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# Population Monitoring for Acute Exposure to $^{210}\text{Po}$

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## Learning Objectives

- Compare the distribution of ingested or inhaled radioactive polonium ( $^{210}\text{Po}$ ) with that of other alpha-emitting radionuclides such as uranium and plutonium.
- Recall the urinary detection limit for urinary  $^{210}\text{Po}$  activity and the minimal intake predicted to result in clinically significant effects.
- Conclude whether analysis of single 50-mL void urine samples will reliably identify those individuals who may have been exposed following the intentional dispersal of  $^{210}\text{Po}$ .

## Abstract

**Objective:** To investigate the feasibility of using single void urine samples to monitor internal radiation exposure of first responders and large populations in the event of a radiological incident involving the intentional dispersal of  $^{210}\text{Po}$ .

**Methods:** Urinary excretion of  $^{210}\text{Po}$  was evaluated and organ absorbed and effective doses were calculated subsequent to an acute unit intake of  $^{210}\text{Po}$ .

**Results:**  $^{210}\text{Po}$  can be detected in single void urine samples at levels sufficient to detect effective dose below recommended limits. Minimum intakes of  $^{210}\text{Po}$  that would result in clinically significant effects were estimated. **Conclusions:** Collection and analysis of single void urine samples is adequate to identify persons who may be exposed in the event of a radiological emergency involving  $^{210}\text{Po}$ . Also, the first responder limit appears to be sufficiently protective to prevent clinically significant deterministic effects. (J Occup Environ Med. 2008;50:916–923)

An international radiological incident involving an unknown substance containing a large quantity of the radioactive isotope  $^{210}\text{Po}$  occurred in November 2006 resulting in the rapid death of one person and contamination of several other individuals.<sup>1,2</sup> As a result,  $^{210}\text{Po}$ , a relatively short-lived, alpha-emitting radionuclide, is now recognized as a potential source of acute internal exposure, should it become widely dispersed in a radiological incident.

Ingested or inhaled  $^{210}\text{Po}$  is unique among internal alpha emitters in that, once it passes from the lung or gastrointestinal (GI) tract and enters the systemic circulation (ie, blood), it deposits primarily in soft tissues with higher concentrations in blood cells, spleen, and kidneys.<sup>3</sup> Thus, the distribution of  $^{210}\text{Po}$  in the body is very different from other alpha emitters, such as plutonium and uranium, which primarily concentrate on bone surfaces.

Deterministic effects associated with acute radiation syndrome (ARS) are a series of clinical observations that describe the response of biological systems when the whole body, or a large part of the body, is exposed to ionizing radiation.<sup>4–7</sup> The symptoms and severity of these effects depend primarily on the magnitude of the dose and the organs that have been exposed.<sup>4</sup> Studies of persons acutely exposed to external radiation, such as atomic bomb survivors, Chernobyl first responders, and workers involved in criticality accidents have provided increasing knowledge about the conditions necessary for onset of ARS due to radiation exposure from an external source. In con-

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trast, most of our knowledge about biological response after comparable doses of alpha-emitting radioactive materials has been obtained from research studies with animals.

Current radiation protection standards regarding the intake of radionuclides consider the risks associated with both the immediate onset of deterministic effects and potential for latent effects (ie, cancer). In many cases, separate occupational exposure limits have been established for deterministic and stochastic effects. Biokinetic models are used to predict deposition and retention of radioactive material that enters the systemic circulation. A separate mathematical model is used to predict how much ingested radioactive material enters the systemic circulation (ie, a GI tract model or more recently, the human alimentary tract model). Another mathematical model is used to predict how much inhaled radioactive material is retained in the lungs, absorbed into the systemic circulation or transferred to the GI tract (ie, lung model). The amount of radioactive material expected to be excreted in urine or feces can be estimated using these models. It is conventional practice to determine compliance with occupational exposure limits by monitoring the quantity of radioactivity in excreta from persons with potential for internal exposure to radioactive material. It is expected that such monitoring would also be conducted for first responders and members of the public who are potentially exposed after an intentional dispersal of radioactive material.

The purpose of this article is to develop guidance for clinicians and health providers who may be called upon to monitor large populations for potential exposure to  $^{210}\text{Po}$  in the event of mass contamination resulting from intentional dispersal to the environment or food and/or water supplies. Ingestion via contaminated food/water supply is considered a likely route of intake as demonstrated by the recent poisoning incident.<sup>1</sup> This article also evaluates the current ex-

posure limits for first responders to determine whether these limits are sufficiently protective against deterministic effects from internal exposure to  $^{210}\text{Po}$ .

