Use of ionizing radiation and radionuclides on human beings for medical research, training, and nonmedical purposes

Report of a WHO Expert Committee

Technical Report Series
611

World Health Organization, Geneva 1977

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization

Use of ionizing radiation and radionuclides on human beings for medical research, training, and nonmedical purposes

Report of a WHO Expert Committee

World Health Organization
Technical Report Series
611

World Health Organization Geneva 1977

ISBN 92 4 120611 4

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

PRINTED IN SWITZERLAND

The World Health Organization (WHO) is one of the specialized agencies in relationship with the United Nations. Through this organization, which came into being in 1948, the public health and medical professions of some 150 countries exchange their knowledge and experience and collaborate in an effort to achieve the highest possible level of health throughout the world. WHO is concerned primarily with problems that individual countries or territories cannot solve with their own resources—for example, the eradication or control of malaria, schistosomiasis, smallpox, and other communicable diseases, as well as some cardiovascular diseases and cancer. Progress towards better health throughout the world also demands international cooperation in many other activities : for example, setting up international standards for biological substances, for pesticides, and for pesticide spraying equipment ; compiling an international pharmacopoeia ; drawing up and administering the International Health Regulations ; revising the international lists of diseases and causes of death ; assembling and disseminating epidemiological information ; recommending nonproprietary names for drugs ; and promoting the exchange of scientific knowledge. In many parts of the world there is need for improvement in maternal and child health, nutrition, nursing, mental health, dental health, social and occupational health, environmental health, public health administration, professional education and training, and health education of the public. Thus a large share of the Organization's resources is devoted to giving assistance and advice in these fields and to making available—often through publications—the latest information on these subjects. Since 1958 an extensive international programme of collaborative research and research coordination has added substantially to knowledge in many fields of medicine and public health. This programme is constantly developing and its many facets are reflected in WHO publications.

* * *

Expert committees and other international groups of experts are convened to give advice on technical and scientific matters. Members of such expert groups serve without remuneration in their personal capacity and not as representatives of governments or other bodies. The selection of members of international groups is based primarily on their ability and technical experience, with due regard to adequate geographical distribution.

The WHO *Technical Report Series* is the vehicle of publication of collective reports of such groups. Although these reports do not necessarily represent the views of the Organization, they are taken into consideration when developing programmes.

Annual subscription : Sw. fr. 100.—.

Public health workers and institutions that wish to be kept informed of new reports of expert groups in the *Technical Report Series* can do so by regular reference to the summaries of these reports given in the *WHO Chronicle*, which is published monthly in English, French, Russian, and Spanish.

Annual subscription : Sw. fr. 45.—.

CONTENTS

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization

Use of ionizing radiation and radionuclides on human beings for medical research, training, and nonmedical purposes

Report of a WHO Expert Committee

World Health Organization
Technical Report Series
611

World Health Organization Geneva 1977

ISBN 92 4 120611 4

PRINTED IN SWITZERLAND

CONTENTS

WHO EXPERT COMMITTEE ON THE USE OF IONIZING RADIATION AND RADIONUCLIDES ON HUMAN BEINGS FOR MEDICAL RESEARCH, TRAINING, AND NONMEDICAL PURPOSES

Geneva, 1–8 March 1977

Members : *

Dr B. Kwaku Adadevoh, Director of Medical Research, Medical Research Council of Nigeria, Yaba, Nigeria (*Rapporteur*)

Dr A. R. Gopal-Ayengar, Institute for Biophysics, Technical University of Hanover, Hanover, Federal Republic of Germany

Dr Y. N. Kasatkin, Central Institute for Education of Postgraduate Physicians, Moscow, USSR

Dr M. M. Mahfouz, Professor of Radiotherapy and Nuclear Medicine, Cairo, Egypt (*Vice-Chairman*)

Professor P. Pellerin, Director, Central Service of Protection against Ionizing Radiations, Le Vesinet, France

Sir Edward Pochin, Curridge, Berkshire, England (*Chairman*)

Dr K. E. Scheer, Institute for Nuclear Medicine, Heidelberg, Federal Republic of Germany

Representatives of other organizations : **

International Labour Organisation :

Dr N. Gavrilescu, Occupational Safety and Health Branch, ILO, Geneva, Switzerland

International Atomic Energy Agency :

Professor K. E. Scheer, IAEA, Vienna, Austria

Council for International Organizations of Medical Sciences :

Dr Z. Bankowski, Executive Secretary, CIOMS, Geneva, Switzerland

Mrs K. Carballo, Assistant, CIOMS, Geneva, Switzerland

International Radiation Protection Association and the International Society of Radiology :

Dr G. Poretti, Section of Medical Physics, Department of Radiotherapy, University Hospital, Berne, Switzerland

---

* Unable to attend : Professor C. Chagas, Biophysical Institute, Federal University, Rio de Janeiro, Brazil ; Dr S. Takahashi, Hamamatsu University School of Medicine, Hamamatsu, Japan.

