

Piratome sheet #1 "Treatment principles and choice of antidotes"

General principles relative to treatments to initiate in the very 1st hours (<24 hours) for persons presenting with demonstrated or suspected internal contamination, with one or more radionuclides

The key points to remember for the treatment of victims of internal contamination with radionuclides are as follows:

- → Under all circumstances of exposure to nuclear and radiological agents, the medical-surgical emergency (i.e. the extreme urgency requiring a saving surgical procedure) takes precedence over the treatment of contamination and/or irradiation.
- → Emergency treatment, i.e. within 2 hours of contamination, shall be implemented "preventively" for all persons with suspected contamination, as soon as the potential contaminant radionuclides have been identified. Treatment should be initiated as soon as possible, at the site of the event if necessary. This treatment shall also be initiated or continued at the hospital. This therefore implies very rapidly notifying the healthcare establishments to enable them to obtain emergency supplies of the appropriate products. Table A specifies the type of treatment to initiate according to radionuclide (suspected or identified).
- → The biological samples required in the event of internal contamination are not necessarily collected on-site, they must be scheduled in consultation with the national competent authority in radionuclear safety.

In the event of major radionuclide contamination, precautions relative to excreta (urine and stools) samples from patients must be taken based on advice from a radioprotection expert from a nuclear medicine unit.

The present sheet is intended to provide all information required by persons involved in providing care during the early hours following the attack, in order to allow appropriate treatment of victims. In particular, it states the nature of specific treatments to implement according to the radionuclides involved, while non-specific treatments may also be applied, along with the samples to collect in view of evaluating the exposure of victims contaminated by radioactive elements.

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1. Introduction

The potential scenarios for a radiological or nuclear action may be extremely varied and their operational implementation can be more or less complex. They range from simple spreading of radioactive substances, which is particularly easy to carry out, to the dissemination of radioactive sources or dispersion by conventional explosive of large amounts of radionuclides, whether or not in a confined environment ("dirty bomb"), not forgetting more complex scenarios, such as the attack of a reactor building at a nuclear plant, or the theft of a nuclear weapon. These different radiological scenarios have highly varied short and long-term health impacts, with profound effects on the medical, sanitary and psychosocial management of the crisis.

From the medical management standpoint, scenarios may be event-based, with immediate victims in a finite area, requiring deployment of medical emergency services, or insidious, with victims spread out in both space and time, the consequence of which is the major difficulty establishing a diagnosis of epidemic in relation to ionising radiation. In the first case, massive collective damage is probable and the psychosocial effects are immediate. In the second case, massive collective damage is not systematic and societal impact is delayed.

Amongst the event-based scenarios, that of the "dirty bomb" involves burns, injuries and blasts, associated with both external and internal contamination, with immediate threat to life and a long-term risk of appearance of radio-induced cancer in exposed victims. Another possible scenario consists in the dissemination of high-activity radioactive sources, with very different consequences, such as global irradiation resulting, in clinical terms, in the appearance of an acute irradiation syndrome associated with major short and medium-term threat to life, due in particular to the bone marrow failure that is frequently observed in this type of situation.

Amongst the insidious situations, that of radionuclide spreading will result in strict contamination, with a health impact focused on the risk of appearance of long-term radio-induced cancer. Another scenario, that of the dissemination of moderate activity sources with localised irradiation that may or may not be associated with global low-rate irradiation, will result in the progressive appearance of non-life-threatening radiological skin lesions (such as dry or exudative epidermitis for example).

Nevertheless, whatever the considered scenario, two modes of radionuclide exposure must be considered:

- exposure by external irradiation: this occurs when the radioactive source is located in the exposed individual's close or remote environment; depending on the exposure parameters, it may lead to the appearance, in the more or less short-term, to an acute irradiation syndrome that may or may not be associated with radiological skin burns. If exposure by irradiation is pure, *i.e.* not associated with exposure by internal contamination, victims must be treated in a specialist hospital environment: the recommendations given in the present do not therefore apply to this exposure situation;

exposure by internal contamination: this type of exposure occurs when the radioactive source is incorporated into the body of the exposed individual; if not associated with exposure by external irradiation, internal contamination with radionuclides is nearly always initially silent in clinical terms, unless if associated with external contamination by skin contact (skin burns, with possible necrosis of exposed tissues if a decontamination strategy is not implemented, may then be observed in the short to medium-term in this case). In such an exposure situation, contaminated individuals must be identified through the implementation of relevant examinations (anthroporadiometric measurements, radiotoxicological urine and/or stool analyses) and specific or non-specific treatments must be administered to accelerate radionuclide excretion and/or to prevent binding to target organs: the recommendations given in the present apply to this exposure situation.

