses. This phenomenon is related to the fact that lymphocytes are highly sensitive to radiation. In addition to these cytotoxic effects, radiation can trigger a "danger signal", which can in turn affect the cellular-level immune response. Therefore, radiation exposure should not be categorised with cytotoxic agents (immunosuppressive agents), but should instead be considered an immunomodulatory agent.

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3/ This immunomodulatory action against cancer is now better known. According to conventional theory, malignant tumours may develop if immune surveillance fails to detect them, due either to reduced expression of tumour antigens, or to changes in the immune response. It now appears that immune-related tumour promotion may also be tied to persistent low-level infections, the activation of immature immune cells or antibodies which block cellular activity.

4/ There is disagreement about the effects of low doses (below 200 mGy) and low dose rates (below 100 mGy h⁻¹). In humans, cellular irradiation often produces irregularities interpreted as reduced immune capacity; certain studies suggest that prolonged exposure may result in an adaptive response.

5/ Several questions should be explored in greater depth. They mainly concern: the effects of low doses and low dose rates compared with those of moderate and high doses, the combined effects of irradiation and other agents, the effects of external exposure compared with those of internal exposure, the relationship between immunomodulation and cancer, disruptions in T cell homeostasis, the relationship between immunity and carcinogenesis, and the effects of aging on immune function and the inflammatory response.

2/5

Non-targeted and delayed effects of exposure to ionising radiation

Compared with the previous report (R.638, 2004), the current document is slightly better documented, but the differences are not very significant. In 2004, the subject was truly novel, because in earlier publications and draft publications it had only been addressed in a fragmented, incomplete fashion. This report's strong point is that it is practically the only document focusing on phenomena described relatively recently and in need of further investigation and clarification, particularly because of the potential repercussions on radiological protection standards. The term "non-targeted effects" encompasses effects with various mechanisms, but they share a common characteristic: they are not related to energy deposit in cell nuclei, which until recent years was the central dogma of traditional radiobiology. Consequently, the carcinogenic effects are somehow tied to mutagenic and clastogenic risks. These effects were recently described in an NCRP draft report  on risk



Report R. 659:
Non-targeted and delayed
effects of exposure to ionising
radiation



National Council on Radiation
protection and Measurements.
Extrapolation of risks from
nonhuman experimental
systems to man. NCRP Draft
Report SC 1-4, October 2003

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extrapolation. Current knowledge is based on *in vivo* and *in vitro* findings.

Genomic instability is well known and has been described in the literature for several years. It involves increased changes in the genome and is the first critical step in the development of certain radiation-induced cancers. This concept encompasses both the chromosomal instability of cells not directly irradiated but situated in a radiation-exposed environment, and the instability of cells descended from non-irradiated stem cells. It appears likely that signals from irradiated cells can stimulate chromosomal rearrangements in cells not present at the time of irradiation. Various observations in humans have helped clarify the relationship between irradiation and genomic instability: 1/ instability is found *in vitro* in cultures of irradiated human lymphocytes (from victims of the 1994 radiation accident in Estonia), 2/ chromosomal aberrations found in peripheral blood lymphocytes persist in the Sellafield plutonium workers (undoubtedly due to a selection of irradiated precursors in bone marrow), 3/ a high rate (19/20) of genetic mutations (TP53) is observed in former patients injected with thorostrast, 4/ instability is observed in patients who develop second cancers following radiotherapy for bilateral retinoblastoma, and 5/ chromosomal aberrations and rearrangements are observed in the Hiroshima and Nagasaki survivors who developed acute myeloid leukaemia following exposure to doses above 2 Gy. In contrast, no cellular aberrations were observed in 18 patients exposed to a total of 35–80 Gy administered in a fractionated manner. Certain observations suggest that genomic instability plays a non-negligible role in the development of cancer and support the conclusion that persistent instability may strongly influence the development of leukaemia in humans.

