Radioactive iodine and the thyroid

The radioactive isotopes of iodine follow the same biological pathways as stable iodine. After contamination by radio-iodine, the radiation dose delivered to the thyroid, the primary exposed organ, is 1,000 to 10,000 times greater than that delivered to the other tissues. However, administering large quantities of stable iodine, the thyroid can be protected.

Iodine is used to synthesize thyroid **hormones**, which accounts for its long residence in the thyroid gland. **Radioactive** iodine is concentrated in this gland by the iodide symporter(1) or NIS. Radio-isotopes of iodine have the same biological behaviour as stable iodine (iodine-127). Iodine-131, a **beta** and **gamma** emitter with a **half life** of 8 days, has been used in medicine for over fifty years.

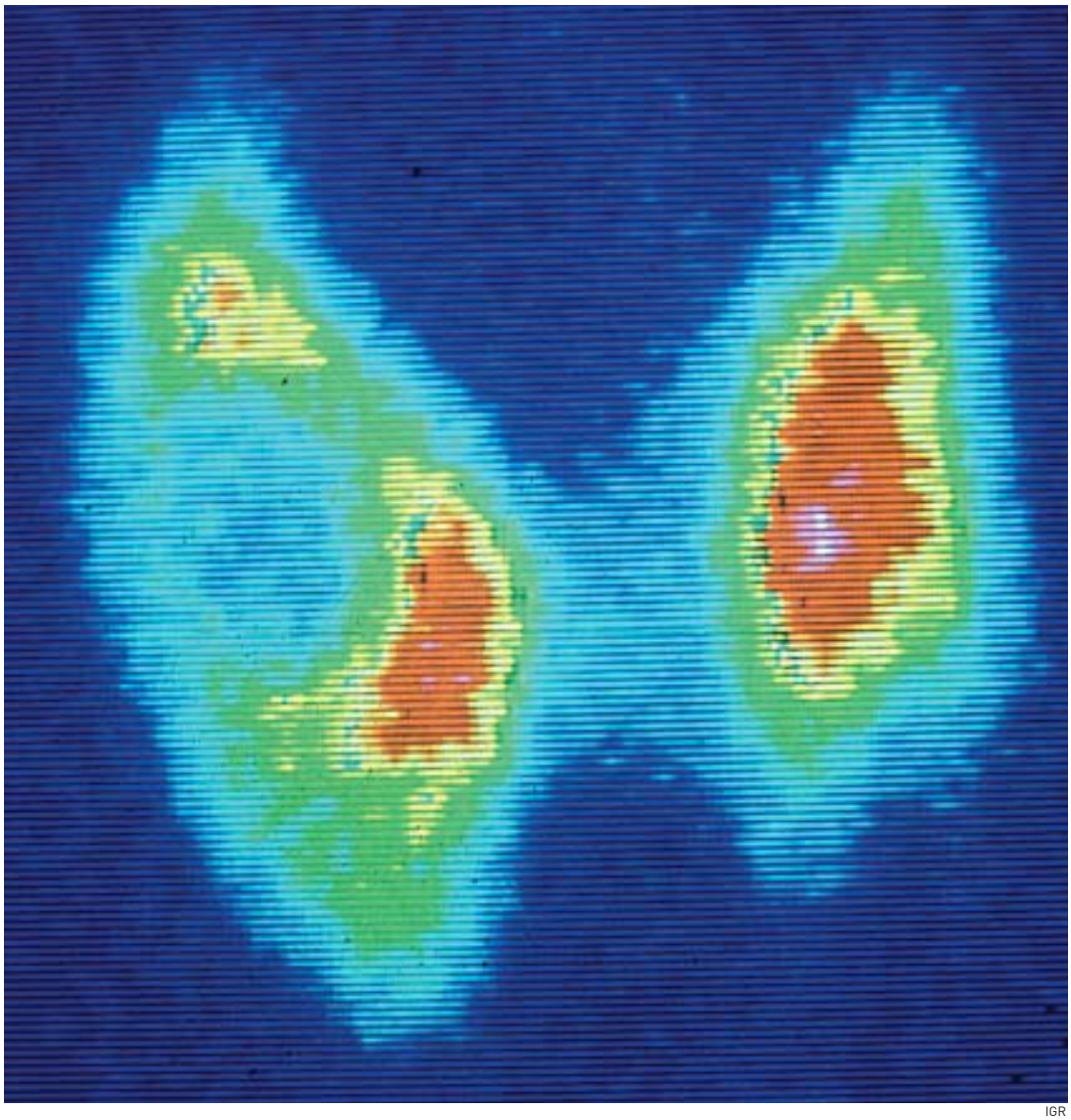
After **contamination** by radio-iodine, the radiation **dose** delivered to the thyroid is 1,000 to 10,000 times greater than that received by the other tissues. Relatively low **activities** can thus result in high radiation doses to the thyroid. Conversely, only high activities can deliver high doses to organs other than the thyroid.