The internal contamination of individuals following the dissemination of a radioactive source is the result of incorporation of substances into the body in one or more of several manners:

- inhalation of radioactive particles present in the atmosphere and in materials re-hanged after having deposited onto the ground or any other surface;
- ingestion of products contaminated by released radioactive substances: contamination by ingestion is determined by diet, population lifestyle, the proportion of contaminated foods consumed, the extent of food contamination and the manner in which the food is prepared (cooking, for example, may render the radionuclides less bioavailable). The ingestion of radioactive particles may also result from hand contamination by contact with contaminated surfaces (hand carriage);
- penetration into subcutaneous tissues or to the systemic environment following breach of the skin barrier: this mode of incorporation may be particularly important in persons presenting with multiple wounds by polyblasting of solid debris during an explosion;
- skin contamination resulting from skin or clothing deposits of particles present in the atmosphere and/or on surfaces.

Whatever their way of incorporation, radionuclides follow a route within the body that is governed mainly by the route of ingress, but also by the physicochemical properties of the concerned radioactive substances (volatility, water-solubility, ionisation, etc.), their affinity for a given target organ or tissue, their mode of excretion and by individual-specific parameters (age and physiopathological status in particular). Thus, after entering the body, all or part of the radioactive materials will reach, *via* the circulatory or lymphatic systems, one or more transfer or storage compartments, within which it may undergo metabolic modifications before being more or less completely and rapidly excreted via urine and/or stools.

2. <u>Determination of chelator treatment according to the radionuclide in the event of internal</u> <u>contamination</u>

The potential efficacy of chelating agents with respect to the elements is ranked, according to levels of scientific efficacy evidence based on data available in the scientific literature, as follows:

Evidence level I - Chemical chelation: complex stability, affinity constant.

Evidence level II - Efficacy in animals: elimination kinetic, effective dose.

Evidence level III - Efficacy in humans: elimination kinetic, effective dose.

Lack of evidence - possibly lack of data, negative study or contradictory results.

These evidence levels are provided for information purposes, without prejudice to the granting of a marketing authorisation (MA) and must be balanced against the chelating agent's tolerance profile.

When an MA was available, the evidence levels were not re-determined.

French temporary specific authorization (TSA granted by Afssaps) are also mentioned for information.

The chelator's efficacy is determined by the chemical element and is independent of its radioactivity. <u>This table can thus also be used for the decorporation of non-radioactive elements</u>. Radionuclides in brackets are provided for illustrative purposes.

The data concerning DTPA apply to Ca-DTPA (or calcium DTPA), an antidote authorised in France. Zn-DTPA (or zinc DTPA) is also available on other markets and may be used in the same indication. Nevertheless, Ca-DTPA is recommended within the first 24 hours following internal contamination. Beyond this period, the efficacy of the 2 antidotes is comparable, though repeated treatment with Ca-DTPA can lead to a depletion of endogenous zinc, that can be treated by supplementation, contrary to Zn-DTPA.

! Do not confuse dicobalt EDTA and disodium calcium EDTA¹ whose pharmacological properties are different.

RADIONUCLIDES	CHELATOR ANTIDOTES	COMMENTS	LEVELS OF SCIENTIFIC EVIDENCE OF EFFICACY	
Americium (²⁴¹ Am)	Ca-DTPA / cf. Sheet no. 4		MA	
Antimony (¹²² Sb, ¹²⁴ Sb, ¹²⁵ Sb)	DMSA or BAL / cf. Sheet no. 3	* DMSA, with its better tolerance profile than BAL, shall be preferred. In cases where the digestive route is not available, BAL should be used.	DMSA: II	BAL: lack of evidence

¹In France, Ca-EDTA is marketed under the name CALCIUM EDETATE DE SODIUM SERB 5%, solution injectable I.V.