The bystander effect is employed in a relatively restricted sense in the report, which states that the bystander effect describes the capacity of cells affected by an external agent to transmit any manifestations to other cells that are not directly targeted or that are capable of expressing the damage. This definition implies that the bystander effect results from a signal produced by a cell interacting with a non-irradiated cell, rather than radiation-induced modifications in the culture medium. Current knowledge is primarily based on *in vitro* experiments. The bystander effect was first demonstrated for alpha emitters and charged-particle microbeams. When these forms of irradiation are focused selectively on a given cellular component, inducing the secretion of one or several substances, they can produce various effects: 1/ stimulation of

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apoptosis, reducing clonal capacity; 2/ increased mutagenesis and higher rates of neoplastic transformation; or 3/ induction of genomic instability in non-irradiated cells. Once irradiated cells are transferred to the culture medium, increased cell death is observed. There is also a decrease in clonal efficiency as well as an increase in neoplastic transformation and genomic instability. Several experiments using low-LET radiation are currently underway; the findings are similar. For example, the irradiation of human keratocytes using ^{60}Co produces a bystander effect for the dose range of 0.01–0.5 Gy and relatively constant independently of the dose level; above 0.5 Gy, cell death is as much a direct result of irradiation as it is a bystander effect. In contrast, cellular responses other than cell death (e.g. proliferation) were observed in cultured human fibroblasts propagated from cells irradiated with an alpha emitter. This contradiction is difficult to explain. Nonetheless, at least *in vitro*, bystander effects can modify cellular response. It remains to be seen whether these effects, which are observed in non-irradiated cells, are determinant in the *in vitro* response of irradiated cells as well as the *in vivo* response of irradiated and non-irradiated cells. The few *in vivo* experiments have been very specific in scope – e.g. formation of chromosomal aberrations, aetiology of micronuclei, embryonic development, regenerative capacities, activation of macrophages and tumour growth - and the findings are difficult to interpret. However it has been shown that the number of liver cancers is not related to the number of cells irradiated. This might be explained by an "amplification" of the biological efficiency and thus more cells exteriorising the harmful effects than the number directly exposed to radiation. This effect predominates at low doses, which allow it to produce a complete cellular response. At this time, the only possible conclusion is that radiation targets an area beyond the physical limits of the nucleus. Another unresolved question concerns the relationship between the bystander effect and genomic instability. Given the similarity of their consequences, these two phenomena may in fact be manifestations of a single process within non-irradiated cells. In this case, the high rate of genomic instability may be explained by bystander-like phenomena.

Abscopal effects refer to responses in other tissues located far from the irradiated zone. For example, after partial irradiation of rat lung, damage may be observed in the DNA of the non-irradiated lung cells. This type of effect has also been observed in humans following radiotherapy, either in a single patient (remission of hepatocellular carcinoma following irradiation of bone metastases) or in groups of patients with chronic leukaemia (haematological

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remission observed in bone marrow after irradiation of the spleen). Some authors, after reviewing all the relevant medical literature, have concluded that it is currently impossible to confirm or reject the existence of bystander effects and, by extension, abscopal effects in irradiated patients.

Clastogenic factors have been brought to light by experiments demonstrating that the plasma of irradiated humans and animals contains factors capable of harming non-irradiated cells. For example, children who underwent isolated spleen irradiation later showed signs of bone marrow damage. Similar damage was also observed in individuals exposed during the Chernobyl accident and in the Japanese A-bomb survivors, in equal proportions. These problems, observed for doses of 200 mGy, persist for around 10 years (as long as three decades for certain Japanese survivors). There is a high degree of individual variability; moreover not everyone is likely to manifest this type of effect. The precise nature of the so-called "clastogenic plasma factors" remains unknown; involvement of endogenous viruses, interference with DNA repair and free radical production have been discussed. At this time, the last of these hypotheses appears most likely. However, the presence of "clastogenic factors" in the peripheral blood of some irradiated individuals raises the question of whether chromosomal rearrangement is an accurate biological dosimeter. If the effects mentioned above are borne out and occur systematically, there may be important public health consequences. For example, it is not impossible to imagine that food products irradiated to enhance preservation could play a role in producing negative health effects. However, the few animal experiments conducted to verify this hypothesis have not demonstrated any consequences, except for an increase in polyploid cells (i.e. with more than two sets of chromosomes) in bone marrow of rats fed irradiated wheat.