** Unable to send representatives : International Commission on Radiological Protection ; United Nations Scientific Committee on the Effects of Atomic Radiation.

Secretariat :

Mr S. Fluss, Senior Editor, Health Legislation, WHO, Geneva, Switzerland

Dr G. Meilland, Medical Officer, Cooperative Programmes for Development, WHO, Geneva, Switzerland

Dr S. B. Osborn, Director, Department of Medical Physics, King's College Hospital, London, England (*Consultant*)

Dr W. Seelentag, Chief Medical Officer, Radiation Medicine, WHO, Geneva, Switzerland (*Secretary*)

USE OF IONIZING RADIATION AND RADIONUCLIDES ON HUMAN BEINGS FOR MEDICAL RESEARCH, TRAINING, AND NONMEDICAL PURPOSES

Report of a WHO Expert Committee

A WHO Expert Committee on the Use of Ionizing Radiation and Radionuclides on Human Beings for Medical Research, Training, and Nonmedical Purposes met in Geneva from 1 to 8 March 1977. Dr L. Bernard, Assistant Director-General, opened the meeting and welcomed the participants on behalf of the Director-General. The task of the Expert Committee was to consider all deliberate irradiation of human beings, particularly in the course of medical research, to evaluate the health risks involved, and to recommend measures for keeping such irradiation under proper control, taking into account the ethical principles laid down by the World Medical Assembly in Helsinki in 1964 and amended in Tokyo in 1975.

The report that follows does not attempt to prescribe exactly which decisions should be taken in specific cases nor what kind of legislation may be desirable to ensure appropriate control over the deliberate irradiation of human beings. It is intended rather to provide some ideas and guidelines that will be helpful for decision-makers, who in any case will have to take into account local conditions and the structure of legislation in the country concerned. Some of the recommendations may not be applicable in all countries ; others may not need to be applied.

1. INTRODUCTION

1.1 Ionizing radiation : benefits and risks

Great benefits to human health have resulted from the use of radiological procedures in medical diagnosis and treatment and more recently in nuclear medicine. Valuable contributions have also been made by types of medical research involving the exposure of human beings to radiation in the course of similar procedures, and it is considered to be of the greatest importance that such research should continue.

At the same time, however, it must be recognized that exposure to large doses of radiation is harmful, and that even exposure to the small doses usually involved in medical diagnosis and research may carry a correspondingly small risk of harmful effects.

1.2 Sources of radiation

All human beings are inevitably and continuously exposed to ionizing radiation from a variety of natural sources : the radioactivity of rocks and of the soil, cosmic radiation reaching the body from space, and naturally radioactive nuclides which become incorporated in the body. To the natural level of ionizing radiation, exposure from man-made sources has now been added. Such sources form an integral part of processes associated with industrial development, which in itself enables considerable contributions to be made to the improvement of human health. However, in order to prevent avoidable harm to human beings any exposure of human subjects to ionizing radiation should be kept as low as practicable.

1.3 Scope of the report

This report deals only with the relatively small proportion of radiation to which people are exposed in the course of medical research, in medical teaching, and in various procedures not directly related to their health needs. It does not deal with deliberate applications of radiation for purposes of diagnosis or treatment (" clinical " exposure), or with occupational exposure to radiation or any other type of exposure occurring incidentally in the use of radiation sources but not planned deliberately. These categories of exposure have been dealt with in detail in a number of reports to which reference should be made—e.g., on clinical exposure (*10*, *11*, *15*, *22*), on occupational exposure (*2*, *4*, *7*, *12*, *14*, *15*), on environmental and incidental exposures (*15*, *19*), and on public health aspects (*20*, *21*).

1.4 Previous work

A consultation was held by WHO and IAEA in November 1972 on the use of ionizing radiation on human beings for medical research and training, including the use of radioactive materials. The report of this consultation (unpublished) was sent to a number of different experts for comment. The report and the comments have been taken into account in preparing the present report. The Committee has, however, also included a review of matters that were not dealt with by the 1972 consultation, so as to cover the whole subject of the deliberate exposure of human beings apart from diagnostic and therapeutic procedures. Until now, few international or national recommendations have been made in regard to such exposure. Its increasing occurrence, particularly in pharmaceutical investigations with radioactively labelled drugs and in the evaluation of new radiological methods, makes it essential to have internationally accepted guidelines on the subject.

In this report, references to medical uses of radiation are intended to cover dental uses also, where appropriate.