RADIONUCLIDES CHELATOR ANTIDOTES		COMMENTS	LEVELS OF SCIENTIFIC EVIDENCE OF EFFICACY		
Arsenic (⁷⁶ AS)	DMSA or BAL / cf. Sheet no. 3	Cf. comments *	DMSA: III In acute phase	BAL: MA In acute phase	
Bismuth (²⁰⁷ Bi, ²¹⁰ Bi)	BAL or DMSA /cf. Sheet no. 3		DMSA: III	BAL: II	
Cadmium (¹⁰⁹ Cd)	BAL or DMSA /cf. Sheet no. 3	BAL is an efficient chelating agent, though it aggravates the nephrotoxic effects of cadmium. DMSA should be used preferentially as it has no nephrotoxic effects.	DMSA: II	BAL: III	
Californium (²⁵² Cf)	Ca-DTPA / cf. Sheet no. 4			I	
Cerium (¹³⁹ Ce, ¹⁴¹ Ce, ¹⁴⁴ Ce)	Ca-DTPA / cf. Sheet no. 4			II	
Caesium (¹³⁴ Cs, ¹³⁷ Cs)	Prussian Blue/ cf. Sheet no. 2	** Intraluminal effect of Prussian Blue, that is not absorbed. Prussian Blue blocks the enterohepatic cycle.	III TSA in France and MA in the United States		
Chromium (⁵¹ Cr)	Ca-DTPA / cf. Sheet no. 4		Lack of evidence		
Chromium (⁵¹ Cr)	Deferoxamine		Lack o	of evidence	
Cobalt (⁵⁷ Co, ⁵⁸ Ćo, ⁶⁰ Co)	Ca-DTPA / cf. Sheet no. 4		МА		
Copper (⁶⁴ Cu, ⁶⁷ Cu)	Ca-EDTA or Penicillamine		Ca-EDTA : III	Penicillamine : MA in Wilson's disease (copper)	
Curium (²⁴² Cm, ²⁴⁴ Cm)	Ca-DTPA / cf. Sheet no. 4			MA	
Erbium (¹⁶⁹ Er)	Ca-DTPA / cf. Sheet no. 4		Lack of evidence		
Europium (¹⁵² Eu, ¹⁵⁴ Eu, ¹⁵⁶ Eu)	Ca-DTPA / cf. Sheet no. 4				
Iron (⁵² Fe, ⁵⁵ Fe, ⁵⁹ Fe)	Ca-DTPA / cf. Sheet no. 4			MA	
Iron (⁵² Fe, ⁵⁵ Fe, ⁵⁹ Fe)	Deferoxamine		МА		
Gallium (⁶⁶ Ga, ⁶⁷ Ga, ⁶⁸ Ga)	Ca-DTPA / cf. Sheet no. 4		I		
Indium (¹¹¹ In, ^{115m} In)	Prussian Blue/ cf. Sheet no. 2	Cf. comments**	I		
lodine (¹²³ I, ¹²⁵ I, ¹³¹ Í, ¹³² I)	Iodine does not	require chelator treatment, but ra	ther competitor treatment w	vith potassium iodide	
Iridium (¹⁹² Ir)	Ca-DTPA / cf. Sheet no. 4		Lack c	of evidence	
Lanthane (¹⁴⁰ La)	Ca-DTPA / cf. Sheet no. 4		ll		
Manganese (⁵² Mn, ^{52m} Mn, ⁵⁴ Mn)	Ca-DTPA / cf. Sheet no. 4		III		
Manganese (⁵² Mn, ^{52m} Mn, ⁵⁴ Mn)	Deferoxamine		Lack of evidence		
Mercury (¹⁹⁷ Hg, ²⁰³ Hg)	DMSA or BAL / cf. Sheet no. 3	Cf. comments *	DMSA: MA	BAL: MA	

