GLOBAL NETWORKING FOR BIODOSIMETRY LABORATORY CAPACITY SURGE IN RADIATION EMERGENCIES

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Abstract—For the public health management of radiation emergencies, one of the essential components of integrated risk assessment is to quickly and accurately assess and categorize the exposure. In addition to other methods, biodosimetry is instrumental to support decision-making for: 1) efficient secondary triage in a hospital response phase; 2) multi-parameter approach for defining best-treatment strategies for those severely exposed; 3) clinical prognosis and assessment of risk; and 4) reassurance and psychological support for those potentially exposed, or “worried-well.” In large-scale events, the number of victims, and especially those worried-well, is likely to overwhelm hospital and laboratory capacities in the accident area. This is already being addressed through the networking approach within several countries and/or regions of the world. The paper reports about WHO’s activity toward coordination of these regional efforts and the international collaborative network of biodosimetry laboratory services, WHO BioDoseNet. The network includes more than 30 laboratories around the world and supports the implementation of the revised International Health Regulations, the scope of which since 2007 also covers the field of radionuclear incidents. Health Phys. 98(2):168–171; 2010

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INTRODUCTION

Since the 1950s, there has been a shift in global security and focus of preparedness for radiation emergencies. During the 1970s to 1990s, the Three Mile Island and Chernobyl accidents shaped the focus of emergency preparedness planning when countries were mostly concerned about the possibility of nuclear power plant accidents. During the last decade, the main preoccupation has shifted toward malevolent event scenarios, especially after the 11 September 2001 terrorist attack. The all-hazard-based preparedness plan concept has become a priority in many countries, considering unified response planning for biological, chemical and radionuclear (BCRN) threat scenarios. What threats the future will bring is not known, but neither war, accidents, nor terrorism are expected to disappear soon.

These changes in the nature of global threats call for a change in preparedness and response planning approaches in many fields. The vision of the World Health Organization (WHO) is one of a more secure world that is on the alert and ready to respond collectively to any public health emergency. One of the several strategic objectives of WHO work is the implementation of an international alert and response system, which is based on strong national public health systems and on an effective international system prepared to deal with specific threats and to coordinate international response.

A MANDATE FOR STRENGTHENING PUBLIC HEALTH RESPONSE TO RADIATION EMERGENCIES

As a specialized UN agency on health, WHO has taken a lead in the field of global health security because it has both a mandate to protect human health and a strong expertise in preparedness and response to public health emergencies of any nature. It has the privileged position of working directly with national health authorities in its 193 member states. The following general functions of WHO are relevant to radiation emergencies preparedness and response (WHO 2006):

- to act as the directing and coordinating authority on international health work;
- to establish and maintain effective collaboration with the United Nations, specialized agencies, governmental health administrations, professional groups and such other organizations as may be deemed appropriate;
- to furnish appropriate technical assistance and, in emergencies, necessary aid upon the request or acceptance of governments;
- to promote, in co-operation with other specialized agencies where necessary, the prevention of accidental injuries;
• to provide information, counsel and assistance in the field of health; and
• to assist in developing an informed public opinion among all peoples on matters of health.

In addition to the WHO Constitution, the legal framework for WHO’s mandate related to radiation emergency response includes the Emergency Conventions (IAEA 1986a, b; IAEA 1987), the International Health Regulations (2005), and the World Health Assembly Resolutions (WHO 2002, WHO 2006). WHO co-sponsors the Joint Radiation Emergency Management Plan of the International Organizations† (EPR-IPlan; IAEA 2007). The IPlan outlines respective responsibilities of the International Organizations and their collaboration under the existing international arrangements coordinated by the International Atomic Energy Agency (IAEA). In the field of radiation emergency, WHO and IAEA work together in a coordinated manner according to the bilateral agreement between the two agencies, with WHO having the primary responsibility for public health preparedness and response, including prevention, intervention, and long-term mitigation and follow-up components as applicable to human health.

