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MEDICAL PREPAREDNESS AND PATIENT MANAGEMENT IN SWEDEN

In the light of the current war waged by Russia against Ukraine, the Swedish medical regulatory authority has asked the Swedish Radiation Emergency Medicine Centre (SREMC, the national WHO REMPAN liaison institute and an EBMT member dept) to provide advice on the medical consequences of high exposures to ionising radiation and the management of highly exposed persons. As a starting point, SREMC used a worst-case scenario (provided by the Swedish Defence Research Agency) of a nuclear weapon explosion at a Swedish coastal town. Our advice discussed four situations: 1) Radiation incident at a Ukrainian NPP (unlikely to seriously affect the Swedish population); 2) Spectator case of a nuclear weapon explosion in a neighbour country (limited effects for the Swedish population); 3) Requests for assistance with medical care in Sweden for Ukrainian radiation victims (a possible result of cases 1 and 2); and 4) Nuclear weapon explosion in Sweden (disastrous consequences for the Swedish population). We described the likely medical effects and suggested how medical establishments might prepare for these cases. In a second document, we suggested what medical countermeasures the authorities should stockpile. Finally, we list some desirable future developments in radiation emergency medicine.

Key words: *emergency planning, nuclear explosions, radiation harm, ARS, MCM.*

Introduction

The Russian full-scale invasion of Ukraine has aroused fears of threats to health and safety due to radiation incidents at nuclear power plants or even use of nuclear weapons. Hence the National Board of Health and Welfare (the Swedish medical regulatory body) has requested the Swedish Radiation Emergency Medicine Centre (SREMC, which is the national WHO REMPAN liaison institute, and a member department of EBMT NAC, the nuclear accident committee of the European blood and marrow transfusion group) to provide information about the medical results of

high doses of ionising radiation, and advice on how medical institutions could prepare for the management of affected patients.

Aided by a worst-case scenario of a ground level 100 kton nuclear explosion on a November weekday with no previous warning, at the small Swedish coastal town of Nynäshamn, devised by the Swedish Defence Research Agency, Goliath et al. (2021), SREMC outlined 4 cases to consider in the planning:

1) *A radiation incident at a Ukrainian nuclear power plant.* Attacks on, or careless activities at, nuclear installations could, in unfortunate circumstances, lead, to uncontrolled releases of radioactive material over large areas, with consequences similar to those after the 1986 Chornobyl accident (UNSCEAR, 2008) or the 2011 Fukushima accident (UNSCEAR, 2022). While such events could become challenging for people in the Ukraine, it is very unlikely that they would necessitate in Sweden any health protective actions like sheltering or stable iodine intake. Some restrictions on foodstuffs and agriculture could become advisable, though.

2) *The 'spectator case' of a nuclear weapon explosion in a neighbour country.* If a nuclear weapon is employed in Ukraine, the local consequences would of course be very serious, but due to the distance the effects in Sweden would be limited. A first approximation of the possible results could be gleaned from the 'Nynäshamn scenario' mentioned above. Neither sheltering, relocation, nor intake of stable iodine would be relevant, but if the weather conditions lead to radioactive fallout in Sweden, restrictions on foodstuff production may become necessary.

3) *Requests for assistance with medical care in Sweden for Ukrainian radiation victims.* Both case 1 and case 2 above could conceivably generate appeals to the Swedish (and other) governments requesting such assistance. If such a potential appeal were received, it is reasonable to assume that Sweden would accept a limited number of patients for treatment and care, either through existing bilateral assistance agreements, via assistance arrangements which are in place via UN and EU (Swedish Government, 2024), or perhaps through the EBMT network of some 600 clinics in Europe (<https://www.ebmt.org/nuclear-accident-committee>). According to preliminary assessments, a handful of patients with Acute Radiation Syndrome (ARS) could be treated at highly specialised haematology units in Sweden.