Readers who desire comprehensive and detailed information on acute toxicity and biokinetics of  $^{210}\text{Po}$  are referred to Stannard and Casarett,<sup>8</sup> Leggett and Eckerman,<sup>9</sup> Harrison et al,<sup>1</sup> and Scott.<sup>2</sup> An exhaustive discussion of the relative biological effectiveness (RBE) of alpha particles is beyond the scope of this article.

## Materials and Methods

IMBA Expert™ ORAU Edition (ACJ and Associates and Health Protection Agency, Radiation Protection Division (HPA). Incorporating HPA's IMBA Suite ©1997–2005. IMBA Expert ORAU Edition © 2000–2005.) (IMBA), a computer program for calculating intakes and organ doses from internally deposited radioactive materials, was used to predict the daily excretion of  $^{210}\text{Po}$  in urine and to estimate organ doses associated with an acute intake of  $^{210}\text{Po}$  via inhalation or ingestion. IMBA uses the polonium biokinetic model described by the International Commission on Radiological Protection (ICRP) in Publication 67.<sup>10</sup> The predicted urinary excretion of  $^{210}\text{Po}$  (Bq per day) was determined subsequent to a unit acute intake of  $^{210}\text{Po}$  via inhalation (type F and M) and ingestion. Comparison of the measured excretion of  $^{210}\text{Po}$  with the predicted excretion per unit intake can be used to determine the quantity of  $^{210}\text{Po}$  inhaled or ingested by a potentially

exposed individual. Uncertainty in the estimated intakes was evaluated using Monte Carlo methods.

Table 1 shows the whole body external radiation absorbed doses,  $D_{\text{body}}$ , at which the different subtypes of ARS may be observed.<sup>6,7</sup> Absorbed dose, which is the energy absorbed per unit mass, is defined in terms that allow it to be specified at a point, but it is used by the ICRP in Publication 60<sup>11</sup> to mean the average dose over a tissue or organ. The ICRP states that the average absorbed dose is not directly relevant to deterministic effects unless the dose is fairly uniformly distributed over the tissue or organ because the dose-response relationship is not linear for deterministic effects.<sup>11</sup> For radiation protection purposes, the ICRP uses the equivalent dose which is the absorbed dose over a tissue or organ (rather than a point) weighted based on the RBE of the radiation. The equivalent dose is then further weighted based on the contribution of the organ or tissue to the total detriment due to these effects resulting from uniform irradiation of the whole body.<sup>11</sup> These doubly weighted organ absorbed doses are summed to produce an effective dose which represents the combination of different doses to several different tissues and organs that correlates with the total of stochastic effects.

The damage to tissue by ionizing radiation is the same regardless of the type of radiation, although the degree of damage varies with the effectiveness of the radiation (ie, RBE).<sup>12</sup> Just as certain tissues or

**TABLE 1**  
Whole Body Absorbed Doses,  $D_{\text{body}}$ , at Which ARS May Be Observed

$D_{\text{body}}$ (Gy)*	ARS Subtype	Effect
0.50	Blood changes (BC)	Mild depression of lymphocyte count
2	Hematopoietic syndrome (H)	Bone marrow depression to ablation
10	Gastrointestinal syndrome (GI)	Desquamation of intestinal epithelium, death likely
20	Central nervous system syndrome (CNS)	Unconsciousness, death

\*Dose refers to whole body absorbed dose from external radiation source.

organs are associated with the probability of certain cancers (eg, irradiation of the bone marrow may result in leukemia), different organs and organ systems are associated with the different syndromes that make up ARS (eg, irradiation of the bone marrow causes hematopoietic syndrome). Direct and indirect damage of tissue in select organ systems gives rise to a generalized systemic disease. In addition, organs that participate in the response to the damage, such as the bone marrow, kidney, and liver, are also damaged.<sup>12,13</sup> The spleen also has lymphatic tissue that can compensate for bone marrow depression after acute radiation exposure.<sup>14</sup>

It is proposed here that the systemic response of the organism to internally deposited radiation is a function of the combined effects of the exposed tissues. It is assumed that the sum of absorbed doses to organs associated with the syndromes of ARS (red bone marrow, small intestine and colon, brain) and the doses to organs critical to the response (kidneys, spleen, and liver) is proportional to the whole body dose sufficient to induce the subtypes of ARS. The red bone marrow, small intestine and colon, and brain are assumed to be the critical organs in the hematopoietic, GI, and central nervous system syndromes, respectively. Organ absorbed dose conversion factors,  $DCF_i$ , due to an acute unit ingestion of  $^{210}\text{Po}$  were calculated for kidneys, spleen, liver, bone marrow, small intestine, colon, and brain and cumulated for 20 days. The quantity of ingestion intake,  $I_j$ , was determined that produces summed organ absorbed doses,  $D_{abs}$ , equal to the threshold doses,  $D_{\text{body},j}$ , for induction of each of the four subtypes,  $j$ , of ARS.