Hereditary effects are those observed in the offspring of irradiated parents (one or both parents exposed). They have been at the centre of numerous contradictory debates and certain conclusions are regularly challenged. The subject is particularly well documented for certain animal species; the effects have been observed and described and the risk factors evaluated. For humans, the situation is completely different; to date researchers have been unable to demonstrate any radiation-induced hereditary effects, whether in the offspring of cancer victims treated with radiotherapy and/or chemotherapy, in women irradiated during childhood to treat haemangioma or in Japanese A-bomb survivors (the cohort included 31,150 children). A recent study on the inhabitants of the

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Mogilev region of Belarus, particularly contaminated by fallout from the Chernobyl accident, is an exception because it appears to demonstrate such effects. But it has been severely criticised by British researchers, who questioned the use of a non-exposed population in the United Kingdom as the control group for exposed parents in Belarus. It was further noted that other pollutants and viral diseases had been overlooked, and the biological significance of certain mutations was challenged. The increased risk of cancer in the offspring of humans irradiated before their children's conception is equally controversial. The abnormally high incidence of leukaemia and lymphoma in children whose fathers worked in the reprocessing facility in Sellafield has been the subject of fierce debate for a number of years, but cannot be completely dismissed.

The main conclusions of the report are as follows:

- 1/ The role of non-targeted and hereditary effects in cancer induction remains unclear ;
- 2/ As for radiation-induced genomic instability, its role in initiating and mediating genetic modifications, which could induce genomic damage and thereby facilitate carcinogenesis, is still based on speculation. This working hypothesis is further tempered by the fact that very high rates of genomic instability are observed both *in vivo* and *in vitro* and saturation is rapidly reached at low doses. However, the issue of inherited hypersensitivity is far from resolved and may have important implications;
- 3/ In the past, most estimates of hereditary risk were based on classic mutations observed in very large populations of easy-to-study mammals. Based on recent studies, it does not appear necessary to modify the quantification of genetic risk proposed in earlier UNSCEAR reports. However, there is absolutely no proof that radiation-induced transgenerational instability leads to a proliferation of clinically significant effects in successive generations. Since UNSCEAR currently supports the position that first generation risk for a number of effects is transmitted to successive generations, the few cases of proliferation do not justify a modification of current risk estimates;
- 4/ With regards to the bystander effect, it is included in the risk estimation because it only affects the exposed organ and because the associated risk factors involve organs rather than cells ;
- 5/ It is generally agreed that understanding of these effect types – genomic instability, bystander effects, abscopal effects, clastogenic factors and hereditary effects – is far from complete. These effects appear to amplify the impact of a given dose; the

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result is more cells manifesting the damage than the number directly irradiated.

6/ If all types of radiation are shown to systematically induce these effects, existing radiological protection hypotheses would underestimate risk, at least for everyday levels of exposure. However, the remarkable capacity of biological systems to adapt to their exposure environment, particularly at low doses, should not be forgotten. Furthermore, the multiple uncertainties and the inconclusive data on the actual consequences of these effects suggest that current risk estimates for cancer and hereditary effects should not be modified.

7/ It is essential to reconsider the concepts of dose and target.

8/ It would be advisable to examine direct and indirect effects in combination for modelling radiation-induced carcinogenesis.

9/ Finally, it should be noted that non-targeted effects can be produced by harmful agents other than radiation.

3/

Reports in progress

3/1

Effects of ionising radiation on non-human biota¹

This 102-page document is relatively new. It is the follow-up to a 1996 report based on data of limited quantity and quality. The 1996 report concluded that radiation exposure caused by human activities adds significantly to the impact of natural exposure. The main activities cited were those involving radon and its progeny (affecting terrestrial environments), polonium-210 (affecting aquatic environments) and alpha emitters (affecting terrestrial and aquatic environments). In 2005 it was decided that UNSCEAR should concentrate on assessing the levels and effects of non-human exposure, therefore working upstream of the ICRP and the IAEA, which shape protection policies. The 2006 version of the report appears to be a relatively exhaustive review of: 1/ the methods used to assess the levels of exposure and results obtained (reference organisms, transfers in terrestrial, aquatic and marine environments), and 2/ the somatic and genetic effects observed in terrestrial plants and in terrestrial, aquatic and marine animals, considered individually or collectively. The report's objective is to complement publications on the same subject by other international or national bodies, such as the ICRP (2003)², the IAEA (2005)³, the Chernobyl Forum organised under the aegis of the United Nations (2005)⁴, FASSET (2004)⁵, ERICA (2003)⁶, the United States Department of Energy⁷ and the Canadian authorities⁸. The French UNSCEAR delegation recently proposed adding a chapter on the biological mechanisms of biota responses to radiation exposure, which would allow appropriate monitoring methods to be defined for many species. The French proposal on which issues to address in this new chapter was well received, but as the scope seemed too ambitious for the next report, the members of the delegation were asked to prepare a summary, focusing on 1/ the main parameters affecting biological responses