Hypothyroidism due to cell death can appear during the years following irradiation of the thyroid at high doses. Above all, the thyroid is one of the most sensitive organs to the **carcinogenic** effects of **ionising radiation**. Several conclusions have been drawn from **epidemiological** studies of persons irradiated externally.

First, **external irradiation** increases the risk of thyroid tumours. One third of these tumours are cancers, most often papillary and therefore with favourable outcome. They are often multicentric and should be treated by total thyroidectomy. **Chromosomal** rearrangements of the RET/PTC type are found in 5 to 15% of non-radio-induced papillary cancers, and in 60 to 80% of papillary

(1) Symporter: membrane transport **protein** carrying two soluble species across the membrane in the same direction. The sodium/iodide symporter, Na/I symporter or NIS, cloned in 1996, is a key agent in thyroid function.

Thyroid scintigraphy reveals a cold nodule.



IGR

cancers occurring after cervical irradiation during childhood, and this permits molecular epidemiology studies.
Second, the increase in thyroid tumour incidence starts after a latency period of about ten years, peaking some twenty years after irradiation, after which the risk declines, although it remains significantly elevated for at least forty years.
Third, the risk is significant for doses delivered to the thyroid as low as 100 milli**grays** (mGy), and above that level increases linearly with dose up to 10-15 grays. When low doses have been delivered to the thyroid, most patients have normal thyroid function when the tumour is discovered. Above a few tens of grays, owing to cell death processes the risk is high but no longer increases with dose.
Last, the most significant risk factor is age at the time of radiation exposure. Subjects aged below 5 years at the time of exposure have the greatest risk. The risk then decreases with age at irradiation, and is no longer significant beyond an age of 15 to 20 years at exposure. In young children the excess risk factor after a dose of 1 Gy is 7.7, which is a very high figure.
The other factors liable to influence risk include sex, thyroid tumours after irradiation being 2 to 3 times more common in women than in men. Genetic susceptibility factors are probably also involved. However, the characteristics of the radiation, in particular **dose rate** and exposure pattern have little influence on the risk.
After exposure to radioactive iodine (iodine-131) for medical purposes either for diagnosis by **scintigraphy** (average thyroid dose about 1 Gy), or for hyperthyroidism therapy (thyroid dose 100 Gy), no increase in thyroid cancer rate has been observed. This is because thyroid disorders appear in adulthood at an age when the thyroid is much less sensitive to the cancer-inducing action of exposure to radioiodine. In contrast, medical data available for children are insufficient to rule out a cancer risk, and the use of radioiodine should be limited in young subjects. We can note that an activity of iodine-131 of 2 méga**becquerels** (MBq) will deliver to the thyroid of a young adult a dose for which tumour-inducing effects have been demonstrated after external irradiation, i.e., about 100 mGy.
No carcinogenicity outside the thyroid has been observed after exposure to iodine-131 for scintigraphy or treatment of hyperthyroidism. In patients treated for thyroid cancer with high activities of iodine-131 amounting to several gigabecquerels (GBq), an increased risk of leukemia has been demonstrated for high activities, together with a smaller increase in solid cancer risk. Also, the evolution of pregnancies after treatment of thyroid cancer by iodine-131 is identical to that of pregnancies with no treatment.
The thyroid has attracted renewed attention since the Chernobyl accident. A considerable increase in the incidence of thyroid cancer has been observed in Ukraine and Belarus in children who were heavily contaminated by radio**isotopes** of iodine (iodine-131 and short half life isotopes iodine-132 and -133) and who received doses to the thyroid of several hundred mGy. Most children who developed thyroid

Cogema

"Ghost" for the calibration of a thyroid irradiation detector at the medical service of Cogema Marcoule.