$$I_j = \frac{D_{\text{body},j}}{\sum_i DCF_i} \quad (1)$$

and

$$D_{\text{abs},i} = I_j \cdot DCF_i \quad (2)$$

$^{210}\text{Po}$  is tightly bound to hemoglobin proteins in blood and is transported to all tissues of the body similar to the manner in which hemoglobin transports oxygen to and carbon dioxide from tissues.<sup>15</sup> Organ and tissue damage may occur via radiation injury to vascular endothelial cells, with greater damage expected in well-vascularized tissues.<sup>16</sup> Therefore, it is also proposed that the organ absorbed doses should be weighted according to organ vascularity, blood volume, or blood flow rate. Blood flow rates (BFR) as a percentage of cardiac output<sup>17</sup> for each of the organs of interest were summed and normalized to unity creating a weighting factor,  $w$ , for each organ,  $i$ .

$$w_i = \frac{BFR_i}{\sum_i BFR_i} \quad (3)$$

The  $DCF_i$  were multiplied by the appropriate BFR weighting factor,  $w_i$ , and then summed to determine the quantity of ingestion intake,  $I_j$ , that produces summed weighted organ absorbed doses equivalent to the threshold doses,  $D_{\text{body},j}$ , for induction of each of the four subtypes,  $j$ , of ARS

$$I_j = \frac{D_{\text{body},j}}{\sum_i DCF_i \cdot w_i} \quad (4)$$

and

$$D_{\text{abs},w,i} = I_j \cdot DCF_i \cdot w_i \quad (5)$$

Systemic uptakes ( $\text{MBq kg}^{-1}$ ) were calculated from the ingestion intakes and compared to animal toxicity data.

Other than the recent poisoning case,<sup>1,2</sup> the only reported incidence of fatality from internal exposure to  $^{210}\text{Po}$  was reported by Gasteva.<sup>18</sup> The case involved acute inhalation of a  $^{210}\text{Po}$  aerosol of unknown particle size distribution and solubility and the individual died 13 days after the incident. Absorbed organ doses from inhalation were calculated using IMBA and default parameters for the

lung model described in ICRP Publication 66.<sup>19</sup> Values for absorption type and particle size were adjusted to match predicted urinary and fecal excretion rates reported by Gasteva. The quantities of inhaled  $^{210}\text{Po}$  that would result in clinically significant effects were also calculated.

The US Department of Homeland Security<sup>20</sup> has adopted a 50-year committed effective dose limit of 250 mSv for emergency first responders. IMBA was used to determine the quantity of  $^{210}\text{Po}$  activity taken into the body via ingestion or inhalation that would deliver an effective dose equal to 250 mSv. The ICRP 66 lung model<sup>19</sup> and tissue and radiation weighting factors recommended in ICRP Publication 60<sup>11</sup> were adopted for these calculations. The calculated intakes were compared to animal toxicity data and the quantity of activity estimated to induce subtypes of ARS to determine whether 250 mSv is a sufficiently protective dose limit to prevent the occurrence of ARS in emergency first responders.

## Results

Predicted excretion of  $^{210}\text{Po}$  in urine for up to 30 days after acute exposure to 1 Bq of  $^{210}\text{Po}$  via inhalation or ingestion is shown in Fig. 1. For comparison, the expected excretion of  $^{210}\text{Po}$  in urine from natural sources in diet is also included in Fig. 1 for smokers and nonsmokers. The ICRP reference man<sup>21</sup> is assumed to ingest approximately 0.12 Bq  $\text{d}^{-1}$  of  $^{210}\text{Po}$  in food and water. Note that these values are subject to day-to-day variability and are very dependent upon diet.

Excretion of  $^{210}\text{Po}$  in a 24-hour sample of urine on any day postexposure to 1 Bq is predicted by the three curves in Fig. 1 which can be used to estimate the level of acute intake if the suspected date of exposure is known. Population monitoring after a radiological incident will likely involve collecting single void samples of urine that require rapid analysis so that results can be reported to authorities with little delay,