1

Report R.662:
Effects of ionising radiation on
non-human biota

2

ICRP: International Commission on
Radiological Protection. ICRP
Publication 91: A Framework for
Assessing the Impact of Ionising
Radiation on Non-human Species.
Annals of the ICRP, Vol. 33(3).
Pergamon Press, 2003

3

IAEA: International Atomic Energy
Agency. Draft plans of activities on
the radiation protection of the
environment. IAEA, GOV/2005/49,
24 August 2005

4

The Chernobyl Forum: Chernobyl's
legacy: Health, Environmental and
Socio-economical impacts and
Recommendations to the
Governments of Belarus, the
Russian federation and Ukraine.
IAEA, WHO, FAO, UNDP, UNEP,
UN-OCHA, UNSCEAR. IAEA,
Vienna, 2005

5

FASSET: Framework for
Assessment of Environmental
Impact, Final Report. Developed
under EC 5th Framework Program.
Contract FIGE-C

6

ERICA: Environmental Risk from
Ionizing Contaminants:
Assessment and Management.
Developed under EU 6th
Framework Program. Contract
FIGR-CT-2004-508847, 2003

7

United States Department of
Energy. A graded approach for
evaluating radiation doses to
aquatic and terrestrial biota. DOE-
STD-1153-2002, US DOE, 2002

to radiation, and 2/ the importance of understanding these phenomena when assessing the biological effects. Given that reproductive change is a more sensitive indicator than mortality, UNSCEAR believes that for the majority of terrestrial species, prolonged irradiation at dose-rates below $100 \mu\text{Gy h}^{-1}$ should not significantly affect the most exposed individuals. Similarly, for aquatic species the Committee believes that dose-rates up to $400 \mu\text{Gy h}^{-1}$ should have no harmful effects in a given population.

3/2

Exposures from radiation accidents

This relatively short report is very recent. The objective was to draw up a list of accidents involving various sources of radiation. Although the forward clearly states that the document is not intended as an exhaustive inventory, it seems odd that some severe accidents are not included while several others with little impact on the victims, society and/or the environment are discussed in detail. It is of course impossible to provide a complete overview of all accidents, especially since the definition of the term "accident" remains vague, but the radiation sources and their activities found in the report might give a false idea of the distribution and gravity of radiological accidents. Consequently, it is not necessarily clear to the reader that the "deadly" sources are those which emit high-energy radiation (e.g. cobalt-60), whereas most accidents involve relatively small industrial sources (e.g. iridium-192). Obviously it is not the role of UNSCEAR to study the lessons which can be derived from these accidents (the IAEA conducts an in-depth review of each severe accident, examining the causes, circumstances and lessons), but the Committee could have done more than list some accidents according to a classification based on source utilisation (civil and military uses [there is a marked preference for criticality accidents], industry, orphan sources, transportation and medicine).

3/3

Exposures of the public and workers to various sources of radiation

This voluminous report serves to update the data in earlier UNSCEAR reports. The subject matter is one of the body's reasons for existing and is thus regularly examined. The report successively reviews 1/ sources of exposure for the public: natural sources in general, those whose impact is increased by human activity, civil and military sources; and 2/ sources of exposure for workers:

•3/ Reports in progress

8

Advisory Committee on Radiological Protection (ACRP22). Protection of non-human biota from ionizing radiation. Canadian Nuclear safety Commission (CNSC), INFO-0703, March 2003

1

Report R.660 : Exposures from radiation accidents

2

Report R.656: Exposures of the public and workers to various sources of radiation

methods of dose assessment, natural sources, civil and military sources. The report contains 110 detailed tables (114 pages) and 47 figures (56 pages), which are valuable sources of reference. The main conclusions are as follows:

1/ The estimate of average natural exposure remains unchanged at around 2.4 mSv per year, mostly due to radon. Doses for all terrestrial surfaces have a lognormal distribution and in the largest number of cases, exposure is within the range of 1–10 mSv per year;

