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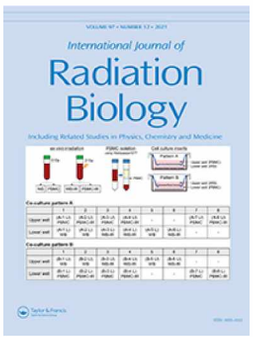

International Journal of Radiation Biology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/irab20

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To cite this article: Harold M. Swartz, Ruth C. Wilkins, Elizabeth Ainsbury, Matthias Port, Ann Barry Flood, François Trompier, Laurence Roy & Steven G. Swarts (2021): What if a major radiation incident happened during a pandemic? – Considerations of the impact on biodosimetry, International Journal of Radiation Biology, DOI: 10.1080/09553002.2021.2000659

To link to this article: https://doi.org/10.1080/09553002.2021.2000659

Published online: 17 Nov 2021.

INTERNATIONAL JOURNAL OF RADIATION BIOLOGY
https://doi.org/10.1080/09553002.2021.2000659

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COMMENTARY

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What if a major radiation incident happened during a pandemic? – Considerations of the impact on biodosimetry

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ARTICLE HISTORY Received 30 July 2021; revised 21 October 2021; accepted 25 October 2021

Introduction

In this paper, we consider the issues associated with and the potential impact on biodosimetry, i.e. screening for medically significant exposure to radiation, if a major radiation incident were to happen during a pandemic. We focus on those aspects that are likely to have greatest impact and/or to require modifying usual practice, because of the simultaneous needs to address the problems and synergistic risks that may occur. In particular, from the point of view of carrying out effective biodosimetry, we consider what will be the special challenges and how to plan and prepare to meet those challenges.

While this paper reports on the preparations (or the lack thereof) that biodosimetry laboratories made for handling a possible radiation incident during the COVID-19 pandemic, the lessons and inferences that we draw will be applicable to the co-occurrence of a radiation incident and other types of pandemics as well as other large population-scale emergencies.[1]

Premise of this paper: Major assumptions and context

Assumptions:

- The risk of another pandemic occurring is very high but with unpredictable incidence, distribution, and impact (Wister and Speechley 2020).
- A radiation accident, i.e. not deliberately instigated, could coincidently occur during a pandemic.
- Due to factors that contribute to increased social and economic instability during a pandemic, there is an increased risk of a deliberate, i.e. malicious, radiation event co-occurring during a pandemic (Counter-Terrorism Committee Executive Directorate (CTED) 2021).
- Biodosimetry laboratories and personnel, with their expertise in testing in the context of carrying out rigorous security and safety protocols, are likely to be called upon to help meet the needs associated with pandemic testing and treatment (Kulka et al. 2018). This was clearly seen during the COVID-19 pandemic particularly in government funded or affiliated laboratories including Public Health England (PHE), Institut de Radioprotection et de Sûreté Nucléaire (IRSN), Bundeswehr Institute of Radiobiology (BIR) and Bundesamt für Strahlenschutz (BfS), where biodosimetry specialists, individuals with transferable skills including project management, emergency response communication and laboratory techniques, were redeployed to focus on the pandemic response.

Based on these assumptions, it is desirable to develop advanced plans for how to (re)deploy biodosimetry resources (both facilities and personnel). These resources will be needed to carry out their primary responsibility to conduct biodosimetry testing during a radiation event (especially a large scale incident) as soon as they are needed, while potentially also continuing to safely and securely carry out testing and other responsibilities during a pandemic.

If the number of individuals at risk of radiation exposure during a pandemic is small, then it is likely that the responding team will be able to adequately deal with the challenges, without needing to prioritize tasks or modifying protocols for treating patients during a pandemic (Kulka et al. 2018).

If, however, the number of individuals potentially exposed to radiation levels that could lead to the acute radiation syndrome (ARS) is too large to be accommodated in the available health care facilities, then it will be very

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important to have a means to identify those potential victims who are at highest risk for having clinically significant effects of radiation in order to triage them to receive medical attention. Then the capacities will depend on the staff available given that the pandemic may have caused a reduction in staff or resources available to carry out biodosimetry to support the medical management with dose estimates.

In either small- or large-scale radiation events, modifications to usual practices may be necessary because of the potential for irradiated victims to be ill from the agent producing the pandemic. The medical and laboratory personnel may need to modify their usual emergency procedures in order to avoid getting ill or spreading the infection that is causing the pandemic. Biodosimetry will be a paramount need, and planning should take into account how to deploy biodosimetry experts and facilities who may face conflicting expectations and/or modified procedures and reduced staff if an incident occurs during a pandemic.