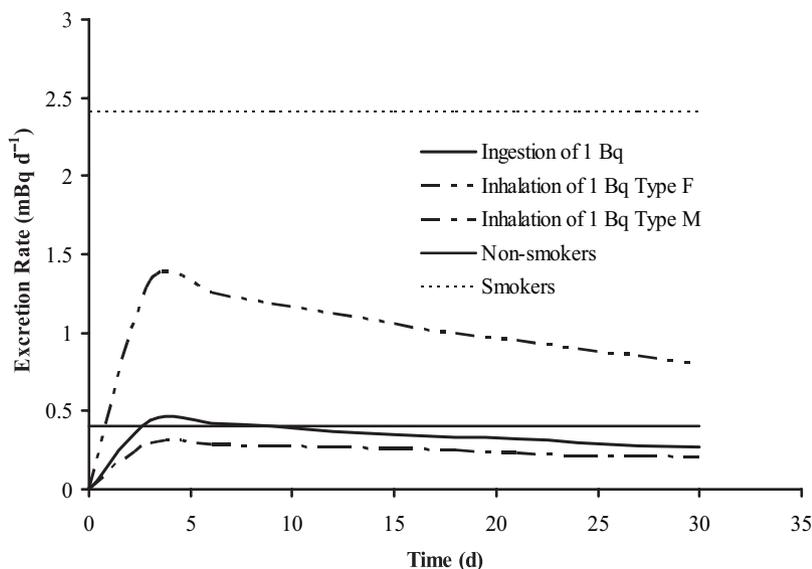


Fig. 1. Urine excretion after acute exposure to 1 Bq of <sup>210</sup>Po. Also shown are the background urine excretion levels of <sup>210</sup>Po for nonsmokers and smokers (ICRP 1975).

should remedial actions or countermeasures be required. Using the method of spontaneous deposition and alpha spectrometry, the detection limit for <sup>210</sup>Po in a single void (50 mL) sample of urine is approximately 20 mBq which equates to 640 mBq of <sup>210</sup>Po excreted per day determined by normalizing the single void urine sample volume to 1.6 L d<sup>-1</sup>. According to Fig. 1, between 3 and 9 days postintake, the urine excretion rate per Bq intake is about 0.3 mBq d<sup>-1</sup> (type M inhalation), 0.4 mBq d<sup>-1</sup> (ingestion), and 1.2 mBq d<sup>-1</sup> (type F inhalation). Table 2 shows the minimum intakes and effective doses that can be confirmed if single void urine samples are collected within a few days postexposure. For inhalation of a type F material or ingestion, the minimum detectable effective dose is less than 1 mSv, which

is the annual dose limit for members of the public recommended by the ICRP.<sup>11</sup> For inhalation of a type M material, the minimum detectable effective dose is about 5 mSv.

Table 2 also shows the 90% confidence interval (CI) for the calculated minimum detectable intakes and effective doses evaluated using Monte Carlo analysis to propagate uncertainty. It was assumed that the uncertainty associated with the various models used to interpret a urine sample result followed a lognormal distribution with a geometric standard deviation of 1.6.<sup>22</sup> Additional uncertainty is introduced by the normalization factor (1.6 L d<sup>-1</sup>), which was estimated using data provided by studies of 24-hour voiding among asymptomatic men and women.<sup>23,24</sup> If the 24-hour excretion volume of

urine varies lognormally, then median and 95th percentile 24-hour urine volumes for 137 women and 284 men can be used to determine a geometric standard deviation of 1.6.

Calculated organ absorbed DCF for ingestion are shown in Table 3. BFR as a percentage of cardiac output for each of the organs of interest are also shown in Table 3 as well as the calculated normalized weighting factors.

Table 4 shows the quantities of <sup>210</sup>Po activity ingested that result in the summed weighted organ absorbed doses that are predicted to result in subtypes of ARS. Organ absorbed doses do not account for the RBE of alpha radiation. The limited time period adopted for cumulating absorbed dose is similar to that experienced by an acutely exposed person (ie, ~20 days) who died from complications associated with ARS as a result of exposure to <sup>210</sup>Po.<sup>1</sup> For comparison, the systemic burden that results in 50% lethality for Sprague-Dawley rats at 20 days<sup>25</sup> is 1.3 and 1.6 MBq kg<sup>-1</sup> for women and men, respectively, which is equivalent to an uptake of 90 to 110 MBq for a 73-kg man and an ingested amount of 900 to 1100 MBq, assuming a fractional absorption from the GI tract of 0.1. The summed weighted organ absorbed dose is 16–19 Gy, which is above the threshold whole body absorbed dose predicted to result in GI syndrome. The body burden which gives a summed weighted organ absorbed dose of 0.5 Gy (0.04 MBq kg<sup>-1</sup>), the threshold whole body external dose for blood changes, is within the range of body burden (0.04 to 0.4 MBq kg<sup>-1</sup>) that has been observed to result in temporary reduction of white blood cells in animals.<sup>1</sup>

Gasteva<sup>18</sup> estimated an inhalation intake of approximately 110 MBq for the reported <sup>210</sup>Po fatality case. Retention in the lung and whole body at death (day 13) was estimated to be about 13 MBq and 100 MBq, respectively, suggesting rapid and relatively complete absorption similar to that of a compound assigned to Absorption type F using ICRP criteria.<sup>26</sup> Measured urine and fecal ex-