2/ Exposure to natural sources of radiation that have been modified by humans is becoming particularly significant as a result of newly identified sources whose dose estimates are based on various scenarios. However, it is not yet possible to provide a global assessment of these sources, the kind that would allow an extrapolation for the entire planet;

3/ In this category of sources, mine residues represent enormous quantities of matter with higher concentrations of natural radionuclides than normally found in the environment. As a result, these residues are problematic in terms of both storage and site clean-up. The public exposure associated with these residues is not high, but the number of people exposed to low doses can be high ;

4/ Civil nuclear reactors have not released large quantities of radioactive substances; the associated doses are thus low. For the entire nuclear cycle, collective local and regional exposure is estimated at 0.72 man Sv (GW a)⁻¹. Therefore, for a yearly energy production of 272 GW, the collective dose per production year is approximately 196 man Sv. For a local and regional population of around 250 million, this collective dose corresponds to an average individual dose of less than 1 µSv per year. If nuclear reactors maintain their energy production capacity over the next 100 years, the average individual dose for the global population will have a maximum value of 0.2 µSv, which is small, compared to the dose from background radiation;

5/ In terms of man-made radiation sources, atmospheric testing of nuclear weapons accounts for the largest portion of the collective dose. The resulting exposure is local, regional and global since there are radioactive deposits over the earth's entire surface. According to estimates, individual doses peaked at 110 µSv in 1963 and have decreased since then to 5 µSv (mainly due to ¹⁴C, ⁹⁰Sr and ¹³⁷Cs) ;

6/ For populations living near test sites, the level of exposure is now known and may be high, particularly when these populations return to their former habitats. At the Semipalatinsk site, residual

contamination is considerable, but on the atolls of Moruroa and Fangataufa it plays a very moderate role in overall exposure. On the Marshall Islands and Maralinga, such contamination depends largely on inhabitants' lifestyles ;

7/ When nuclear arsenals were being developed, and particularly from 1945 to 1960, large populations were exposed to releases from military installations. It is difficult to accurately assess the damage because the quality of monitoring was poor and the risks were hidden ;

8/ Enrichment processes generate large quantities of depleted uranium. The properties of this very dense metal explain its numerous civil and military uses. Depleted uranium has been used in recent conflicts. In numerous areas, such as Kosovo, Serbia, Bosnia and Montenegro as well as Kuwait and Iraq, the public is constantly exposed to the resulting residues. Several eventualities have been considered in order to assess the potential consequences of this exposure. Notwithstanding a few rare scenarios, the estimated levels of exposure are low. The long-term fate of depleted uranium and whether it will contaminate underground water remains unknown.

9/ There are still numerous civil sites which once used radioactive substances and remain contaminated today. Most are contaminated with radium and have been identified; many have undergone decontamination and are generally closed to the public unless they have been rehabilitated. There are similar problems with residues from former mine sites. The clean-up programmes aim to bring exposure levels within acceptable ranges for such ongoing practices.

10/ In general, accidents only affect a limited number of people, but the doses may be high. Exceptions include the 1983 accident in Mexico City, the 1987 accident in Goiânia and the 1982–1984 accident in Taiwan. The first resulted in relatively low exposure levels for the population and was due to the use of ^{60}Co for the manufacture of concrete reinforcing bars and furniture parts. The second accident had far more serious consequences; a medical source of ^{137}Cs was mishandled by several people, resulting in widespread exposure. Four people were killed and 28 suffered serious burns. In Taiwan several apartment buildings were built with reinforcing bars contaminated with ^{60}Co . Although the residents were exposed over several years, the levels of exposure remained moderate.

3/4

Medical radiation exposures¹

This very well-documented report (192 pages including 60 pages of text, 110 pages of tables and 10 pages of forms and questionnaires) is much improved compared to the previous document, which included only a very brief discussion of radiotherapy and nuclear medicine even though these two fields contribute substantially to the public's level of medical exposure. The report in question does a better job of reviewing these fields, but there are still numerous gaps. For example, doses associated with diagnostic radiology, including certain recent techniques which are particularly powerful (e.g. computed tomography, interventional radiography, mammography and bone densitometry) and which often involve high exposure levels for patients, are far better documented than doses associated with radiotherapy and nuclear medicine. The report lists the doses received by patients exposed to during paediatric and dental radiology procedures, as well as fetal doses. The dosimetric assessment of these now widely used techniques is of great interest to the healthcare professionals who use them; most of these professionals are not familiar with all the potential risks for their patients because in general they are not radiologists but rather cardiologists, paediatricians, traumatologists, etc. Techniques involving particularly high radiation doses for patients are well documented. Certain sections have yet to be written due to a lack of appropriate documentation and references.