Brief summary of radiation biodosimetry

Biological and physical retrospective biodosimetry uses well-established techniques to assist in triage and management of individuals suspected of being exposed to ionizing radiation following a radiation accident or incident (Ainsbury et al. 2011; ICRU 2019). The techniques are based on radiation-induced changes in the person themselves, either physical changes (e.g. the generation of long-lived free radicals in teeth or fingernails) or biological responses to radiation damage (e.g. changes in white blood cells such as the generation of chromosomal aberrations, changes in blood cell count or changes in levels of gene expression) (Jaworska et al. 2015; Kulka et al. 2018).

However, because of the perceived low risk of a mass casualty radiation event, these capabilities are not routinely available onsite (or even in the country as a whole in some cases), especially in the amount needed in the event of a large radiation incident. There are some national efforts to stockpile biodosimetric resources and to identify key persons to utilize them when needed. Furthermore, for some of these techniques for which only a small number of laboratories worldwide are equipped to carry out these measurements, in recent years a large effort has been focused on networking between the different countries and regions, in order to have an adequate capability to respond to such an incident (Kulka et al. 2018). To date, however, such plans have rarely taken into account the co-occurrence of a radiation event and a pandemic.

Overview of planning for triage following a radiation event that occurs during a pandemic

Although this manuscript is very much informed by our perspective as biodosimetry experts and the COVID-19[2] pandemic, it is important to realize that it is quite likely that, in one form or another, the virus and its derivatives will persist at significant levels for many years, with surges and ebbs. Also, there are likely to be other infectious agents that will arise and lead to widespread risk. Moreover, the risk of having a simultaneous occurrence of a radiation event in the midst of an active COVID-19 or similar epidemic is sufficiently likely so as to warrant planning for how the pandemic would impact how radiation biodosimetry would be carried out.

The presence of a pandemic at the time of a radiation event would impact biodosimetry on several different and interacting levels, including:

- Reduced availability of staffing and reduced readiness of the emergency response network, because of diversion of expert personnel, illness, or requirements to minimize staff interactions and/or a shortage of consumable supplies.

This occurs because of the overlap in the expertise required to prepare to test for radiation exposures and COVID-19 but also in the overlap in wider 'transferable' skills required for any emergency response including management and communication skills. All employees of PHE in the UK, for example, hold multiple emergency responsibilities, depending on their expertise. Because of the overlap in skill sets, at least some members of biodosimetry teams are likely to be deployed to assist with national COVID-19 responses. Due to the rareness of biological, chemical, radionuclear or even mass casualty incidents, some countries have decided to pool their biological/medical preparedness activities within one institution. Some nations have opted not to consider the risk of a co-incident pandemic in their preparation for possible radionuclear events (NATO research task group, personal communication, August and September 2020). This consolidation, while potentially efficient, also has the potential to decrease the ability of these abovementioned countries to respond to a radiation event in the midst of a pandemic. Therefore, some groups have started to give consideration as to how and how soon teams can be redeployed back to their original radiation emergency response roles and how the resulting gaps in COVID-19 response can be filled, should a radiation accident occur. Planning for this possibility will be required to take into account the individual resources and needs of the country or region.

- Potential changes in the validity or practicality of some types of radiation biodosimetric assays, due to changes in the biological responses to radiation when the person is infected with the virus; conversely, tests for the presence of the virus may be impacted by having been exposed to radiation.

While some of the assays such as the chromosome based and physically based dosimetry techniques are unlikely to be impacted by changes due to COVID-19, other assays such as genetic and metabolically based assays theoretically could be impacted, particularly if markers are related to the immune response (Rogan et al. 2020; Park 2021; Rios et al. 2021). However, even though we believe that COVID-19

infection does not significantly affect chromosome-based assays, this could be completely different for other infectious diseases leading to a major decrease or loss in function of peripheral lymphocytes (Baeyens et al. 2010). Even when there is a known systematic effect on the marker for a given test, testing may be further complicated by needing to test for the presence of the virus. These considerations in turn highlight the need to determine which types of tests or procedures may actually be affected by the virus, which may in turn determine which biodosimetric tests should be used if there is a pandemic. In a similar light, tests for the presence of the virus may be impacted by having been exposed to radiation. Therefore, the effects of radiation exposure on the performance of various viral testing methods will need to be assessed in order to identify those test methods whose outcomes are sufficiently refractory to an individual's exposure to radiation. It is also important to note that such reassessment may need to be carried out rapidly, in response to the particular characteristics of the emerging threat, which may not be possible to predict in advance.