TABLE 2

Minimum Detectable Intakes and Doses Following Inhalation or Ingestion of <sup>210</sup>Po Based on the Predicted Excretion of 1 Bq Between 3 and 9 d and a Detection Limit of 20 mBq in a Single Void Urine Sample

Type Intake	Median Minimum Predicted Intake (90% CI) (Bq)	Median Minimum Predicted Effective Dose (90% CI) (mSv)
Ingestion	1600 (550–4800)	0.39 (0.14–1.2)
Inhalation (type F)	530 (62–1600)	0.39 (0.13–1.2)
Inhalation (type M)	2300 (770–6700)	4.9 (1.7–15)

The 5th and 95th percentile intakes and doses were determined by Monte Carlo methods.

**TABLE 3**

Calculated Organ Absorbed Dose Conversion Factors (*DCF*) and Blood Flow Rates (*BFR*), as a Function of Percent Cardiac Output (From Leggett and Williams 1995) Used to Calculate Normalized Weighting Factors (*w*) for Deterministic Detriment

Organs ( <i>i</i> )	Dose Conversion Factors ( <i>DCF<sub>i</sub></i> ) (Gy MBq <sup>-1</sup> )	Blood Flow Rates ( <i>BFR<sub>i</sub></i> ) (% Cardiac Output)	Normalized Weighting Factors ( <i>w<sub>i</sub></i> )
Kidneys	0.0375	19.0	0.33
Spleen	0.0323	3.0	0.05
Liver	0.0194	6.5	0.11
Red bone marrow	0.0078	3.0	0.05
Colon	0.0024	4.0	0.07
Small intestine	0.0010	10.0	0.17
Brain	0.0008	12.0	0.21

Calculated *DCF*s are cumulative average absorbed dose to the organ at 20 d after an acute ingestion intake.

**TABLE 4**

Quantities of  $^{210}\text{Po}$  Activity ingested and the Resulting Weighted Organ Absorbed Doses,  $D_{abs,w}$ , at 20 d That are Predicted to Result in ARS Subtypes Based on the Summed Weighted Organ Doses

Syndrome	BC	H	GI	CNS	LD <sub>50(20)</sub> Females	LD <sub>50(20)</sub> Males
Threshold dose of syndrome (Gy)	0.5	2	10	20		
Ingestion intake (MBq)	29	116	582	1164	913	1132
Systemic uptake* (MBq)	3	12	58	116	91	113
Body burden† (MBq kg <sup>-1</sup> )	0.04	0.2	0.8	1.6	1.3‡	1.6‡
$D_{abs,w}$ (Gy)						
Kidneys	0.36	1.44	7.21	14.42	11.31	14.03
Spleen	0.05	0.20	0.98	1.96	1.54	1.91
Liver	0.06	0.25	1.28	2.55	2.00	2.48
RBM	0.01	0.05	0.24	0.47	0.37	0.46
Colon	0.00	0.02	0.10	0.19	0.15	0.19
SI	0.00	0.02	0.10	0.20	0.16	0.19
Brain	0.01	0.02	0.10	0.21	0.16	0.20
Sum of doses	0.5	2	10	20	16	19

Organ absorbed doses due to systemic uptake that results in lethality predicted from animal toxicity studies are also shown.

\*Fractional uptake from the GI tract was assumed to be 0.1.

†Calculated for a 73-kg man.

‡Data for Sprague-Dawley rats reported in Cowden (1952).

cretion rates averaged over days 10 to 12 postexposure were 0.41 and 0.55 MBq d<sup>-1</sup>, respectively. IMBA was used with the ICRP 66 lung model and ICRP 67 polonium biokinetic model to predict excretion of  $^{210}\text{Po}$  in urine and feces averaged over days 10 to 12 postintake. For an intake of 110 MBq of a rapidly absorbed (type F) compound, and default deposition parameters (5- $\mu\text{m}$  aerosol), the average excretion rates were predicted to be 0.13 and 0.26

MBq d<sup>-1</sup>, respectively. The predicted and observed excretion rates are relatively consistent considering the uncertainties associated with the models and the severely impaired health of the exposed worker. If a larger intake of 290 MBq is assumed, predicted urine and fecal excretion rates averaged 0.33 and 0.69 MBq d<sup>-1</sup>, respectively, which is closer to the reported excretion rates for the exposed worker. Table 5 shows the organ absorbed *DCF*s cumulated for

13 days, and the weighted and summed organ doses for each of the two intake levels. Table 6 shows the quantities of inhaled  $^{210}\text{Po}$  that result in the summed weighted organ absorbed doses that are predicted to result in subtypes of ARS. Quantities are calculated for both a type F and type M material.

