

# Acute radiation syndrome and chronic radiation syndrome

Philip Grammaticos<sup>1</sup> MD, PhD,  
Evanthia Giannoula<sup>2</sup> MD,  
George P. Fountos<sup>2</sup> PhD

1. Professor emeritus of Nuclear  
Medicine

2 Department of Nuclear Medi-  
cine, Theageneion Anticancer  
Hospital, Thessaloniki, Greece

3. Technological Educational  
Institute (TEI) of Athens/ Depart-  
ment of Medical Instruments  
Technology, Ag. Spyridonos,  
12210, Athens, Greece

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## Correspondence address:

Philip Grammaticos MD, PhD  
51 Hermou St, 54623  
Thessaloniki, Macedonia, Greece  
Tel-Fax: +30 2310 229133  
E-mail: fgr\_nucl@otenet.gr

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## Abstract

Acute radiation syndrome (ARS) or sickness or poisoning or toxicity is induced after a whole body exposure of men to high doses of radiation between 1-12Gy. First symptoms are from the gastrointestinal system, which together with bone marrow are the most sensitive parts of our body. Chronic radiation syndrome (CRS) may be induced by smaller than 1Gy radiation doses or after a mild form of ARS. Prophylaxis and treatment suggestions are described. *In conclusion*, in cases of ARS, a large part of the exposed population after proper medical care may survive, while without medical care this part of the population will be lost. Prophylaxis may also save another part of the population.

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## Introduction

Acute radiation syndrome (ARS) or sickness or poisoning or toxicity is induced after a whole body exposure of men to high doses of radiation between 1-12Gy. Doses as high as 1-2Gy, 2-6Gy, 6-8Gy or 8-12Gy induce the mild, median, grave or instant form of ARS, respectively. The grave form of ARS is usually not-treatable. First symptoms are from the gastrointestinal system, which together with bone marrow are the most sensitive parts of our body.

Atomic bombs and nuclear accidents are the main causes for ARS. Till 2000 more than 417 nuclear accidents have been reported with 127 casualties [1], while others state that the nuclear accidents were 580 and fatal casualties 180 [2]. These figures may be even higher. Nuclear accidents may terrorize communities, far away from the site of the actual accident [3].

In our times all Great Powers worldwide have nuclear factories and nuclear weapons, so that they may use these weapons during the Third World War. It is thus wise to know much about ARS and especially prophylaxis and possible treatment of this devastating syndrome.

Chronic radiation syndrome (CRS) may be induced by smaller than 1Gy radiation doses or after a mild form of ARS.

The present review aims to describe clinical and laboratory effects of ARS and CRS on men.

In cases of ARS, a large part of the exposed population after proper medical care may survive, while without medical care this part of the population will be lost. Prophylaxis may also save another part of the population exposed to high radiation doses.

## Forms or stages of ARS

Acute RS may also be induced after internal radiation intake.

Radiation exposures to high doses from nuclear accidents, atomic bombs, the use of radioactive products by terrorists or for radiotherapy are the main causes for ARS [4].

Whole body radiation doses of 1-2Gy and 2-6Gy induce mild and median forms of ARS that are treatable, while the grave form of ARS after whole body exposure to 6-8Gy is usually not treatable. The instant form of ARS induced by 8-12Gy is definitely untreatable.

## Symptoms-signs and laboratory findings

*Mild and median forms of ARS* have a characteristic incubation stage lasting from 6 to 2h before first symptoms appear from the gastrointestinal system. The two other and more grave forms of ARS have a shorter stage of incubation from 1h till 10min.

The first symptoms in mild ARS are nausea, vomiting, diarrhea, headache and fever [4].

*In median and grave forms of ARS*, 1-4 weeks after the gastrointestinal symptoms, patients have dizziness, fatigue, disorientation, hematemesis, melaina, loss of hair, hypotension and dermal injuries which may be infected [4].

*In the instant form of ARS* all symptoms as above shall appear immediately or very soon after the accident.

*In the two milder forms of ARS*, after months or few years of serenity we may diagnose chronic radiation syndrome (CRS) with: leukemia, anemia, leucopenia or various types of cancers due to DNA radiation damage.

*In the grave and instant form of ARS* death is expected within 2-14 days with very few exceptions for the grave ARS [4].

Symptoms related to the hemopoetic system appear in adults after radiation absorbed in the sternum or the pelvic area. These symptoms are mild, not noisy and may escape our attention. They may appear after smaller doses like those of 1Gy [5]. In these cases we find: low white blood cells, low platelets and signs of aplastic anemia [6].

Symptoms from gastrointestinal system (nausea and vomiting) may appear in 5% of the population exposed to whole body absorption of 1Gy, while after 8Gy almost all patients have these symptoms [6]. Diarrhea starts after 2Gy in about 5% of the patients and is of a grave form in all patients who received 8Gy or more [6]. The same is true as for the induction of fever.