cancer were aged under 10 years at the time of the accident. This increase contrasts with the absence of any increase in other cancers or leukemia in these children, which is attributable to the low doses of irradiation delivered to the organs other than the thyroid.
It is noteworthy that outside Ukraine, Belarus and Russia no adverse health impact due to this accident has been observed, in particular in France, where the thyroid dose in a few young children was at most some tens of mGy. There is no scientific evidence to suggest that this accident may have caused an increase in the incidence of thyroid cancer in France.
Thus irradiation of the thyroid in children can cause the appearance of a cancer whatever the nature of the radiation, especially in younger children. If the contamination is atmospheric, young children should be protected as a priority, through general measures (confinement, dietary restrictions, sometimes evacuation), and above all by administration of potassium iodide (KI).
Potassium iodide can totally prevent the concentration of radio-iodine in the thyroid provided a sufficiently high dose is administered (adults, including pregnant women: 100 mg of iodide, i.e., 130 mg of KI; children under 13: 50 mg of iodide; children under 3: 25 mg), either before or immediately after the contamination. This is the rationale for pre-distributing KI tablets for the populations living near the French nuclear power stations. KI administration must be repeated in the case of prolonged contamination. By preventing concentration by the thyroid, KI can reduce the health risks due to contamination by radio-iodine isotopes.
The side effects of KI, in the thyroid and other organs, are exceptional in children and are only observed to any extent in adults, in whom the potassium iodide prophylaxis is of limited utility.

To conclude, irradiation of the thyroid during childhood increases the risk of tumour formation, and therefore should be avoided. Prophylaxis by administration of potassium iodide should be implemented in the case of contamination by radioactive iodine isotopes.

> Prof. **Martin Schlumberger**
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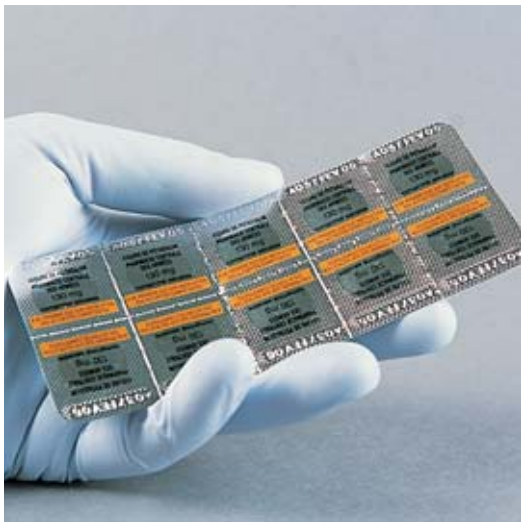


Cyrille Dupont/CEA

Potassium iodide tablets. Distribution of iodine is organised near nuclear power stations to saturate the thyroid gland in the event of dispersion of radioactive iodine isotopes.

E When radionuclides take the place of vital elements

Among the elements necessary for life the human body contains a certain number of naturally-occurring radioactive isotopes. The main ones are carbon-14 and potassium-40, which are responsible for an intrinsic radioactivity of natural origin amounting to *several thousand* becquerels in an adult. In unusual or accidental situations, the body can also be exposed to toxic elements or isotopes. Among those used or generated by the nuclear industry, some are isotopes of physiologically vital elements, such as iodine, while others are non-physiological elements such as cadmium, strontium, cæsium, lead and the actinides.

In addition, certain essential constituents of living matter, formed of stable elements such as iron, manganese or sulphur, have radioactive equivalents among certain activation or corrosion products.

Potential major radiocontaminants include three main groups of radionuclides: iodine (^{131}I and ^{133}I), strontium (^{89}Sr and ^{90}Sr) and cæsium (^{134}Cs and ^{137}Cs). Iodine, which has a biological role, is very readily absorbed and metabolised, whereas strontium and cæsium follow the same metabolic pathways as vital biogenic elements. Thus strontium (^{90}Sr) behaves much like calcium, and so ends up in bone tissue, of which calcium is a major constituent, while cæsium (^{137}Cs) diffuses throughout muscle tissue, following practically the same metabolic pathways as potassium, the main intracellular element.

Although these nuclides follow pathways similar to those by which the transfer to blood of vital elements takes place, often facilitated by specific processes (respiration, digestion, ion transport), the efficiency of their transport is often much lower than that of their biological analogues.