International Health Regulations and radiation emergencies

In 2007, another significant event occurred: The revised International Health Regulations (IHR) came into force. Before revision, the IHR covered few types of infectious diseases. As a result of the revision, the IHR were extended to include other types of public health emergencies, including any infectious disease outbreaks, natural disasters, and chemical and radiation emergencies that represent a potential threat to public health. The IHR are a formal agreement for all 193 member states of WHO and were adopted at the World Health Assembly in 2006 in the context of global preparedness against pandemic influenza. They were then extended and revised, according to instructions transmitted to WHO by member states, and the final draft was established by negotiation among the member states themselves.

The revised IHR came into force on 15 June 2007. They constitute a legally binding framework at the global level, leading to international cooperation for preparedness, notification, alert and efficient response to public health emergencies of all kinds. They include detailed instructions for national capacity evaluation, IHR implementation, monitoring, and reporting. The responsibility for adequate resource mobilization is placed both on governments and on WHO.

Radiation emergency scenarios included under the scope of the revised IHR provide an additional impulse to WHO’s role and involvement in assisting countries to strengthen their preparedness for this specific type of emergency. This is being implemented through an all-hazard approach to the development of tools and recommendations for the member states for assessing their health care systems’ preparedness (e.g., national hospital and laboratory resources surge capacity, partnerships and networking), identifying and closing gaps, and monitoring the efficiency of implemented measures.

BIODOSIMETRY AND RESPONSE TO RADIATION EMERGENCIES

In radiological or nuclear accidents/incidents, one of the main public health management issues is emergency triage allowing assessment of the number of over-exposed persons as well as the severity of each person’s exposure. If this can be done quickly, potential patients can be further triaged in hospitals in an efficient and timely manner, and best available treatment strategies may be selected for those affected. Hence human lives may be saved. This is especially relevant for countries with limited resources with regard to hospital and laboratory capacity, national stockpiles of radiation injury treatment-specific agents, and generic agents for supportive care, so accurate triage and diagnosis will allow a more efficient allocation of those scarce resources.

For management of those exposed to low doses and those worried-well, cytogenetic dosimetry also plays an important role in assessing their risk for reassurance purposes and mitigation of the psychological impact of a radiation emergency. Hence, biodosimetry is instrumental for the management of radiation emergencies; however, substantial technical difficulties stand in the way of rapid triage of radiation emergency victims. These gaps include: 1) lack of a universal technique applicable to various types of radiation and pathways of exposure; 2) the need to combine and optimize the methods for rapid population triage in emergencies; 3) the need for non-invasive, portable, and sensitive techniques; 4) lack of standard protocols for multi-parameter dosimetry-based decision-making (i.e., combining clinical dosimetry-based findings of biological and physical dosimetry) for best treatment strategy choice; 5) low throughput of any

given laboratory alone and limited surge capacity for biodosimetry laboratory services in a given region or a country; and 6) lack of trained personnel and resources, including the stockpile of consumables.

Nevertheless, in supporting the decision-making process for medical and public health response management, dose assessment remains one of the principal tools. This is accomplished through various means, including biological and physical dosimetry as well as observation and recording of clinical symptoms development, use of scenario-based dose reconstruction models and integrated multi-parameter dosimetry combining clinical observations with other dosimetry methods. Hence, dosimetry in general and biodosimetry in particular are important decision-making support tools for the management of victims of radiation emergencies.

Most biodosimetry techniques require several hours, or even days, before yielding results. For example, conventional cytogenetic approaches usually require cultivating a blood sample for 48 h, followed by harvesting the metaphase cells and scoring chromosomal aberrations. This is a labor-intensive task, because automation of metaphase-finding and aberrations-scoring is not yet widely available and cannot be carried out by common cytogenetic laboratory personnel unless appropriately trained. When hospital or clinical cytogenetic laboratories drop their day-to-day work (usually related to genetic counseling) and apply their existing capacity to the emergency at hand, they are unable to increase their throughput without a reduction in quality control. Therefore, the best way to increase performance at short notice is to increase surge capacity through networking with laboratories situated further afield, using protocols which have been agreed upon beforehand for achieving consistent results across the laboratories participating in a network. Among WHO BioDoseNet’s priority tasks is harmonizing the sample preparation, which would assure the consistency of results across the network. This may have been done already in some countries or groups of countries; however, the surge capacity for biodosimetry services in most parts of the world remains insufficient for a large-casualty event.