Symptoms from the neurovascular system start with mild headache after a dose of 1-2Gy. A more intense headache appears after 2-6Gy in 50% of the patients and in all patients after 8Gy. Consciousness is deranged after 2-6Gy and symptoms of decapitation appear after 8-30Gy. Neurovascular symptoms appearing within a few minutes of hours indicate a grave or an instant ARS [6].

The most sensitive tissues are bone marrow, breast in women, thyroid gland and salivary glands [7], while low or no sensitivity to radiation have tissues like the uterine cervix, oral cavity, esophagus, prostate, uterus, pancreas, anus, bile cyst, kidneys, testes and muscles [7].

It has been described that vomiting within the first 4h or 1h, indicates that the whole body absorbed dose was higher than 3.5Gy or 6.5Gy, respectively.

### Laboratory tests

In some cases laboratory blood or serum tests should be performed every 6h. These tests are: Hemoglobulin, hematocrit, white blood cells number, the number of lymphocytes, granulocytes, platelets and tests for blood regulation [4]. The normal count for lymphocytes is 1000-3000mm<sup>3</sup>. In the mild, median, grave and instant forms of ARS, lymphocytes within the first 48h are expected to be, 1000-1500, 500-1000, 100-500 and below 100mm<sup>3</sup>, respectively [8].

Genetic material is also examined within the first 24h after the ARS accident for possible chromosomes damage [9].

*Radiation physicists* are responsible to inform about: a) the kind of radiation emitted ( $\gamma$ -,  $\beta$ -,  $\alpha$ -, neutrons etc.) and b) the whole body dose (or in certain organs) of the people exposed to radiation due to internal contamination or from external radiation sources. The neutron doses cause a sequence of effects and damages, since tissues become secondarily radioactive for a short period of time. Thus, a useful and sufficiently accurate approximation to the dose, used in atomic bomb dosimetry, is given by the Kerma quantity. Kerma is

the acronym for "kinetic energy released in material" and is measured in Gy as the absorbed dose.

The absorbed radiation dose is measured in Grey (1Gy = 1J/kg). One Gy equals to the absorbed dose of 100rad. For  $\gamma$ -rays Gy measures the effective absorbed dose [10, 11]. As an example, we mention that X-rays radiology tests usually induce to men an absorbed dose of less than 0.1Gy [5]. It has been reported that absorbed doses higher than 1.5Gy may be cancerogenic [12]. On 2011 International Commission for Radiological Protection (ICRP) decided to lower the annual dose limit for the induction of eye cataract from 150mSv to 50mSv [13]. A radiation weighting factor that takes account the biological effectiveness of radiation in producing specific biological effects is RBE (Relative Biological Effectiveness) and used in atomic bomb dosimetry. The value of the RBE depends on the characteristics of radiation and its specific biological effects. For example RBE for neutrons ranges from 5 to 20 indicating that neutrons have a higher carcinogenic potency, compared with gamma rays. When RBE is multiplied by Kerma expresses the absorbed dose of gamma rays having the same biological effect.

### Chronic radiation syndrome or Chronic radiation sickness

This syndrome follows after the mild radiation syndrome or after small radiation doses that may be repeated [14]. Furthermore, doses from a flux of radiation greater or about 0.1Gy/h or from an accident during radiotherapy or during a sun exposure emitting radiation, received by astronauts during an interplanetary voyage or absorbed doses from radioactive waste or from accidental misuse of radiopharmaceuticals in medicine may cause CRS.

The experience gained from the nuclear accident of Chernobyl suggests that the main symptoms of CRS are: skin atrophy, fibrous formation of the skin after previous burns and eye cataract [7, 15-17]. Burns may be induced from all kinds of radiation. Specifically, radioactive material emitting  $\alpha$ - and  $\beta$ -rays, which have a short range of activity, must remain for long on the clothing or the skin of the patients before causing burns.

The chance of cancer after whole body radiation is a stochastic effect due to genetic damage and may appear at any time during life [18]. Latent period for a solid form of cancer is 20-30 years, while for leukemia is 7-10 years [7]. There are no indications for future appearance of cancer, for doses as low as 0.05-0.1Gy.

### Treatment

It is considered that the overall condition of patients who received either smaller doses (1-2Gy) or very high doses (8-12Gy) of radiation shall not change much, after medical care and treatment. This is because the small doses group of patients has a 0%-5% chance of fatal results within the next 2 months, while in the higher doses group all patients are expected to die within the next 14 days. For patients who received the intermediate level of doses (between 2-8Gy), medical treatment may increase survival by 50%. Not to forget that in this intermediate group of patients death may also appear in 5% of the cases, unrelated to medical treat-

ment [6]. It has also been reported that without medical care 50% of patients who received more than 4Gy shall die within the next 30 days [19].

In giving medical care and treatment to patients with the ARS, we first, must wash and clean the skin of the contaminated person, from radiation dust and ask him/her to wear clean clothes. We, then, must clean any injuries using warm water and soap and then disinfectant, in order to clean and also lower the radiation emitted from these injuries till twice above background [4]. Note that injuries that have already been healed are sensitive to reoccur even after years [20].