In the event of contamination by radionuclides, these can therefore take the place of vital minerals and trace elements. After ingestion, the metabolised fraction of the radionuclide is distributed throughout the body or is concentrated in particular organs. Although most of the essential elements and some of their analogues (sodium, chlorine, potassium, cæsium, etc.) are distributed fairly evenly in soft tissues, some can accumulate in extracellular storage compartments such as the thyroid for iodine, the liver for plutonium and the bone matrix for the so-called osteotropic elements (calcium, barium, strontium, radium and transuranics).

Thus the membrane transporters facilitate the entry of cæsium and rubidium into cells. Likewise, strontium can be efficiently accumulated in subcellular confinement compartments. Also, certain cotransporters responsible for the capture of divalent metals (iron, copper and zinc ions) also transfer cadmium.

Lastly, the possibility that toxics (whether physiological or not) may be sequestered in each compartment by any of an array of soluble proteins must not be underestimated. Such trapping can be covalent (e.g., iodinated thyroglobulin).

Calcium, or proteins that reduce the free toxic forms of certain vital transition metals (iron, copper, selenium, etc.) are potential complexing agents for non-physiological elements such as uranium or cadmium. The latter metal has few specific effects but tends to take the place of calcium, zinc and copper. Its opportunistic behaviour, which can cause severe physiological disorders, is shared by many other exogenous metals.

A Natural and artificial radioactivity

Everything on the earth's surface has always been exposed to the action of ionising radiation from natural sources. Natural radiation, which accounts for 85.5% of total radioactivity (natural plus artificial), is made up of 71% telluric radiation and about 14.5% cosmic radiation. The radionuclides formed by the interaction of **cosmic rays** arriving from stars, and especially the Sun, with the nuclei of elements present in the atmosphere (oxygen and nitrogen) are, in decreasing order of dose (Box F, *From rays to dose*) received by the population, carbon-14, beryllium-7, sodium-22 and tritium (hydrogen-3). The last two are responsible for only very low doses.

Carbon-14, with a half life of **5,730 years**, is found in the human body. Its activity per unit mass of carbon has varied over time: it has diminished as carbon dioxide emissions from the combustion of fossil fuels have risen, then was increased by atmospheric nuclear weapon tests.

Beryllium-7, with a half life of **53.6 days**, falls onto the leaf surfaces of plants and enters the body by ingestion (Box B, *Human exposure routes*). About 50 Bq (becquerels) per person per year of beryllium-7 are ingested.

The main or **"primordial" radionuclides** are potassium-40, uranium-238 and thorium-232. Along with their radioactive decay products, these elements are present in rocks and soil and are therefore found in many building materials. Their concentrations are generally very low, but vary according to the nature of the mineral. The gamma radiation emitted by these radionuclides forms the **telluric radiation**, which is responsible for the external exposure of the body. The primordial radionuclides and many of their long-lived descendants are also found in trace amounts in drinking water and plants: this results in an internal exposure by ingestion, plus an additional low exposure by inhalation of airborne suspended dust particles.

Potassium-40 is a beta and gamma emitter with a half life of **1.2 thousand million years**, and has no radioactive descendants. This radioactive isotope makes up 0.0118% of all natural potassium, and enters the body by ingestion. The mass of natural potassium in the human body is independent of the quantity ingested.

Uranium-238 is an alpha emitter with a half life of **4.47 thousand million years**. It has thirteen main alpha-, beta- and gamma-emitting radioactive descendants, including **radon-222** (**3.82 days**) and **uranium-234** (**0.246 million years**). Uranium-238 and its two descendants **thorium-234** (**24.1 days**) and **protactinium-234m**(1) (**1.18 min**), and **uranium-234** are essentially incorporated by ingestion and are mainly concentrated in the bones and kidneys.

Thorium-230, derived from uranium-234, is an alpha emitter with a period of **80,000 years**. It is an osteotrope, but enters the body mainly by the pulmonary route (inhalation). **Radium-226**, a descendant of thorium-230, is an alpha emitter with a half life of **1,600 years**. It is also an osteotrope and enters the body mainly *via* food. Another osteotrope, **lead-210** (**22.3 years**), is incorporated by inhalation though mostly by ingestion.