Previous UNSCEAR reports have shown that of all human activities, medicine plays the largest role in the global population's exposure to radiation. Medical radiation involves three different types of sources: 1/ x-rays used for diagnosis and interventional radiology, 2/ various radionuclides used for diagnosis and treatment, and 3/ various types of radiation used mainly for cancer treatment. The use of radiation has increased over time, independently of the quality of care in the countries studied. The upward trend is primarily due to increasingly widespread use of medical equipment that utilises radiation sources. Moreover, the global trend towards urbanisation has given more people access to radiological treatment. Medical radiology is constantly evolving, thanks to continual innovation in the area of equipment. Techniques allowing outpatient exploration and treatment are popular amongst patients and healthcare professionals. This continual positive pressure promotes new techniques such as interventional radiology (used in cardiology and neurology), helical computed tomography and digital imaging.

•3/ Reports in progress



Report R.655 :
Medical radiation exposures

Despite the increased number of examinations and techniques involving radiation, there has been a significant effort to reduce individual doses. This effort is primarily focused on technical advances in equipment, protocol standardisation, measurement of doses actually delivered to patients, quality assurance programmes, etc.

Diagnostic radiology exposure is continually on the rise; the primary reason is the increasing number of x-ray exams. There was an estimated number of examinations of 1.9 billion between 1991 and 1996 (versus 1.6 billion between 1985 and 1990), which is equivalent to a rate of $330 \cdot 10^{-3}$ (versus $300 \cdot 10^{-3}$). And that does not include an additional 520 million dental examinations (rate of $90 \cdot 10^{-3}$). The collective dose for all diagnostic exams is $2.33 \cdot 10^6$ man Sv for the period of 1991–1996, which is equivalent to an average individual dose of 0.4 mSv ($1.6 \cdot 10^6$ between 1985 and 1990, or an average of 0.3 mSv per person). There is enormous variation in the global distribution of x-ray examinations due to differing levels of healthcare in the countries studied: for the period of 1991–1996, 74% were performed in countries with advanced healthcare (rate of $920 \cdot 10^{-3}$), 25% in countries with adequate healthcare ($50 \cdot 10^{-3}$) and only 1% in countries with limited healthcare ($20 \cdot 10^{-3}$). For the same period, the average effective dose per exam is 1.2 mSv, compared with 1 mSv for the preceding 5-year period. According to the distribution of exposure levels between the various types of exams, computed tomography (CT) predominates by a large margin, especially in countries with advanced healthcare, where it accounts for 34% of the total dose. CT takes the place of the former "leading" exam, gastrointestinal radiography, which now accounts for only 14% of the total dose. This distribution varies from country to country depending on the level of healthcare development: chest radiography still accounts for 50% of the collective dose in moderately developed countries and CT accounts for only 2% of the collective dose in less developed countries. The number of CT scans has considerably increased in countries with particularly advanced medical infrastructure. In certain European countries it has risen by a factor of 6. The use of increasingly sophisticated equipment, like helical scanners, should have diminished exposure, but this trend has not been able to offset the growing number of exams.

The use of specialised equipment has led to a decrease in mammography doses in recent years. Initially doses of 100 mGy per exam were common; they were first reduced by a factor of 3, then a factor of 10, resulting in doses to the breast of 1–2 mSv.

In contrast to exposure resulting from medical diagnostic radiology, exposure resulting from dental diagnostic radiology has decreased over time: 14,000 man Sv, or 0.002 mSv per person, for the period of 1991–1996 (compared to 18,000 man Sv, or 0.003 mSv per person for the period of 1985–1990). Medical examination doses cannot be translated directly into potential risks, because the individuals who receive these doses are for the most part elderly and/or sick and thus not representative of the entire population. The reverse is true for dentistry: patients are increasingly young.