- Changes in the rigor and safety procedures for carrying out biodosimetry, because of concerns about exposure to the infectious agent.

Additional, externally imposed regulations or established laboratory specific precautions for handling potentially infected samples could impact biodosimetry at several levels, e.g. it may reduce the rate at which samples could be processed or, in some cases, prevent the sample from being analyzed. Particularly, during a radiological emergency, it is not practical to determine the infectious status a potentially radiation exposed individual prior to sampling and some laboratories would not be able to receive samples of unknown viral status even with COVID-19. This would be even more pronounced for possible infectious agents needing biosafety level three or four facilities. At the regulatory level, concerns over spreading the pandemic could severely impact the ability to ship samples to other sites in a network, especially across international boundaries, e.g. medical shipments may be required to be irradiated, thereby ruining the sample for dosimetry.

Within an individual laboratory, procedures will vary depending on the source of the sample, for example blood or saliva samples for biological biodosimetry or teeth for physical retrospective biodosimetry (e.g. Electron Paramagenetic Resonance (EPR), luminescence) and how the virus is transmitted. If the tests require obtaining blood or saliva samples, there may need to be special handling procedures at the point of obtaining samples as well as how to handle them in the laboratory, especially if the virus is blood-borne. On the other hand, techniques such as saliva for assessing radiation-induced changes in gene expression (Ostheim et al. 2020) or in vivo EPR to measure teeth (Williams et al. 2011) for biodosimetry may require special procedures to protect operators and to avoid transmission to future subjects, especially if the virus is spread by airborne means.

Some labs might have protocols that apply to all samples regardless of source or virus associated with the pandemic (e.g. the laboratory protocol may assume that any blood sample has the potential to contain an infectious agent) while others may have sample-specific or victim-specific precautions (e.g. if the blood or saliva sample is from a person unlikely to be infected, such as someone vaccinated against COVID-19, no special precautions may be needed; however, when there is no definitive information about virus status, the sample may need to be treated as potentially infected). The resulting difficulties might shift decisions as to what biodosimetry tests should be utilized. The required extra steps would not only impact throughput but also could increase the cost of the biodosimetry tests.

In the case of a highly transmittable and blood borne virus (e.g. Ebola), some assays such as Dicentric Chromosome Assay (DCA) or Cytokinesis-Block Micronucleus Assay, which need a culture of viable blood, would not be executable within a standard radiobiology laboratory due to health and safety regulations. In such cases, all tests that are severely affected or impossible to conduct, due to the necessity of inactivating the virus within the sample, would be unusable. The subsequent reduced availability of viable assays for biodosimetry is an additional reason to develop and stockpile supplies for several different assays and methods and not limit the preparedness to a very narrow set of diagnostic procedures that are viable only under more 'ideal' circumstances.

- There is the potential for an increased health risk of subjects from simultaneously having an active infection and being exposed to significant amounts of radiation.

It is important to note that, due to a number of potential commonalities between infectious responses and radiation exposure (including, for COVID-19, immune dysregulation), the impact on illness could be additive or potentially synergistic (Rios et al. 2021). The possibility of poorer outcomes on people dually exposed could place added requirements on biodosimetry to detect such multiplicative effects and/or to provide results more quickly so that those at higher risk could be prioritized for medical care.

- The need based on explicit orders from government official for increased readiness for a radiation event occurring during a pandemic because of the heightened risk of malicious attacks, to take advantage of governments and health care specialists being distracted by having to deal with the virus and its concomitant societal disruptions, such as on the economy.

Terrorists might well conclude that this would be an easier opportunity to carry out a malicious action since the focus of international and national attention is on the pandemic and many types of personnel are diverted to deal with it. They also might recognize that the resulting terror and disruption from a radiation event would likely be heightened and the response would be delayed and

otherwise complicated by the simultaneous need to deal with the risks from both the pandemic and radiation event. The vulnerabilities include the potential for computer or security sabotage as well as radiation terrorist events. It also might be easier to recruit people into terrorist activities due to the societal economic and humanitarian impacts of the pandemic (Counter-Terrorism Committee Executive Directorate (CTED) 2021).

Experience during the COVID-19 pandemic

The following summary of some of the changes and adjustments made by dosimetry laboratories during the COVID-19 pandemic is based on an informal survey by the authors from many individuals and laboratories within the biodosimetry community.