Thorium-232 is an alpha emitter with a half life of **14.1 thousand million years**. It possesses ten main alpha-, beta- and gamma-emitting radioactive descendants including **radon-220** (**55 s**). Thorium-232 enters the body mainly by inhalation. **Radium-228**, a direct descendant of thorium-232, is a beta-emitter with a half life of **5.75 years**. It enters the body mainly in food.

Radon, a gaseous radioactive descendant of uranium-238 and thorium-232, emanates from the soil and building materials, and along with its short-lived alpha-emitting descendants constitutes a source of internal exposure through inhalation. Radon is the most abundant source of natural radiation (about 40% of total radioactivity).

The human body contains nearly 4,500 Bq of potassium-40, 3,700 Bq of carbon-14 and 13 Bq of radium-226 essentially imported in food.

Natural radiation is supplemented by an anthropic component, resulting from the medical applications of ionising radiation and to a lesser extent from the nuclear industry. It accounts for about 14.5% of the total radioactivity worldwide, but much more in the developed countries. In the medical field (more than 1 mSv/year on average in France), irradiation by external sources predominates: radiodiagnosis (X-rays) and radiotherapy, long based on cæsium-137 and cobalt-60 sources, but now more and more often using linear accelerators. Irradiation by internal routes (curietherapy with iridium-192) has more specialised indications (cervical cancer, for example). The metabolic and physicochemical properties of some twenty radionuclides are put to use for **medical activities** and in **biological research**. The medical applications comprise radiodiagnostics (scintigraphy and radio-

(1) m for metastable. A nuclide is said metastable when a transition delay exists between the excited state of the atom and the stable one.

immunology), and treatment, including thyroid disorders using iodine-131, radioimmunotherapy in certain blood diseases (phosphorus-32) and the treatment of bone metastasis with strontium-89 or radiolabelled phosphonates alongside other uses of radiopharmaceuticals. Among the most widely used radionuclides are: **technetium-99m** (half life **6.02 hours**) and **thallium-201** (half life **3.04 days**) (scintigraphy), **iodine-131** (half life **8.04 days**) (treatment of hyperthyroidism), **iodine-125** (half life **60.14 days**) (radioimmunology), **cobalt-60** (half life **5.27 years**) (radiotherapy), and **iridium-192** (half life **73.82 days**) (curietherapy). The average contribution of radiological examinations to total radioactivity amounts to 14.2%.

The **early atmospheric nuclear weapon tests** scattered fallout over the whole of the earth's surface and caused the exposure of populations and the contamination of the food chain by a certain number of radionuclides, most of which, given their short radioactive half lives, have now vanished. There remain **cæsium-137** (**30 years**), **strontium-90** (**29.12 years**), some **krypton-85** (**10.4 years**) and **tritium** (**12.35 years**), and the isotopes of **plutonium** (half lives **87.7 years** to **24,100 years**). Currently, the doses corresponding to the fallout from these tests are essentially attributable to fission products (cæsium-137) and to carbon-14, rather than activation products and plutonium.

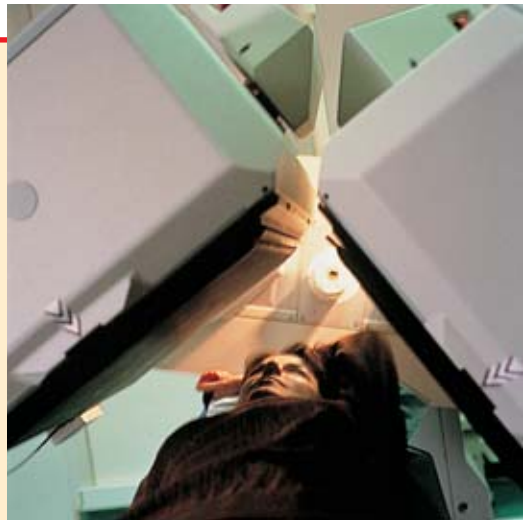
In the **Chernobyl accident** (Ukraine), which occurred in 1986, the total radioactivity dispersed into the atmosphere was of the order of 12 milliard milliard (10^{18}) becquerels over a period of 10 days. Three categories of radionuclides were disseminated. The first consisted of volatile fission products such as **iodine-131**, **iodine-133** (**20.8 hours**), **cæsium-134** (**2.06 years**), **cæsium-137**, **tellurium-132** (**3.26 days**). The second was composed of solid fission products and actinides released in much smaller amounts, in particular the strontium isotopes ^{89}**Sr** (half life **50.5 days**) and ^{90}**Sr**, the ruthenium isotopes ^{103}**Ru** (half life **39.3 days**) and ^{106}**Ru** (half life **368.2 days**), and **plutonium-239** (**24,100 years**). The third category was rare gases which although they represented most of the activity released, were rapidly diluted in the atmosphere. They were mainly **xenon-133** (**5.24 days**) and **krypton-85**.