The exposure data for children and fetuses are particularly interesting. The studies of children come from paediatric departments in Belgium, the United Kingdom and Spain. The Belgian study shows that computed tomography delivers individual doses (effective dose) of 0.4–2.3 mSv to the skull, 1.1–6.6 mSv to the thorax and 2.3–19.9 mSv to the abdomen. The treatment of varicocele in adolescents delivers an effective dose of 18 mSv. The studies performed on fetuses come from Iran, the United Kingdom, the United States and Germany. For 1,300 pregnant Iranian patients who underwent CT scans for mild gastrointestinal or urinary problems, the dose to the fetus (4 weeks old on average) was 6–8 mGy. Most English women examined presented more than 8 weeks into their pregnancies; 85% of the fetuses were exposed to a dose below 5 mGy (only five fetuses received more than 10 mGy). The American study on exams involving helical CT (detection of pulmonary embolism in the mother) shows fetal doses of 3.3–20.2 μ Gy for the first trimester and of 51.3–130.8 μ Gy for the third trimester. These doses are high, but they are still lower than doses delivered by scintigraphy under the same circumstances.

The number of deterministic effects in patients treated with interventional radiology is markedly underestimated; these effects are not reported on a regular basis because patients often receive insufficient follow-up from their physicians, who are not always aware of the possible complications of radiotherapies.

Bone densitometry is used in children to monitor bone growth and in older people to assess the risk of fracture, especially in menopausal women. The report provides effective doses which on average range from a few mSv to a few tens of mSv, depending on the type of exam. Unfortunately, the report does not provide doses absorbed by bone, which would be more interesting if only for the purposes of comparison.

There is a clear commitment on the part of the authorities, equipment designers and healthcare professionals to reduce the

levels of patient exposure. Personnel education and training can reduce doses up to 40%. The ICRP Publication 73¹ (1996) and the European Directive 97/43/EURATOM² (1997) provide reference levels for diagnosis, including optimal levels for each type of exam. Moreover a number of techniques allow considerable dose reduction. By limiting the number of redundant films, doses can be reduced up to 40%; by using pulsed fluoroscopy for angiographies and in a large proportion digital imaging and other procedures, doses can be reduced by 32% to 66%. As for the UNSCEAR report, it complements the recent ICRP reports^{3,4,5,6,7} concerning radiology practices involving particularly high doses for patients and healthcare professionals.

Nuclear medicine regularly uses various radioactive substances for diagnostic or treatment purposes, primarily ^{99m}Tc , ^{123}I , ^{125}I , and ^{131}I . The report provides data on the size of patient populations affected by diagnostic procedures: throughout the world there were 32.5 million examinations per year between 1991 and 1996, which is equivalent to a rate of $5.6 \cdot 10^{-3}$ (24 million for the period of 1985–1990, or a rate of $4.5 \cdot 10^{-3}$); this figure is small compared to the diagnostic radiology figure. The majority of these examinations and treatments (89%) took place in more developed countries. A small number (11%) took place in moderately developed countries and a very small number (less than 1%) took place in less developed countries. The corresponding collective effective dose – 150,000 man Sv or 0.03 mSv per person for the period of 1991 to 1996 – is unchanged compared to the preceding period, indicating decreased exposure levels for each type of exam given that the number of exams has risen. There are 400,000 treatments per year involving radionuclides, which is equivalent to a rate of $0.065 \cdot 10^{-3}$. The same figure applies to brachytherapy.

Radiotherapy is used primarily for patients with cancer. This type of treatment is often used in association with surgery and/or chemotherapy. The proportion of patients treated by radiation may vary considerably from one country to the next. There are two treatment techniques: teletherapy, which uses an external beam of radiation directed at the target area, and brachytherapy, which uses a radioactive source placed directly in a natural cavity or organ. Unsealed source radiotherapy and monoclonal antibodies are also used to treat metastases. There are four families of teletherapy radiation: 1/ ^{60}Co gamma radiation, 2/ ^{137}Cs radiation (but 50–300 kVp x-rays are increasingly used as an alternative), 3/ electrons and x-rays produced by linear accelerators, and 4/ protons and charged particles from cyclotrons and synchrotrons. Particle accelerators are

•3/ Reports in progress

1

International Commission on Radiological Protection. ICRP Publication 73: Radiological Protection and Safety in Medicine. Annals of the ICRP, Vol. 26(2). Pergamon Press, 1996