4) *A fictitious nuclear weapon ground-level explosion in Sweden.* In the 'Nynäshamn scenario' referred to above, over 90% of the 14 000 population would die, primarily due to trauma and burns, but many ARS cases would also ensue. Significant devastation of the infrastructure and high levels of radiation from deposition of radioactive particles would make rescue operations practically impossible within a few km from the explosion site. Depending on weather conditions, radioactive fallout at longer distances (50–100 km from the explosion site) could also lead to radiation levels causing lethal acute radiation harm within hours/days/weeks.

A nuclear explosion well above rather than at the ground level would generate much less radioactive fallout, but would also significantly increase the area where trauma and burns are induced,

Medical consequences. 'Deterministic', usually acute, tissue/organ reactions include skin damage, ranging from erythema and epilation to burns and wounds; temporary or permanent sterility; antenatal brain damage (but other radiation-induced malformations are rare in humans); and Acute Radiation Syndrome (ARS) with haematological, gastro-intestinal, and central nervous system subsyndromes. Long-term exposures can also lead to a Chronic Radiation Syndrome (Akleyev, 2021). 'Stochastic', late effects include cancer and (very rarely) genetic effects. Radiation can also contribute to multifactorially determined conditions such as coronary heart disease. Useful summaries and background information are available in UNSCEAR (1988), Kai et al. (2020), and Valentin and Stenke (2022).

Symptoms of ARS, or other deterministic radiation harm, depend on the absorbed dose of radiation. At doses exceeding 8–10 Gy, nausea, vomiting and disturbed consciousness will set in within minutes to hours. Palliative care is called for, but life-saving efforts are regarded as hopeless. At somewhat lower doses the initial prodromal symptoms are milder and may be followed by some days or weeks with no complaints, then followed by bleeding and infections due to serious bone marrow failure. For such patients, adequate hospital care (preferably at specialised haematological units and/or burns centres in collaboration with other specialists) can be curing and life-saving.

For triage and classification of patients on the basis of prodromal symptoms and blood tests, the pocket guide of EBMT NAC (2017) and the web applications of REAC/TS (Oak Ridge Institute for Science and Education, 2021) and REMM (2024) are recommended. Table 1 summarises data from primarily EBMT (2017) and ICRP (2005; Stewart, et al., 2012; Kai et al., 2020) for initial assessment of radiation victims and suggests levels of medical care.

A further medical complication is that in many possible scenarios, radiation victims are likely to suffer from combined injuries, frequently with surgical trauma and burns which add to the risk of serious infections and impair the prognosis. Patients exposed to lower doses, less than about 1 Gy, will not develop ARS. While not needing hospital care for their radiation exposure, they may need to have their doses assessed, and be offered outpatient follow-up. There will also be persons with very low or no doses, some in shock or other extreme stress and some 'worried well' who will require balanced medical information.

Administrative recommendations. SREMC and the Board of Health and Welfare also suggested a number of actions to be taken by regional medical authorities, as listed in Table 2.

Stockpiling of medical countermeasures (MCM). SREMC has also provided advice to the National Board of Health and Welfare regarding specific pharmaceuticals that should be stockpiled for acute use in case of a major radiation incident. The advice does not focus on risks of late harm or long-term needs of medications. Again, the "Nynäshamn scenario" mentioned above was used as an input to the planning. WHO (2023) has issued advice on national storage of pharmaceuticals useful in radiological and nuclear emergencies. The US Food and Drug Administration has approved a number of pharmaceuticals for radionuclear emergencies under the 'Animal rule', see. MacVittie and Farese (2021) and FDA (2024).