As shown in Table 7, the quantity of  $^{210}\text{Po}$  activity ingested that produces a committed (50-year) effective dose equal to 250 mSv is 1.02 MBq, which is considerably less than the amount (29 MBq) predicted by the proposed model to result in clinically significant effects (Tables 4 and 6). Less activity is needed via the inhalation pathway to produce a 250 mSv effective dose. This is because of the more complete absorption in the lung in the case of type F material compared to the GI tract. In the case of type M material, higher retention in the lung results in a higher equivalent dose to the lung which is heavily weighted relative to other organs in the calculation of effective dose.

## Discussion

Deterministic effects after exposure to radiation are those effects for which above a certain threshold dose the response is certain, with an intensity that is directly related to the dose.<sup>7,27</sup> The existence of a threshold is a result of the ability of many organs and tissues to exhibit adequate function after the loss of substantial numbers of cells. Nevertheless, if enough cells are damaged, there will be observable loss in tissue or organ function.

There is currently no model to address deterministic effects from internal exposure to radionuclides. For stochastic effects, the ICRP uses average absorbed dose to predict risk based on the linearity of the dose-response relationship and the assumption of a linear-no-threshold dose-response relationship at doses less than 100 mSv.<sup>11</sup> Total detriment to health (or risk) from stochastic effects is determined using a doubly weighted absorbed dose, where weighting is based on radiation qual-

**TABLE 5**  
Organ Absorbed Dose Conversion Factors,  $DCF_i$ , at 13 d After an Acute Inhalation Intake of a Type F  $^{210}\text{Po}$  Compound

Organs	Absorption			
	Type F	Type M	Type F	
	$DCF_i$ (Gy MBq <sup>-1</sup> )		$D_{abs,w}$ (Gy), Intake = 110 MBq	Intake = 290 MBq
Kidneys	0.0757	0.0174	2.75	7.26
Spleen	0.0652	0.0149	0.37	0.99
Liver	0.0392	0.0090	0.49	1.28
Red bone marrow	0.0157	0.0036	0.09	0.24
Colon	0.0021	0.0010	0.02	0.04
Small intestine	0.0018	0.0005	0.03	0.09
Brain	0.0017	0.0004	0.04	0.11
Sum			3.8	10

BFR-weighted (see Table 3) organ absorbed doses,  $D_{abs,w}$ , for two intake levels estimated from the Gasteva (2001) data are also shown.

**TABLE 6**  
Quantities of  $^{210}\text{Po}$  Activity Inhaled and the Resulting Weighted Organ Absorbed Doses,  $D_{abs,w}$ , at 13 d That are Predicted to Result in ARS Subtypes Based on the Summed Weighted Organ Doses

Syndrome	BC		H		GI		CNS	
Threshold dose of syndrome (Gy)	0.5		2		10		20	
Absorption type	F	M	F	M	F	M	F	M
Inhalation intake (MBq)	14	63	58	251	290	1254	580	2509
$D_{abs,w}$ (Gy)								
Kidneys	0.35	0.36	1.45	1.44	7.26	7.21	14.51	14.43
Spleen	0.05	0.05	0.20	0.20	0.99	0.97	1.97	1.95
Liver	0.06	0.06	0.26	0.26	1.28	1.28	2.57	2.55
RBM	0.01	0.01	0.05	0.05	0.24	0.24	0.48	0.47
Colon	0.00	0.00	0.01	0.02	0.04	0.09	0.08	0.17
SI	0.00	0.01	0.02	0.02	0.09	0.11	0.18	0.22
Brain	0.01	0.01	0.02	0.02	0.11	0.10	0.21	0.21
Sum of doses	0.5	0.5	2	2	10	10	20	20

Intakes and doses for both absorption Type F and M are shown.

**TABLE 7**  
Quantities of  $^{210}\text{Po}$  Ingested or Inhaled That Result in Committed (50-yr) Effective Dose of 250 mSv

Type of Intake	Ingestion	Inhalation, Type F	Inhalation, Type M
Intake Amount (MBq)	1.02	0.343	0.116
	Absorbed Dose (Gy)		
Kidneys		0.130	0.0132
Spleen		0.112	0.0113
Liver		0.067	0.0068
Red bone marrow (RBM)		0.027	0.0027
Colon		0.004	0.0004
Small intestine (SI)		0.003	0.0003
Brain		0.003	0.0003

Absorbed doses (unweighted) for organs considered relevant in ARS are also shown. Absorbed doses do not account for RBE of alpha radiation.

ity and the relative contribution of an individual organ or tissue to the total detriment.