RADIONUCLIDES	CHELATOR ANTIDOTES	COMMENTS	LEVELS OF SCIENTIFIC EVIDENCE OF EFFICACY			
Nickel (⁶³ Ni, ⁶⁵ Ni)	DMSA or BAL / cf. Sheet no. 3	Cf. comments *	DMSA: II		BAL: Lack of evidence	
Gold (¹⁹⁸ Au)	DMSA or BAL / cf. Sheet no. 3	Cf. comments *	DMSA: II		BAL: MA	
Lead (²¹⁰ Pb)	Ca-EDTA or DMSA + BAL/ cf. Sheet no. 3	A second chelating agent, such as BAL, is used to buffer that is released by Ca-EDTA, particularly in cases of massive lead intoxication, in order to avoid aggravation of encephalopathy.	Ca-EDTA : MA In lead poisoning	DMSA	A: MA	BAL: MA
Plutonium (²³⁸ Pu, ²³⁹ Pu, ²⁴⁰ Pu)	Ca-DTPA / cf. Sheet no. 4		MA			
Polonium (²¹⁰ Po)	DMSA or BAL / cf. Sheet no. 3	Cf. comments *	DMSA: II BAL: II		BAL: II	
Praseodymium (¹⁴³ Pr, ¹⁴⁴ Pr)	Ca-DTPA / cf. Sheet no. 4		III			
Rubidium (⁸⁴ Rb, ⁸⁶ Rb, ⁸⁸ Rb)	Prussian Blue/ cf. Sheet no. 2	Cf. comments**	II			
Prometheum (¹⁴⁷ Pm)	Ca-DTPA / cf. Sheet no. 4		III			
Ruthenium (¹⁰³ Ru, ¹⁰⁶ Ru)	Ca-DTPA / cf. Sheet no. 4		I			
Samarium (¹⁵³ Sm)	Ca-DTPA / cf. Sheet no. 4					
Scandium (⁴⁶ Sc, ⁴⁷ Sc)	Ca-DTPA / cf. Sheet no. 4		III			
Thallium (²⁰¹ Tl, ²⁰⁴ Tl)	Prussian Blue/ cf. Sheet no. 2	Cf. comments**	III TSA in France and MA in the United States			
Thorium (²³² Th)	Ca-DTPA / cf. Sheet no. 4		II			
Uranium (²³⁵ U, ²³⁸ U)		Chelator treatment is not relevant to uranium intoxication				
Ytterbium (¹⁶⁹ Yb)	Ca-DTPA / cf. Sheet no. 4					
Yttrium (⁹⁰ Y)	Ca-DTPA / cf. Sheet no. 4					
Zinc (⁶⁵ Zn)	Ca-DTPA / cf. Sheet no. 4		III			
Zirconium 95 (⁹⁵ Zr)	Ca-DTPA / cf. Sheet no. 4		Lack of evidence			

3. <u>Treatments</u>

The main treatments described below concern the early treatment of internal contamination. In all cases, **internal contamination must be treated as rapidly as possible**, possibly through the combined administration of several molecules, for example Prussian Blue and Ca-DTPA, failing rapid and precise initial identification of the radionuclides involved, except if the on-site measurement data point towards a treatment to administer.

The long-term continuation of treatment for internal contamination should be assessed according to the estimated extent of incorporation according to the anthroporadiometric and/or radiotoxicological examination (cf. C/ Samples to collect for radiotoxicological examination following internal contamination).

3.1. Specific treatments

In order to keep radionuclide diffusion within the body to a strict minimum, where it will in most cases be bound to endogenous molecules that are highly difficult to mobilise in pharmacological terms, the treatment of internal contamination must be applied whenever possible from the contaminant's point of entry. The other therapeutic alternative consists mainly in the administration of decorporating agents that will accelerate radionuclide excretion. Thus, we can distinguish evacuation treatments that reduce the absorption of toxic compounds and purification treatments that increase its elimination; the aim of both of these strategies is to reduce the duration of intoxication and, consequently, the exposure to radionuclides, thus helping reduce the dose received by the exposed person, without however correcting the symptoms.

3.1.1. <u>Treatments intended to reduce radionuclide absorption</u>

This type of treatment is applied to prevent radionuclides from passing the intestinal barrier in the event of ingestion of radioactive particles or contaminated food, or to reduce radionuclide binding to target organs once the element has passed into the bloodstream.