Table 1

**A scoring table for initial assessment of irradiated patients
and suggested level of care**

Level of care Clinical observation*)	Score I Outpatients	Score II Hospital care Curing intent	Score III Hospital care Palliative intent
Time from exposure to debut of symptoms	< 12 h	< 5 h	< 30 minutes
Erythema	0	+/-	+++ within 3 h
Asthenia	+	++	+++
Nausea	+	+++	(-)
Vomits per 24 h	Max 1	1-10	> 10, serious
Stools/diarrhoeas / 24 h	Max 3, shaped	2-9, soft	> 10, watery
Abdominal pain	Minimal	Intensive	Unbearable
Headache	None	Manifest	Unbearable
Temperature	< 38° C	38° - 40° C	> 40° C
Systolic blood pressure	Normal	Normal or a bit low	< 80 mm Hg
Temp. loss of conscience	0	0	+/coma
Lymphocytes at 24 h in blood	> 1.5*10 ⁹ /l	< 1.5*10 ⁹ /l	< 0.5*10 ⁹ /l
at 48 h	> 1.5*10 ⁹ /l	< 1.5*10 ⁹ /l	< 0.1*10 ⁹ /l
Medical actions	Polyclinical follow-up Benign prognosis	Highly specialised haematological care (antibiotics, transfusions, cytokines etc) Grave, but care increases survival probability	Palliative care Even if blood formation is restored (maybe with stem cell transplantation), Multi-Organ Failure will follow Survival unlikely
Representative whole-body dose**)	~(500) 1000 – 2000 mSv	~2000 – 8000 mSv	More than ~8000 mSv

*) Clinical observations 1-2 days after a single whole-body exposure to ionising radiation

**) While more familiar to laymen, the unit mSv refers to effective dose and is not defined for doses exceeding 1000 mSv. The values really refer to absorbed doses in mGy, where however the numerical value in many cases agrees with values stated in mSv.

Table 2

**Actions to be taken by regional medical authorities in preparation
for a possible foreign nuclear explosion**

Short-term (as soon as possible)	
Where/what	Action
Pre-hospital organisation, A&E depts, emergency care wards	Update and rehearse medical RN plans
Measurements	Co-ordinate, nationally (through radiation regulator) and locally, have medical physicist stationed at A&E dept
Contaminated patients	Check equipment, rehearse decontamination
Health care providers	Prepare to receive a few foreign ARS and/or trauma patients at specialist units; formalise medical management, check resources
Longer term	
Set up a training and education programme. What is already available? What support is required, and from whom?	

The SREMC advice points out that patients who have been exposed to radiation may need both specific medical countermeasures, which are not used in other contexts and should therefore be stocked and supplied by the national healthcare authority, and medications which are routinely used in health care, such as bone-marrow stimulating growth factors, antibiotics, and antiemetics which should primarily be stocked and supplied by regional authorities within the regular health care framework.

Preventing uptake of selected nuclides. For preventive administration in case of internal contamination, stable iodine in the shape of potassium iodide is the classical example. This can prevent accumulation of radioactive iodine in the thyroid. Contamination with radioiodine is not a primary concern for members of the public after nuclear explosions (prophylaxis may however be indicated for responders), but is a major risk after accidents at nuclear power installations. Because of this, stable iodine is already available in all regions with NPPs, and pre-distributed to households in the immediate vicinity of the installations. Thus, no further stockpiling is necessary.

Increasing excretion of selected nuclides. *Prussian blue* (Radiogardase; ferrihexacyano ferrate) can bind caesium (Cs) and thallium (Tl) ions in the intestine, thus increasing excretion with faeces. Available as 500 mg capsules for oral intake. *DTPA* (pentetic acid) is used to de-corporate transuranics (Am, Pu, Cm, Cf, Bk) and many polyvalent cations (Ac, Ce, Cr, Co, Es, Eu, In, La, Mn, Nb, Pd, Ru, Sc, Th, Y, Zn, Zr, and Pm). DTPA forms water-soluble chelate complexes with the ions, thus increasing urine excretion. It is unsuitable for U, Np, or Cd de-corporation due to the risk of nephrotoxicity. Available as Ca-DTPA or Zn-DTPA injection solutions. *Gaviscon* (sodium alginate and Al antacids) increases excretion of Sr by substituting it for sodium which is excreted. Available as tablets and as 50 mg/ml oral suspension (recommended). *Baking soda* (sodium hydrocarbonate) alkalises urine and forms uranyl tricarbonat, thus increasing urine excretion of uranium. Available as tablets or solution for intravenous treatment.