- Increased vigilance for the increased risk of terrorism.
  Many institutions conducting biodosimetry were asked to ensure their institutions were maintained in a heightened state of readiness due to an increased risk of terrorism. This was required while simultaneously minimizing the number of onsite staff to adhere to the COVID-19 protocols of the workplace. They, and other institutions involved in responses to radiological emergencies, were asked to be prepared to respond to such an event within their area of responsibility at any time. In order to fulfill this duty, clear organization and rigorous preparedness is required to avoid complete shutdown even in the event of infection of the staff (Bundeswehr, personal communication March, 2020).
- Preparations to remain fully capable of responding to radiation emergencies, while dealing with the restrictions on personnel and activities that were part of the general limitations of activities to minimize spread of COVID-19.
  Measures taken by laboratories included local separation of groups of personnel (to minimize cross contamination and maximize the ability to function as teams), partial shutdown of laboratory activities, on-call standby of all personnel 24/7, deferral of all non-essential operations while maintaining equipment in a state of readiness to respond, stockpiling reagents and assay specific consumables and personal protection equipment (PPE) in anticipation of shortages, establishing remote access for analysis (e.g. using remote connections to automated metaphase finders for scoring), and an early and all-embracing implementation of hygiene policies including defining appropriate social behavior such as social distancing, minimizing social gatherings etc., organizing workspaces to create appropriate social distancing, and providing medical preparedness activities, ranging from early test strategies up to psychological support. All these efforts were included in and supported by a governmental response plan, or an intra-ministry action plan, at the various different international laboratories (U. Oestreicher, personal communications, June 23, 2021; A. Balajee, personal communication, June 28, 2021).
- Efforts were redirected from usual responsibilities of responding to radiation events, to respond to COVID-19. Illustrating the requirement for and complexity of needing the same public health experts and laboratories to handle both types of crises, the World Health Organization (WHO) conducted a survey in 2021 of its BioDoseNet laboratories in which laboratory directors were asked about their laboratory's preparedness and ability to perform biodosimetry during a pandemic such as COVID-19. Of 62 responding laboratories, representing 42 countries, about 53% of respondents indicated that they had considered the changes and challenges of conducting biodosimetry in the case of dual emergencies. Their changes involved developing new protocols to improve safety measures of handling potentially infected samples (e.g. increased use of PPE), updating equipment and facilities with improved biosafety features, such as establishing processes for scoring remotely. Forty percent of the respondents stated they could still accept biodosimetry samples as usual for analysis. Eighteen percent stated that they would not be able to accept any biodosimetry samples for analysis during a pandemic, with the remaining 42% able to receive a reduced number. The main precaution reported to handle this situation was the need to minimize the risk of infection to laboratory staff by having improved protocols for blood sampling and handling; half of the respondents reported already having these protocols in place (submitted manuscript).

Although the need for these protocols would not be consistent with known pathways for transmission of the COVID-19 virus, they may be relevant for other types of pathogens. Also, however, it is likely that many dosimetry laboratories have established procedures that treat all blood samples as potentially infected and handle them accordingly. Most of the laboratories (76%) stated that they did not have the expertise, capability and capacity to assist with other diagnostic testing. Of those that did, molecular genetics and polymerase chain reaction (PCR) was the most common expertise described. Although some laboratories mentioned that they have been recruited to deal with the COVID-19 response, these laboratories also stated that they would be released from these duties if biodosimetry analysis were required (submitted manuscript).

Emergency centers must be prepared to respond to any emergency situation, regardless of the occurrence of simultaneous events or another crisis. A recent example is the activation of the French National Nuclear and Radiological Emergency Center at IRSN following the contaminated forest fires in Ukraine. This incident, although resolved otherwise, could have led to a potential release of radioactive materials into the atmosphere in the spring of 2020, i.e. during the national COVID-19 lockdown.

Such multi-emergency scenarios are indeed plausible and therefore require planning to mobilize personnel and maintain the activities of the emergency center regardless of the duration of any concomitant crises. As occurred in this

example, preparations for handling both types of emergencies may necessitate keeping personnel locked up 24/7 on a secure site—a significant logistical problem that must be anticipated in preparedness planning.

The importance of networking

Even if a pandemic is global or almost global, any concurrent radiation event is likely to be relatively localized. Hence, the importance of active networking in radiation emergency preparedness cannot be overstated (Kulka et al. 2018).

The WHO BioDoseNet network in 2021 was comprised of over 80 laboratories, which were distributed globally, with varying levels of capacity to conduct biodosimetry and readiness to respond to an imminent emergency. To date, this network, along with smaller regional networks, has enabled extensive harmonization to occur, from sharing of protocols to conducting inter-laboratory comparisons.