As an example, Prussian Blue (ferric ferrocyanide) can be administered in the event of contamination with caesium, for which it blocks the enterohepatic cycle by insolubilisation in the intestinal lumen, thus preventing its transfer to the bloodstream. This treatment was successfully administered to 46 victims (including 13 children) during the Goiana accident: administered at daily doses of 1 to 3 grams, though this was increased to up to 10 grams in the most highly contaminated individuals, it reduced the biological half-life of caesium by a factor of 3.

The digestive absorption of substances such as strontium 90 could also be reduced by oral administration of 10 to 20 grams of sodium alginate that, by coating the gastrointestinal mucosa, prevents the radionuclide from passing into the blood compartment, thus avoiding durable binding to bone tissue, the major target tissue of strontium.

3.1.2. Treatments intended to increase radionuclide elimination

In this case, the therapeutic approach implemented consists in the administration of so-called "decorporating" agents that accelerate the excretion of radionuclides that entered the body. Most frequently, these molecules are chelating agents that complex with the radionuclide, thus enabling its rapid elimination, mainly in urine. When administered, for example, at a slow intravenous dose of 1 gram per day, Ca-DTPA is strongly indicated in cases of plutonium and americium contamination, but its efficacy has not been demonstrated for the treatment of uranium contamination. Besides Ca-DTPA, chelating agents such as Ca-EDTA, DMSA and BAL can also be used (this latter should be administered with great precaution due to its toxicity).

Though recommended, the treatment consisting in complexing uranium with an isotonic solution of sodium bicarbonate is not advised as its efficacy is dubious and is can cause metabolic alcalosis. Moreover, it may lead to uranium salt precipitation in the kidneys, thus aggravating the renal toxicity of uranium.

Once the emergency phase has passed, continued treatment with chelating agents shall be decided according to the progression of radionuclide retention and/or excretion; it should never be needlessly continued. Chelation must be adapted to the element's kinetics, taking into account redistribution from

the storage organs. Thus, in certain cases, the courses of treatment should be short, whereas in other cases, they will be longer and, in certain cases, therapeutic windows will be required.

It should be noted that other molecules also serve to increase radionuclide elimination. Thus, the oral administration of water can be used to treat internal tritium contamination by isotope dilution. Moreover, the administration of stable isotopes of the incriminated radionuclide, or of stable isotopes with similar kinetics to those of the incriminated radionuclide, should serve to displace the radionuclide from its binding sites. Thus, stable strontium gluconate may be useful to displace strontium 90 from its bone binding sites. Similarly, calcium gluconate may compete with strontium 90 or calcium 45 bound to the bone matrix.

Finally, in the event of an accident involving the release of radioactive iodine isotopes into the environment, the therapeutic strategy consists in the oral administration of stable iodine in the form of potassium iodide, at a dose of:

- 130 mg (*i.e.* 100 mg of iodine element) in adults;
- 65 mg (*i.e.* 50 mg of iodine element) in children between the ages of 36 months and 12 years;
- 32.5 mg (i.e. 25 mg of iodine element) in new-borns aged between 1 and 36 months;
- 16.25 mg (*i.e.* 12.5 mg of iodine element) in new-borns under the age of 1 month.

To ensure optimum efficacy, the iodine should be administered on formal instruction by the competent authorities as soon as the alert is raised, ideally before propagation of the radioactive cloud and at the worst within the first hours post-exposure. Thus, thyroid saturation with stable iodine will prevent binding of radioactive isotopes that are then excreted in urine.

3.2. <u>Non-specific treatments in the event of internal contamination with one or more radionuclides</u> in situations involving large numbers of victims

3.2.1. <u>Treatments adapted to radionuclide dispersion methods</u>

Radionuclide dispersion by fire or explosion may lead to large numbers of contaminated victims, who may also be traumatised, burnt, or blasted. Some of these victims may be in life-threatening condition. In this case, treatments of life-threatening distress take precedence over radiological decontamination. These victims must therefore be taken to healthcare establishments with the facilities required to receive them (protected and trained personnel), on medical decision, without passing through decontamination structures, after taking some elementary precautions to prevent particle dispersion:

- protection of healthcare teams at all stages of the trip;
- complete victim undressing;
- victim transported according to the double jacket principle;
- hospital path marking and protection.

3.2.2. <u>Non-specific treatments aimed at reducing internal contamination</u>

In the event of suspected internal contamination with one or more radionuclides, non-specific treatments may be initiated, without waiting for definitive identification of the concerned radionuclide. These are intended to reduce absorption, block binding or facilitate elimination.