The contributions of the early atmospheric nuclear weapon tests and the Chernobyl accident to the total radioactivity are roughly 0.2% (0.005 mSv) and 0.07% (0.002 mSv) respectively.

The whole of the **nuclear-powered electricity production** cycle represents only about 0.007% of total radioactivity. Almost all the radionuclides remain confined inside the nuclear reactors and the fuel cycle plants. In a nuclear reactor, the reactions that take place inside the fuel yield transuranics. **Uranium-238**, which is non-fissile, can capture neutrons to give in particular plutonium isotopes ^{239}**Pu**, ^{240}**Pu** (half life **6,560 years**) and ^{241}**Pu** (half life **14.4 years**), and **americium-241** (**432.7 years**). The main fission products generated by the fission of **uranium-235** (**704 million years**) and **plutonium-239** are **iodine-131**, **cæsium-134**, **cæsium-137**, **strontium-90** and **selenium-79** (**1.1 million years**).

The main radionuclides present in releases, which are performed in a very strict regulatory framework are, in liquid release, **tritium**, **cobalt-58** (**70.8 days**), **cobalt-60**, **iodine-131**, **cæsium-134**, **cæsium-137** and **silver-110m** (**249.9 days**). In gaseous releases **carbon-14** is the most abundant radionuclide, emitted most often as carbon dioxide. In all the reactors in the world, the total production of radiocarbon dioxide amounts to one tenth of the annual production formed naturally by cosmic radiation.

In addition, certain radionuclides related to the nuclear industry exhibit chemical toxicity (Box D, *Radiological and chemical toxicity*).



Laurence Médard/CEA

Classical scintigraphy performed at the Frédéric-Joliot Hospital Service (SHFJ). The gamma-ray camera is used for functional imaging of an organ after administration, usually by the intravenous route, of a radioactive drug (radiopharmaceutical) to the patient. The radionuclides used are specific to the organ being studied: for example, technetium-99m for the kidneys and bones, thallium-201 for the myocardium. The injected radiopharmaceutical emits gamma photons, which are captured by two planar detectors placed at 180° or 45° according to the examination.

B Human exposure routes

Human **exposure**, i.e., the effect on the body of a chemical, physical or radiological agent (irrespective of whether there is actual contact), can be external or internal. In the case of **ionising radiation**, exposure results in an energy input to all or part of the body. There can be direct **external irradiation** when the subject is in the path of radiation emitted by a radioactive source located outside the body. The person can be irradiated directly or after reflection off nearby surfaces.

The irradiation can be **acute** or **chronic**.

The term **contamination** is used to designate the deposition of matter (here **radioactive**) on structures, surfaces, objects or, as here, a living organism. Radiological contamination, attributable to the presence of **radionuclides**, can occur by the **external** route from the receptor medium (air, water) and vector media (soils, sediments, plant cover, materials) by contact with skin and hair (cutaneous contamination), or by the **internal** route when the radionuclides are **intaken**, by **inhalation** (gas, particles) from the atmosphere, by **ingestion**, mainly from foods and beverages (water, milk), or by penetration (injury, burns or diffusion through the skin). The term **intoxication** is used when the toxicity in question is essentially chemical.

In the case of **internal contamination**, the dose delivered to the body over time (called the **committed dose**) is calculated for 50 years in adults, and until age 70 years in children. The parameters taken into account for the calculation are: the nature and the intaken quantity of the radionuclide (RN), its chemical form, its **effective half life**[1] in the body (combination of **physical** and **biological half lives**), the type of **radiation**, the mode of exposure (inhalation, ingestion, injury, transcutaneous), the distribution in the body (deposition in target organs or even distribution), the radiosensitivity of the tissues and the age of the contaminated subject.

Lastly, the **radiotoxicity** is the toxicity due to the ionising radiation emitted by the inhaled or ingested radionuclide. The misleading variable called **potential radiotoxicity** is a *radiotoxic inventory* that is difficult to evaluate and made imprecise by many uncertainties.