For example, during the active stages of the COVID-19 pandemic, the RENEB network organized and conducted a large international biodosimetry exercise. More than 40 laboratories and more than 100 researchers from all over the world took part, including several authors of this manuscript. Although the analysis of this exercise is incomplete at the time of preparing this manuscript, preliminary results suggest that, at least at the status of the pandemic in mid-2021, biodosimetry laboratories could continue to function and international shipments of samples between laboratories would be possible with no more constraints than usual. In early 2020 it would have been impossible to conduct this exercise due to shutdowns within the participating laboratories, special orders to manage the pandemic, or a shortage of consumables.

Furthermore, the current experience with networks suggests that collaborations between laboratories enable the development of new biodosimetry methods (e.g. those using PCR), which could result in dually-prepared laboratories, i.e. with the ability to conduct COVID-19 testing as well as biodosimetry. This capability would be especially helpful if the laboratory is assisting in a dual event, where victims being tested for radiation may also have been exposed to the pandemic agent. It would also increase the flexibility of these laboratories to assist in either type of emergency. Networks need to continue to provide shared training and expertise with its members, which will strengthen the capacity of the international biodosimetry network. This will enable laboratories to come to the assistance of others, which may be in a heightened status of pandemic conditions at the time of a radiation incident and less able to deal with it (Kulka et al. 2018).

Conclusions and recommendations

Given the history of pandemics throughout human history, the recurrence of pandemics is expected but with unpredictable incidence and impact. There is a possibility for concurrent radiological incidents during a pandemic, which, for the most part, are expected to consist of small radiation incidents of one or two cases, as was witnessed during the current COVID-19 pandemic in several laboratories including PHE, IRSN, Bfs, the Radiation Emergency Assistance Center/Training Site and Health Canada (personal communication). However, there remains the possibility of more impactful, larger radiological scenarios occurring during a pandemic that arise from malicious acts or large scale accidental release events. In these large-scale radiological situations occurring within a pandemic, the ability to address the radiological emergency will be adversely affected due to limitations placed on personnel, resources, and processes as a consequence of the pandemic. However, the impact of these limitations can be reduced through advanced planning and preparation. Based on the experience gained during the current COVID-19 pandemic and past radiological incidents, we make the following recommendations:

- In the ideal situation, within reason, be ready for anything! Flexibility in addressing radiological emergencies within pandemic emergencies requires knowing the capabilities and limitations of biodosimetry laboratories in addressing the situation.
- Plan to reorganize/release staff as needs shift between support of pandemic and radiation dosimetry response.
- Develop operational plans to prevent or minimize contact with contagion within lab personnel, including isolation protocols.
- Maintain a reserve of personnel or laboratory networks in a position to fill in for those who become ill from exposure to the contagions or are directed toward addressing testing needs in the screening of infected individuals.
- Establish which labs are able to receive human samples based on biosafety level of the pathogen, recognizing that not all labs are able to work with potentially infectious samples.
- Establish protocols to address appropriate level of biosafety level of infectious agent, including protocols defining proper containment equipment and engineering, as well as stock piling of personal protective equipment appropriate for the biosafety level of the pathogen.
- Establish procedures to address limited availability of reagents and consumables in the event that supply chains are impacted by pandemic.
- Establish shipping protocols specific to pathogen biosafety. Shipping of samples may be impacted by pandemic or the biosafety level of the pathogen. Additionally, where possible, protocols defining proper and effective inactivation methods of pathogens within human samples are needed for both the shipper and receiver for sample transport, especially for contagions with biosafety levels of 3 or greater.
- Plan to seek help from wider network of response-ready partners. Networks need to continue to provide training and sharing expertise to continue to increase the strength and capacity of the international biodosimetry network.

By implementing these recommendations, international biodosimetry networks can be prepared to address large-scale radiological incidents within the context of a pandemic

and ensure the safety of biodosimetry personnel as well as victims in such dual emergencies.

Notes

1. There is a related white paper in preparation by the same authors reporting the lessons learned from the biodosimetry community's actual participation in planning and responding to COVID-19. This report, in contrast, focuses on the possibility of there being the dual need for biodosimetry laboratories and experts to help with a major radiation incident and a pandemic.
2. COVID-19 is used throughout the rest of the paper in a generic sense of referring to a world-wide infectious based pandemic, unless otherwise specified.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The authors reported there is no funding associated with the work featured in this article.

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