Similar reasoning is proposed by the authors to address a new model to predict the occurrence of deterministic effects from internal exposure. First, it is reasonable to use the average absorbed dose to an organ or tissue because the dose-response relationship may indeed be linear if one is considering cellular or tissue response other than clonogenic survival.<sup>16</sup> Also, detriment to organs or tissue is likely due to damage to the vascular endothelium.<sup>16,28,29</sup> Recent research has shown that radiation damage to the microvascular endothelium is the primary lesion in the pathogenesis of the GI syndrome.<sup>30</sup> Another study showed that hematopoietic recovery and survival of lethally irradiated mice is mediated by transplantation of primary endothelial cells.<sup>31</sup>

Animal toxicity studies have indicated hemorrhagic syndromes in animals injected with  $^{210}\text{Po}$ .<sup>32</sup> Gasteva<sup>18</sup> described the symptoms in a worker acutely exposed to  $^{210}\text{Po}$  that included vomiting within 5 to 6 hours after the exposure, epigastric pains, dyspnea, headache, and excitation. By the 6th day, there was general hemorrhagic syndrome, although platelet counts were relatively high, indicating injury of the microcirculatory network (capillaries). Prolonged retention of  $^{210}\text{Po}$  in the blood apparently caused secondary dystrophy of the liver and kidneys (discovered at autopsy). The clinical presentation of this patient is quite similar to that of other workers who received lethal doses of external ionizing radiation.<sup>4,12,13</sup>

Organ and tissue injury due to damage to the microcirculation (capillary system) such as reported by Gasteva<sup>18</sup> is not addressed in current dosimetry models, although evidence suggests that this damage may play a significant role in initiating local and systemic responses that could lead to multiorgan failure such as is seen in ARS. The model proposed in this article is reasonable in that it utilizes the average absorbed dose, a well-

known quantity that can be calculated relatively easily, and applies a weighting factor which represents the relative contribution of that organ or tissue to the total detriment due to these effects resulting from uniform irradiation of the whole body. The choice of the weighting factor is also reasonably based on the relative vascularity of the organ or tissue, which is represented by blood flow rate as a percentage of cardiac output.

## Conclusions

Assessing exposure to  $^{210}\text{Po}$  by measuring the amount excreted in urine is most reliable if 24-hour urine samples are collected because the biological models are based on the amount of activity excreted per day. Nevertheless, in response to a radiological emergency where accuracy may need to be superseded by other civic requirements, it has been shown that analysis of single void urine samples is adequate to identify persons who may be exposed above the recommended public dose limit of 1 mSv for ingestion or inhalation of type F materials. For inhalation exposure to type M material, the minimum detectable dose is about 5 mSv.

The US Department of Homeland Security<sup>20</sup> has issued draft guidance for emergency responders involved in life and property saving activities in the event of a radiological dispersal device or improvised nuclear device incident. The guideline of 250 mSv is intended to “provide assurance that exposure will not result in detrimental deterministic health effects (ie, prompt or acute effects).” The level of intake ( $\leq 1.02$  MBq) that results in a 250 mSv effective dose appears to be below the level of intake (14 MBq) at which deterministic effects may present clinically.

A model has been proposed that can be used to predict deterministic effects from an intake of  $^{210}\text{Po}$  that uses the sum of weighted doses to seven organs/tissues thought to be critical in the pathogenesis of ARS. The choice of weighting factors based on organ/tissue blood flow rate

appears to be reasonable and the model appears to correlate well with animal and human toxicity data. This model should be further examined using experimental animal toxicity data for other radionuclides and different routes of exposure.