2

European Union. Council Directive 97/43/EURATOM on Health protection of individuals against the dangers of ionizing radiation in relation to medical exposure, and repeating Directive 84/486/EURATOM, 1997

3

International Commission on Radiological protection. Radiation dose to patients from radiopharmaceuticals. ICRP Publication 80, Pergamon Press, Vol. 28, N° 3, 1998

4

International Commission on Radiological protection. Pregnancy and medical radiation. ICRP Publication 84, Pergamon Press, Vol. 30, N° 1, 2000

5

International Commission on Radiological protection. Avoidance of radiation injuries from medical interventional procedures. ICRP Publication 85, Pergamon Press, Vol. 30, N° 2, 2000

6

International Commission on Radiological protection. Prevention of accidental exposures to patients undergoing radiation therapy. ICRP Publication 86, Pergamon Press, Vol. 30, N° 3, 2000

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International Commission on Radiological protection. Managing patient dose in digital radiology. ICRP Publication 93, Pergamon Press, Vol. 34, N° 1, 2004

still rare and are concentrated in Europe, the United States and Japan. The total number of external or internal radiotherapy treatments provided throughout the world between 1991 and 1996 is estimated at 5.1 million (90% involved teletherapy), which is equivalent to a rate of $0.9 \cdot 10^{-3}$. The same figure applies to the period of 1985–1990. As for diagnostic radiology, there are major variations depending on the level of healthcare development: 51% of treatments occurred in more developed countries (rate of $1.7 \cdot 10^{-3}$), 43% in moderately developed countries (rate of $0.7 \cdot 10^{-3}$), 6% in less developed countries (rate of $0.5 \cdot 10^{-3}$) and 1% in the poorest countries (rate of $0.07 \cdot 10^{-3}$).

Intravascular radiotherapy, which is technically comparable to interventional radiology, involves introducing a sealed source in the lumen of a stenotic blood vessel. The report offers little discussion of this localised technique, which is used to treat many vascular diseases, but it does provide a table of doses including most of the commonly used procedures. Local doses are rarely less than a few tens of mGy and often above a few hundred mGy, even reaching a few Gy in some cases.

The report also shows that the number of machines varies greatly from one country to the next, depending on the level of development. For example, the linear accelerator capacity (number per million inhabitants) is 3.04 in more developed countries, 0.26 in moderately developed countries, 0.06 in less developed countries and nonexistent in the least developed countries. The range of variability is broad: there are no linear accelerators in either Lithuania or Ecuador whereas the United States has 7.28 per million inhabitants. The number of patients treated is directly proportional to the number of machines available. Likewise, the frequency of teletherapy treatment is 30 times higher in the best-equipped countries than in the poorest countries. In a sample of 28 more developed countries, treatment frequency is between $0.7 \cdot 10^{-3}$ and $37 \cdot 10^{-3}$; in a sample of 19 moderately developed countries, the range is from $0.05 \cdot 10^{-3}$ to $3.1 \cdot 10^{-3}$; finally, in a sample of 6 less developed countries, the range is from $0.05 \cdot 10^{-3}$ to $2.1 \cdot 10^{-3}$.

In conclusion, this report is incomplete in several areas. The questionnaires supplied at the end should allow many of the gaps to be filled in the areas of nuclear medicine and biomedical research, and also with regard to many developing countries. Obviously radiological protection is not the subject of this report, but it is unfortunate that it does not assess exposure among healthcare professionals, which is becoming problematic for certain newer

methods of investigation. Another shortcoming is the lack of information about the dosimetric impact of systematic screening using diagnostic radiology.

•3/ Reports in progress

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Conclusion

The UNSCEAR reports summarised in the present document can be divided into two groups: 1/ technical reports, which are part of UNSCEAR's primary mission and closely tied to its reasons for existing, i.e. identification of all radiation sources and quantification of public and professional exposure, detailed analysis of exposure due to radon, assessment of medical exposure and evaluation of the effects of radiation on humans as well as plants and animals; and 2/ scientific reports, which are upstream of the technical reports and explore the aetiological and physiopathological aspects of the various effects of radiation, i.e. mechanisms and epidemiology of radiation-induced carcinogenesis, mechanisms of noncancer effects, immune system reactions to radiation, and non-targeted and delayed effects.