They are administered based on presumptive arguments and are not intended to replace specific antidote treatments.

It should be possible to administer these non-specific treatments at the site of the event, in a support zone, due to the possible duration of undressing and decontamination operations. They must therefore conform to a certain number of requirements:

- a. distribution without individual medical prescription;
- b. *per os* administration only;
- c. no noteworthy contraindications or adverse events;
- d. no special post-administration monitoring.

They must be associated with steps intended to limit the risk of over-contamination:

- a. water spraying to avoid dispersion of radioactive dust during undressing, if possible;
- b. undressing;
- c. hand washing, in particular when taking medicine per os;
- d. distribution of breathing apparatus.

Under these conditions, the distribution of certain drugs may be considered:

- a. potassium iodide;
- b. sodium alginate;
- c. Prussian blue;
- d. Ca-DTPA: may be used in solution for wound decontamination.
- 3.2.3. Other non-specific purification treatments
 - a. emetics;
 - b. gastric lavage;
 - c. laxatives and purgatives;
 - d. broncho-alveolar lavage.

These treatments can only be considered on a case by case basis, in a healthcare establishment, after determination of the extent of internal contamination by anthroporadiometry and on specialist advice.

4. <u>Samples to be collected for radiotoxicological tests following</u> internal contamination with radionuclides

The evaluation of the dose received by an individual following incorporation of a radioactive substance requires knowledge of changes to this substance's activity over time in the body and calculation of the dose received by the various tissues and organs. The determination of incorporated activity is based on retention measurements, whole body or pulmonary, thyroid or bone, according to preferential binding sites of radionuclides and their urinary and faecal excretion.

a. Measurement of radionuclide retention by anthroporadiometry

Anthroporadiometric measurement consists in determining the activity of radionuclides incorporated into the body by detecting the external X and gamma radiation that they emit. Requiring no biological sampling, this technique can be used to identify the radionuclide or radionuclides involved according to the energy of their emissions, to quantify the activity retained at a given time and to estimate the initial incorporation from this value.

The main benefits of anthroporadiometric measurement relate to its non-invasive nature and rapid implementation, this technique requiring no special patient preparation as long as a specific facility is available nearby.

Nevertheless, this technique is not always sufficient to characterise internal contamination, particularly in the case of incorporation of radionuclides that do not emit X or gamma radiations (such as strontium 90 for example, or any radionuclide that emits only alpha particles, such as plutonium 210 for example) and rapid elimination radioactive substances for which radiotoxicological urine and/or stool analysis is necessary.

Furthermore, an anthroporadiometric measurement performed on a person presenting only with external contamination will give a false positive result that will only be revealed by an excreted activity analysis. In practice, anthroporadiometry should therefore be performed on subjects for whom external contamination has first been eliminated by undressing followed by showering.

b. Measurement of radionuclide excretion by radiotoxicological analysis

Radiotoxicological *excreta* analysis consists in determining the activity of radionuclides excreted in urine and/or stools, following incorporation of radioactive substances. Less demanding than anthroporadiometry in terms of the nature of radiation that can be detected, **these analyses** are used to measure all types of radioactive emissions (alpha, beta and gamma), but they **nevertheless require the implementation of complex logistics that are incompatible with direct** *in situ* examinations. Indeed, considering the volume of samples required and to take daily elimination fluctuations into consideration, they require 24-hour collection periods for urine and up to 3 days for stools. The samples must then be sent to a radiotoxicological analysis laboratory and processed according to the nature of the radionuclides to measure.

Moreover, the type of sample to collect (urine and/or stools) is governed by numerous parameters such as the nature of incriminated radionuclides, their physicochemical form and their route of ingress

into the body: the information pertaining to the biological samples to collect shall preferably be provided after consultation with an expert in radiological field.

Thus, although complementary to anthroporadiometric measurements and frequently essential for correct assessment of the level of contamination, **radiotoxicological analyses of** *excreta* are unable **to provide objective elements supporting the triage of victims of an NRBC attack**. Nevertheless, the collection of samples, urinary in particular, from the immediate crisis management phase, will provide subsequent information concerning radionuclide elimination during the 24-hour period following the attack and hence elements allowing the *post-event* calculation of the dose received by exposed victims.