## References

- Harrison J, Leggett R, Lloyd D, Phipps A, Scott B. Polonium-210 as a poison. *J Radiol Prot.* 2007;27:17–40.
- Scott BR. Health risk evaluations for ingestion exposure of humans to polonium-210. *Dose-Response.* 2007;5:94–122.
- Stannard JN. Distribution and excretion of polonium-210. I. Comparison of oral and intravenous routes in the rat. *Radiat Res.* 1964;(suppl 5):49–59.
- Hempelmann LH. The acute radiation syndrome. *Med Radiogr Photogr.* 1953;29:42–46.
- Anno GH, Baum SJ, Withers HR, Young RW. Symptomatology of acute radiation effects in humans after exposure to doses of 0.5–30 Gy. *Health Phys.* 1989;56:821–838.
- Cember H. Biological effects of radiation. *Introduction to Health Physics.* New York: McGraw-Hill, Inc.; 1992:180–183.
- Alpen EL. Acute lethal response in mammals. *Radiation Biophysics.* New York: Academic Press; 1998:255–263.
- Stannard JN, Casarett GW. Metabolism and biological effects of an alpha particle emitter, polonium-210. *Radiat Res.* 1964;Suppl 5.
- Leggett RW, Eckerman KF. A systemic biokinetic model for polonium. *Sci Total Environ.* 2001;275:109–125.
- International Commission on Radiological Protection. *Age-Dependent Doses to Members of the Public From Intake of Radionuclides: Part 2-Ingestion Dose Coefficients.* Tarrytown, NY: Elsevier Science Inc.; 1994. ICRP Publication 67. Annals of the ICRP 23 (3/4).
- International Commission on Radiological Protection. *1990 Recommendations of the International Commission on Radiological Protection.* Tarrytown, NY: Elsevier Science Inc.; 1991. ICRP Publication 60. Annals of the ICRP 21 (1–3).
- Hempelmann LH, Lisco H, Hoffman JG. The acute radiation syndrome: a study of nine cases and a review of the problem. *Ann Intern Med.* 1952;36:279–510.
- Azizova TV, Semenikhina NG, Druzhenina MB. Multi-organ involvement and failure in selected accident cases with acute radiation syndrome observed at the Mayak Nuclear Facility. *BJR Suppl.* 2005;27:30–35.
- Jacobson LO, Marks EK, Gaston EO, Robson M, Zirkle RE. The role of the spleen in radiation injury. *Proc Soc Exp Biol Med.* 1949;70:740–742.
- Thomas RG. The binding of polonium by red cells and plasma proteins. *Radiat Res.* 1964;(suppl 5):29–39.
- Thomas PA, Tracy BL, Ping T, Wickstrom M, Sidhu N, Hiebert L. Relative biological effectiveness (RBE) of  $^{210}\text{Po}$  alpha-particles versus X-rays on lethality in bovine endothelial cells. *Int J Radiat Biol.* 2003;79:107–118.
- Leggett RW, Williams LR. Suggested reference values for regional blood volumes in humans. *Health Phys.* 1991;60:139–154.
- Gasteva GN. Acute radiation sickness caused by uptake of polonium. In: Gusakova AK, Selidovkin GD, eds. *Human Radiation Injuries.* Moscow: Izdat; 2001:99–103.
- International Commission on Radiological Protection. *Human Respiratory Tract Model for Radiological Protection.* Tarrytown, NY: Elsevier Science Inc.; 1994. ICRP Publication 66. Annals of the ICRP 24 (1–3).
- Department of Homeland Security. Preparedness Directorate-Protective Action Guides for Radiological Dispersal Device (RDD) and Improvised Nuclear Device (IND) Incidents; Notice. *Fed Regist.* 2006;71:174–196.
- International Commission on Radiological Protection. *Report of the Task Group on Reference Man.* Elmsford, NY: Pergamon Press; 1975. ICRP Publication 23.
- Boecker B, Hall R, Inn K, et al. Current status of bioassay procedures to detect and quantify previous exposures to radioactive materials. Bioassay Procedures Working Group. *Health Phys.* 1991;60(suppl 1):45–100.
- Fitzgerald MP, Brubaker L. Variability of 24-hour voiding diary variables among asymptomatic women. *J Urol.* 2003;169:207–209.
- Latini JM, Mueller E, Lux MM, Fitzgerald MP, Kreder KJ. Voiding frequency in a sample of asymptomatic American men. *J Urol.* 2004;172:980–984.
- Cowden RN. Histopathological Study of Sprague-Dawley Rats Injected Intravenously With Varying Amounts of Polonium. MLM-761. Mound Laboratory. Miamisburg, Ohio: Monsanto Chemical Company; 1952.
- International Commission on Radiological Protection. Annexe D. Assignment of Compounds to Absorption Types from Experimental Data. *Age-Dependent Doses to Members of the Public from Intake of Radionuclides: Part 4-Inhalation Dose Coefficients.* Tarrytown, NY:

- Elsevier Science Inc; 1996. ICRP Publication 71. Annals of the ICRP 25 (3–4).
27. Fry RJ. Deterministic effects. *Health Phys.* 2001;80:338–343.
  28. Akashi M. Role of infection and bleeding in multiple organ involvement and failure. *BJR Suppl.* 2005;27:69–74.
  29. Gaugler MH. A unifying system: does the vascular endothelium have a role to play in multi-organ failure following radiation exposure? *Br J Radiol.* 2005; (suppl 27):100–105.
  30. Paris F, Fuks Z, Kang A, et al. Endothelial apoptosis as the primary lesion initiating intestinal radiation damage in mice. *Science.* 2001;293:293–297.
  31. Chute JP, Muramoto GG, Salter AB, et al. Transplantation of vascular endothelial cells mediates the hematopoietic recovery and survival of lethally irradiated mice. *Blood.* 2007;109:2365–2372.
  32. Casarett GW. Pathology of orally administered polonium. *Radiat Res.* 1964; (suppl 5):361–372.