Antibiotics should be given against both aerobic and anaerobic bacteria. If we use an antibacterial drug like metronidazole against the anaerobic bacteria we may as a side effect encourage the aerobic bacteria to grow [21]. It is suggested to give a broad spectrum antibiotic, especially against aerobic Gram negative bacteria of the intestine, such as enterobacter and pseudomonas. These two bacteria cause about 1/3 of septicemia after ARS. One may subscribe quinolones (ciprofloxacin or levofloxacin) or cephalosporines of 3<sup>rd</sup> or 4<sup>th</sup> generation or an aminoglycoside such as gentamycin or amikacin [22]. Gram positive aerobic bacteria such as a-hemolytic streptococcus are the cause of septicemia in 1/4 of the cases. For them we also use broad spectrum antibiotics [23].

*If needed, we administer by parenteral infusion:* normal saline, red blood cells or platelets. Growth factor or factors for regenerating granulocytes, filgrastim (neupogen) 5mg/kg per day or pegfilgrastim (neulasta) 6mg subcutaneously per week and sargramostin 250mg/m<sup>2</sup> per day are also administered early, starting during the first 1-2 days and till white blood cells are 1000mm<sup>3</sup>, with rather good results [24, 25].

In case of an internal oral contamination diagnosed early, 1-2h before, we can perform gastric lavage [4]. We can also give aluminum hydroxide or magnesium carbonate. Aluminum also binds to radioactive strontium. For faster transport of the radioactive material through the intestine, we subscribe laxatives and enemas [4].

For all the above mentioned forms of ARS, we also use symptomatic treatment with anti-emetics, painkillers, anti-diarrhea drugs and support patients psychologically.

## Prophylaxis

It has been suggested to *use* the following foods: a) *olives, olive oil and sugar*. These foods in their chemical synthesis do not contain iodine, potassium, calcium, cesium or strontium so that it is not likely to be absorbed from the contaminated soil radioactive elements as the above like <sup>131</sup>I or <sup>137</sup>Cs or <sup>89</sup>Sr emitted during nuclear accidents. b) It has also been suggested to use *canned foods and milk in powder*.

It is also suggested to administer orally: a) tablets of *potassium iodide or Lugol*, solution in a daily dose of 3 tablets or 30 drops, respectively, during the first 24h after radioactive pollution. Thus thyroid gland is saturated and cannot absorb radioactive iodine. b) *Prussian blue solution*, which binds to radioactive elements of strontium and thallium and is discarded through feces. c) Solution of the "chelated" drug diethyl-triamin-pentaacetic acid (DTPA), which binds to the radioactive metals americium, polonium and curium, which have a very long half life, and are thus finally discarded through the urine.

*We may have to stay at home* for sometime, in order to avoid exposure to radioactive pollution. In this case we must remain in a central room, close doors, window shutters, curtains and also close airway pipes and air-conditioners. Furthermore, if we have domestic animals, we must bring them home as early as possible.

*If we must move outside the house or to another city* before or after the nuclear accident, it is suggested to carry with us a suitcase in which we have placed: a torch, a radio, spare batteries, a mobile phone, canned food, a bottle of water, some medicine, a can opener, clean clothes and money or credit cards.

*Underground stations*, if we can be there at the time of a nuclear accident, can protect us from the immediate effects of the bomb blast but the air we breathe in these areas will still be contaminated and of course, facilities for a more permanent stay are not available.

Some may wish or may be able to construct a private "*anti-atomic*" shelter underground with facilities for a stay of 1-2 weeks.

*Special clothing* protecting us from external radiation similar to those used by astronauts are now available in the market.

## Discussion

Factors influencing the effect of a high radiation absorbed dose and cause special sensitivity and vulnerability of the patient to radiation are the following: a) *Age*. In children, tissue damages are more intense because young cells are more sensitive to radiation. b) *A previous radiation accident*. This previous accidental radiation burden may be due to high natural radiation or internal intake of radiated food or incidental exposure to radiation sources. c) *The kind of radiation*. Neutrons and  $\alpha$ -rays are more dangerous than  $\beta$ - and  $\gamma$ -rays. d) *Gender*, since women are prone to thyroid and breast cancers [12] and e) *Congenital factors* [12].

We may mention here that medical examinations using radioactive substances or radiation treatment are continuously increasing and participate in more than half to all natural radiation burden [26]. To illustrate this point, it has been reported that patients with renal colic, who were examined by computed tomography, received a total dose between 19.5-153.7mSv [27]. On the other hand, most people living outside but close to Fukushima nuclear accident had received doses up to 20mSv during the accident and during the following year [28]. It is good to know that the upper dose limit, which indicates danger after a nuclear accident, is 250mSv [28].

In order to be aware and consider minimizing medical radiation doses, it has been suggested that every patient must be supplemented with a personal record-card, like a "Smart Card", where all administered doses will be recorded by the physicians [29-32].

*In conclusion*, prophylaxis and medical treatment and care in most of acute and chronic radiation sickness cases increase patients survival.

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