• Urine sampling

Samples are collected in individualized and time-stamped (sample start and end time) plastic containers, that are then stored, whenever possible, at a temperature of +4°C without preservatives. Urine should be collected over a 24-hour period Samples are sent to radiotoxicological medical analyses laboratory..

• Stool sampling

Samples are collected in individualized and time-stamped (sample start and end time) plastic containers, that are then stored, whenever possible, at a temperature of +4°C without preservatives. Whenever possible, stools should be collected over a 72-hour period. Samples are sent to radiotoxicological medical analyses laboratory.

Whether for urine or stool samples, the collection bottles must, while awaiting transport to the analytical laboratory, be stored in a location free from atmospheric radioactive contamination in order to avoid any cross-contamination that would skew the final analytical result.

c. Benefits of blood samples for evaluating internal radionuclide contamination

In light of currently available analytical techniques, blood samples are of no use for assessing exposure to internal radionuclide contamination. However, in addition to the information they provide concerning the victim's general condition, they can be of use in the diagnosis of an acute irradiation syndrome: thus, a Complete Blood Count can be used, for example, to monitor the decrease in white blood cells, observed during the weeks following external irradiation.

Moreover, a blood sample can be collected to assay lymphocyte chromosomal aberrations that may be observed following external exposure to irradiation. Again, with the currently available knowledge and techniques, this type of examination does not allow exposure by internal contamination to be assessed. Furthermore, it must be performed by a cytogenetics laboratory specialising in biological dosimetry and with staff specifically trained in this type of analysis.

5. <u>Reminder of the definitions of the various doses used in</u> <u>radioactivity</u>

To measure the radioactivity (Bq, *Ci*), measured the absorbed dose (Gy, *rad*) and to assess the effects on health (Sv, *rem*) of a person exposed to radionuclides.

- <u>Becquerel (Bq)</u>: the Becquerel is the unit of radioactivity measurement. 1 Becquerel corresponds to one disintegration per second. Previously, the *Curie (Ci)* was used: 1 Curie corresponds to the radioactivity of one gram of radium, *i.e.* 37 billion disintegrations per second.
- <u>Gray (Gy)</u>: the Gray is the unit of absorbed dose measurement, it is the amount of radiation absorbed by matter. 1 Gray corresponds to 1 Joule absorbed by kilogram of matter. Previously (and still in certain countries, such as the USA), the *Röntgen* and, more recently, the *Rad* (abbreviation of "*Radiation Absorbed Dose*") were used: 1 Rad corresponds 10⁻² Gy.
- <u>Sievert (Sv)</u>: the Sievert is a unit used to distinguish the effects induced on living tissues by the different types of radioactive particles and ionising radiation (alpha, beta, gamma, neutron), along with the radiosensitivity differences amongst different organs and tissues. The Sievert is a risk management unit used to assess:
 - <u>Equivalent dose</u>: the equivalent dose shows the effect of the different types of radioactive particles and ionising radiation on tissues. It corresponds to the absorbed dose, expressed in Gy, multiplied by a radiation weighting factors (the greater the energy delivered by the radiation, the higher the weighting factor). Previously (and still in certain countries, such as the USA), the *Rem* (abbreviation of "*Röntgen Equivalent Man*") was used: 1 Rem corresponds to 10⁻² Sv.
 - <u>Effective dose</u>: the effective dose reflects not only the effect of the different types of radioactive particles and ionising radiation on tissues, but also the more or less radiosensitive nature of the exposed tissue or organ. It corresponds to the equivalent dose, expressed in Sv, multiplied by a tissue weighting factor (the more radiosensitive the tissue, the higher the tissue weighting factor).

The following table gives the equivalences between official and former (though still sometimes used) units:

Measured quantify	Official unit	Former unit	Equivalence
Radioactivity	Becquerel (Bq)	Curie (Ci)	1 Ci = 3.7.10 ¹⁰ Bq
Absorbed dose	Gray (Gy)	Rad (rad)	1 rad = 10 ⁻² Gy
Biological effect	Sievert (Sv)	Rem (rem)	1 rem = 10 ⁻² Sv