2. BIOLOGICAL EFFECTS OF IONIZING RADIATION AND RELATED RISKS

2.1 Damage from energy deposition

The biological effects of ionizing radiation depend essentially upon the energy deposited in body tissues by the ionizing action of such radiation and the changes in biologically important molecular structures that may be caused when this energy is delivered to them. Such damage may be induced whether the radiation reaches the body tissues from sources outside the body or from radioactive materials that have become incorporated within the tissues themselves.

Thus, in the case of radiological procedures, the tissues are subjected to " external radiation " from diagnostic X-rays and in most forms of radiotherapy, but to " internal radiation " following the diagnostic or therapeutic administration of radionuclides in nuclear medicine.

2.2 The dose equivalent

Under most circumstances, the frequency with which harmful effects will result from a given exposure depends upon the amount of energy imparted to the tissues by radiation regardless of whether it comes from external or internal sources, and regardless of the type of source or of radioactive material from which it is derived. For this reason, risks of radiation exposure can be expressed in terms of the frequency of harmful effects per unit of energy deposition in the tissues. Traditionally, different levels of " dose equivalent " of radiation have been expressed in rem (see Annex 1). The rem is a unit that not only depends upon the amount of energy from ionization deposited in the tissues but also reflects the rather greater frequency of harmful effects (in some cases greater by a factor of 10) resulting from exposure to certain types of radiation (e.g., from neutrons).

In 1975 the Conférence générale des Poids et Mesures (CGPM) adopted, at the request of the International Commission on Radiation Units and Measurements (ICRU), the gray (Gy) as a special name for the joule per kilogram for the measurement of absorbed dose. The gray is therefore an SI unit and is used for absorbed dose in this report, although equivalent values in rads are also given within parentheses. ICRU made no request regarding a unit for the measurement of dose equivalent. Recently, however, it has been proposed that the sievert (Sv) be used as a special name for the joule per kilogram for this purpose. Since the sievert has not been approved by CGPM, it is not an SI unit and does not have the same status as the gray. For this reason the rem is used for dose equivalent in this report, although equivalent values in sieverts are given within parentheses in the text.

In general, the frequency of harm from a given dose equivalent depends on the tissues irradiated and other factors, but not on the source of radiation involved.

The harmful effects of radiation may manifest themselves either in the individual exposed or in his or her descendants as a result of changes induced in the germ cells at the time of exposure. There is extensive literature on the subject (e.g., *1*, *5*, *6*, *8*, *16*).

2.3 Somatic effects

In the individual, two types of effect are recognized. First, there are the so-called " stochastic " effects, whose frequency depends upon the level of radiation exposure, but whose severity does not. These include the induction of malignant changes that may follow the exposure of certain body tissues, but are typically not detectable until many years after exposure. The other type—" non-stochastic " effects—occurs only after high exposures, and their severity then depends on the dose equivalent received in tissues sensitive to them. Such effects are in general unlikely to occur at the levels of exposure considered in this report (see Annex 2).

Special problems arise, however, in connexion with exposures of the embryo or fetus during pregnancy, since, for example, effects may occur at relatively low levels of exposure early in pregnancy, when damage to a single cell or group of cells may prevent either the normal implantation of the conceptus in the uterine wall or the development of a part of the body during stages of organogenesis. For this reason, radiation exposure during pregnancy demands special precautions.

2.4 Genetic effects

Radiation may also cause damage to the germ cells, leading to abnormalities in children conceived after the irradiation or in members of later generations whose inherited characteristics are derived from the germ cells originally damaged. It follows that inherited abnormalities of this type contribute to the total harm caused by radiation exposure, though to a rapidly decreasing extent in respect of exposures of persons aged 40 and over (particularly females) as the rate of child expectancy declines.

Estimates are available of the frequency with which serious somatic and genetic effects are likely to follow relatively high exposures to radiation; and inferences can be made of the probable frequency, or the maximum likely frequency, with which such effects may follow the much lower exposures with which this report is mainly concerned (see Annex 2). The different categories are suggested below (see section 5.5) in the light of the degrees of risk that might result from exposure at the dose equivalents specified.

3. ETHICAL ASPECTS

3.1 A statement of principles

General ethical principles for research involving human subjects were stated by the Eighteenth World Medical Assembly in Helsinki in 1964 (Helsinki Declaration) and revised by the Twenty-Ninth World Medical Assembly in Tokyo in 1975.[1] While these internationally accepted principles were formulated for biomedical research on human subjects, the Committee considers some of them to be applicable over a wider field of radiation use.

3.2 Ethical considerations in medical research

3.2.1 *The principles*

Medical progress demands that in research the "benefit of the patient" should not be interpreted in a narrow sense, since this could

[1] The full revised text of the declaration was reproduced in: *WHO Chronicle*, **30**: 360–362 (1976).