CYTOGENETIC LABORATORY SURVEY

In 2007, WHO carried out a survey with the purpose of preliminary evaluation of the cytogenetic laboratory capabilities in selected countries. The results of the survey are reported elsewhere (Blakely et al. 2009). The survey proved there was a vast array of untapped resources, and an enormous opportunity was seen in joining these laboratories in a global network that would provide streamlining of efforts towards combining the cytogenetic laboratory services. All 33 laboratories participating in the survey expressed interest in joining a future network. This survey pointed to robust global capability with a clear lack of global leadership and coordination.

2007 GENEVA CONSULTATION

Within this framework, in December 2007, an expert consultation with the leading experts in cytogenetic dosimetry and health security was convened at WHO Headquarters in Geneva, Switzerland. The expert group recommended WHO to facilitate establishment of a global biodosimetry network and decided to focus on cytogenetic laboratories using the “gold standard” biodosimetry method—dienetic assay—with the capacity to provide dose data for radiation disasters. The experts present at the meeting formulated the general scope and framework for the development of the WHO global biodosimetry laboratory network for radiation emergencies. They suggested what the structure of the network might be and defined the respective roles of core, reference, and associate labs in emergencies and during “quiet” time.

The specific recommendations of the meeting were:

- to set up the WHO biodosimetry laboratory services network—BioDoseNet;
- to focus on cytogenetic labs first, further expanding to electron paramagnetic resonance (EPR), radionuclide bioassay, and molecular biomarkers in the future;
- to start with the “gold standard” dienetic assay in both triage and precise-dose-estimation mode; and
- to use the new ISO-21243 report on cytogenetic assessment in radiological mass casualty events as a basis for cytogenetic triage protocol (ISO 2008).

THE ROLE OF WHO BIODOSENET IN ASSISTING RADIATION EMERGENCY MANAGEMENT

BioDoseNet is an agent-specific biodosimetry branch of the WHO Global Laboratory Services Network (GLaDNet). BioDoseNet was formally launched on 7 September 2008 during the first coordination and planning meeting held at Dartmouth University in Hanover, NH, that brought together 30 cytogenetic laboratories—or cytogenetic laboratory networks—in Asia, Australia, Europe, and North and South America.7 The project includes a global cytogenetic dosimetry laboratories network, which will support the implementation of

the International Health Regulations with regard to strengthening the capacity of member states for management of large radiation emergency events when the capacity of any given country alone to process blood samples will be overwhelmed. Another objective for WHO BioDoseNet is to expand toward inclusion of other methods of dosimetry and harmonization of standards for multi-parameter dosimetry, since unified standards are lacking at the global level.

WHO BioDoseNet is building on several existing regional cytogenetic biodosimetry networks that are collaborating with WHO, notably the North American, Latin American (the network set up with the support of IAEA regional Technical Cooperation project), Western European, Scandinavian, former Soviet states, Western Pacific and Southeast Asian regional networks.

The ultimate goal of WHO BioDoseNet is to provide dose assessment capacity for management of mass casualty radiation emergency events by using methods such as cytogenetics, EPR, radionuclide contamination bioassays, and molecular biomarkers. In the absence of emergencies, a major focus of the network’s activities will be on capacity building through exercise and training. Special attention will be paid to large international inter-laboratory comparison studies that will be conducted to ensure consistency and compatibility of the biodosimetry methods used by laboratories participating in the network. Such cooperation will be coordinated by WHO, acting as the network’s secretariat. The member laboratories will have a common framework of protocols not only for dose assessment, but also for communication and reporting during an emergency, sample selection criteria, labeling and shipment, etc. Based on the “cytogenetic” model of BioDoseNet, other types of acute dosimetry labs will be identified in the future and invited to join the WHO BioDoseNet.

REFERENCES