Supportive treatments for barrier injuries and infections. These are standard parts of medical care. Prophylactic antimicrobial fluorokinolones are used, such as *Ciprofloxacin* or *Levofloxacin* (with perhaps broader action against resistant bacteria). Broad-spectrum antibiotics are used if infection is manifest. Antiviral prophylaxis is achieved with *valaciclovir*. Antifungal prophylaxis is primarily achieved with *fluconazol*, but in case of persistent neutropenia, other agents such as *posakonazol*, *isavuconazol* or *voriconazol* may be useful.

Growth stimulating factors support the haematopoietic system which is very sensitive to radiation. Granulocyte colony stimulating factors (G-CSF such as *filgrastim* (*Accofil*, *Neupogen*, *Nivestim*, *Zarzio*) or *lenograstim* (*Granocyte*) are used in haematology and oncology and are used as subcutaneous injections after whole-body exposures to radiation. Granulocyte-macrophage CSFs (GM-CSF, *sargramostim*, *Leukine*, or *molgramostim*, *Leucomax*), while not as frequently used, may also be helpful. Pegylated G-CSF (PEG-G-CSF, *pegfilgrastim*, *Fulphila*, *Neulasta*, *Pelgraz*, *Ziextenso*) acts for longer and thus requires fewer

administrations. Romiplostim (*Nplate*) can prevent or mitigate thrombocytopenia, and this is also true for eltrombopag (*Revolade*).

Soothing treatments for gastrointestinal symptoms. Loperamid (*Dimor*) reduces peristalsis and thereby reduces diarrhoea. 5-HT₃ antagonist (Ondansetron) antagonises 5-hydroxytryptamine receptors in the gastrointestinal tract and thereby is an antiemetic.

How much should be stocked? According to general regulations, sufficient amounts of medications for 1–3 months should be stocked. SREMC recommended that radiogardase and the two varieties of DTPA should be stocked at the 6 university hospitals, for 5 patients per hospital=30 patients. Growth factors should be stocked in sufficient amounts for 1000 patients (~the number of potential survivors with ARS in the 'Nynäshamn case') for 3 months.

Discussion and conclusions

Some remaining problems. The advice summarised above represents, in the authors' opinion, the current state of the art of management of ARS patients. However, research needs and MCM developments were discussed at a US NIH/NIAID workshop on GI-ARS (Winters et al., 2024) and at a yet unpublished companion 2024 workshop on vulnerable and understudied populations (where however SREMC's Valentin was an invited participant). Problems and needs are also summarised by UNSCEAR (2008) and Valentin and Stenke (2022). Based on those references, and on discussions within SREMC regarding the advice provided as mentioned above, our opinion is that the following problems should be addressed:

Research so far and planning are biased towards mass-casualty situations with uniform external whole-body exposures. Vulnerable populations and their special requirements need to be defined. Children are not just smaller adults; they need to be treated on the basis of paediatric data. Inhomogeneous exposures and varying dose rates need to be more carefully regarded. New medical countermeasures need to be developed, for the gastrointestinal subsyndrome of ARS, for skin reactions, for complex multi-organ effects, and perhaps also for paediatric patients.

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References

Akleyev, A.V. (2021). Specific features of medical care provision to the population of the Tcha river side settlements. *J. Radiol. Prot.*, 41, S342–S354.

EBMT. (2017). *European Approach for the medical management of mass radiation accidents*. Pocket Guide. <https://www.ebmt.org/sites/default/files/2018-03/EBMT%20Nuclear%20Accident%20Committee%20Pocket%20Guide%202017.pdf>

FDA. (2024). *Animal Rule Information*. <https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/animal-rule-information>

Goliath, M., Lidström, K., Nylén, T., & Sivertsson, S. (2021) *Kärnvapenscenario för räddningstjänst* [Nuclear weapons scenario for rescue services]. Swedish Defence Research Agency Report FOI-R--5131--SE.

ICRP. (2005). Protecting people against radiation exposure in the event of a radiological attack. ICRP Publication 96. *Ann. ICRP*, 35(1). <https://www.icrp.org/publication.asp?id=ICRP%20Publication%2096>

Stewart, F.A. et al. (2012). ICRP Publication 118: ICRP Statement on Tissue Reactions / Early and Late Effects of Radiation in Normal Tissues and Organs – Threshold Doses for Tissue Reactions in a Radiation Protection Context. *Sage Journals*, 41(1/2). <https://doi.org/10.1016/j.icrp.2012.02.0>

Kai, M.T., Homma, J. Lochard, T., Schneider, J.F., Lecomte, A. Nisbet, S. Shinkarev, V., Averin, & Lazo, T. (2020, Dec 20). ICRP Publication 146: Radiological protection of people and the environment in the event of a large nuclear accident. *Ann. ICRP*, 49(4), 11–135. <https://pubmed.ncbi.nlm.nih.gov/33291942/>

MacVittie, T.J., & Farese, A.M. (2021, Nov 10). Recent advances in medical countermeasure development against acute radiation exposure based on the US FDA animal rule. *J. Radiol. Prot.*, 41(4), S438–S453. <https://pubmed.ncbi.nlm.nih.gov/34433144/>

Oak Ridge Institute for Science and Education. (2021). *REAC/TS RadMed App*. <https://orise.orau.gov/reacts/resources/radmed-app.html>

REMM. (2024). *Guidance on Diagnosis and Treatment for Healthcare Providers*. <https://remm.hhs.gov/index.html>

Swedish Government. (2024). *Sweden's support to Ukraine*. <https://www.government.se/government-policy/swedens-support-to-ukraine/>

UNSCEAR. (1988). *Report to the General Assembly, Scientific Annex G: Early effects in man of high doses of radiation*. https://www.unscear.org/unscear/uploads/documents/publications/UNSCEAR_1988_Annex-G.pdf

UNSCEAR. (2008). *Report to the General Assembly, Scientific Annex D: Health effects due to radiation from the Chernobyl accident*. https://www.unscear.org/unscear/uploads/documents/publications/UNSCEAR_2008_Annex-D-CORR.pdf

UNSCEAR. (2022). *2020/2021 Report to the General Assembly, Scientific Annex B: Levels and effects of radiation exposure due to the accident at the Fukushima Daiichi nuclear power station*. https://www.unscear.org/unscear/uploads/documents/publications/UNSCEAR_2020_21_Annex-B-CORR.pdf

Valentin, J., & Stenke, L. (Eds.). (2022). Special Issue Concerning Medical Management after High-Dose Radiation Exposures. *Journal Radiological Protection*. <https://iopscience.iop.org/journal/0952-4746/page/special-issue-concerning-medical-management-after-high-dose-radiation-exposures>

WHO. (2023). *National stockpiles for radiological and nuclear emergencies: policy advice*. <https://www.who.int/publications/i/item/9789240067875>

Winters, T.A., Marzella, L., Molinar-Inglis, O., Price, P. W., Han, N.C., Cohen, J. E., Wang, S-J., Fotenos, A.F., Sullivan, J.M., Esker, J., Lapinskas, P.J., & DiCarlo, A.L. (2024). Gastrointestinal acute radiation syndrome: Mechanisms, models, markers, and medical countermeasures. *Radiat. Res.*, 201, 628–646.

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МЕДИЧНА ПІДГОТОВЛЕНІСТЬ ТА ЛІКУВАННЯ ПАЦІЄНТІВ У ШВЕЦІЇ

Надано поради, що охоплюють чотири ситуації: 1) радіаційний інцидент на українській АЕС (малоймовірно, що він серйозно вплине на населення Швеції); 2) явний випадок вибуху ядерної зброї в сусідній країні (обмежений вплив на населення Швеції); 3) прохання про надання медичної допомоги у Швеції постраждалим від радіації українцям (можливий наслідок перших двох випадків); 4) вибух ядерної зброї у Швеції (катастрофічні наслідки для населення Швеції). Описано ймовірні медичні наслідки та підготовано пропозиції щодо дій медичних установ у таких випадках. Запропоновано медичні контрзаходи, до яких влада має бути готова. Надано перелік необхідних майбутніх розробок, які були б корисними для екстреної радіаційної медицини.

Ключові слова: *планування на випадок надзвичайних ситуацій, ядерні вибухи, радіаційна шкода, гострий радіаційний синдром, медичні контрзаходи.*

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