(1) The effective half life (Te) is calculated from the physical half life (Tp) and the biological half life (Tb) by $1 / Te = 1 / Tp + 1 / Tb$.

F From rays to dose

Radioactivity is a process by which certain naturally-occurring or artificial **nuclides** (in particular those created by **fission**, the splitting of a heavy nucleus into two smaller ones) undergo spontaneous **decay**, with a release of energy, generally resulting in the formation of new nuclides. Termed **radionuclides** for this reason, they are unstable owing to the number of nucleons they contain (protons and neutrons) or their energy state. This decay process is accompanied by the emission of one or more types of **radiation**, ionising or non-ionising, and (or) particles. **Ionising radiation** is electromagnetic or corpuscular radiation that has sufficient energy to ionise certain atoms of the matter in its path by stripping electrons from them. This process can be *direct* (the case with alpha particles) or *indirect* (gamma rays and neutrons).

Alpha radiation, consisting of helium-4 nuclei (two protons and two neutrons), has low penetrating power and is stopped by a sheet of paper or the outermost layers of the skin. Its path in biological tissues is no longer than a few tens of micrometres. This radiation is therefore strongly ionising, i.e., it easily strips electrons from the atoms in the matter it travels through, because the particles shed all their energy over a short distance. For this reason, the hazard due to radionuclides that are **alpha emitters** is **internal exposure**.

Beta radiation, made up of electrons (beta minus radioactivity) or positrons (beta plus radioactivity), has moderate penetrating power. The particles emitted by **beta emitters** are stopped by a few metres of air, aluminium foil, or a few millimetres of biological tissue. They can therefore penetrate the outer layers of the skin.

Gamma radiation composed of high energy photons, which are weakly ionising but have high penetrating power (more than the **X-ray** photons used in radiodiagnosis), can travel through hundreds of meters of air. Thick shielding of concrete or lead is necessary to protect persons.

The interaction of **neutron radiation** is random, and so it is stopped only by a considerable thickness of concrete, water or paraffin wax. As it is electrically neutral, a neutron is stopped in air by the nuclei of light elements, the mass of which is close to that of the neutron.

• The quantity of energy delivered by radiation is the **dose**, which is evaluated in different ways, according to whether it takes into account the quantity of energy absorbed, its rate of delivery, or its biological effects.

• The **absorbed dose** is the quantity of energy absorbed at a point per unit mass of matter (inert or living), according to the definition of the International Commission on Radiation Units and Measurements (**ICRU**). It is expressed in **grays** (Gy): 1 gray is equal to an absorbed energy of 1 joule per kilogramme of matter. The *organ absorbed dose* is obtained by averaging the doses absorbed at different points according to the definition of the International Commission on Radiological Protection (**ICRP**).

• The **dose rate**, dose divided by time, measures the intensity of the irradiation (energy absorbed by the matter per unit mass and per unit time). The legal unit is the gray per second (Gy/s), but the gray per minute (Gy/min) is commonly used. Also, radiation has a higher **relative biological effectiveness (RBE)** if the effects produced by the same dose are greater or when the dose necessary to produce a given effect is lower.

• The **dose equivalent** is equal to the dose absorbed in a tissue or organ multiplied by a **weighting factor**, which differs according to the nature of the radiation energy, and which ranges from 1 to 20. Alpha radiation is considered to be 20 times more harmful than gamma radiation in terms of its biological efficiency in producing random (or **stochastic**) effects. The equivalent dose is expressed in sieverts (Sv).

• The **effective dose** is a quantity introduced to try to evaluate harm

Foulon/CEA

Technicians operating remote handling equipment on a line at the Atalante facility at CEA Marcoule. The shielding of the lines stops radiation. The operators wear personal dosimeters to monitor the efficacy of the protection.

in terms of whole-body stochastic effects. It is the sum of *equivalent doses* received by the different organs and tissues of an individual, weighted by a factor specific to each of them (weighting factors) according to its specific sensitivity. It makes it possible to sum doses from different sources, and both external and internal radiation. For internal exposure situations (**inhalation**, **ingestion**), the effective dose is calculated on the basis of the number of **becquerels** incorporated of a given radionuclide (**DPUI**, **dose per unit intake**). It is expressed in sieverts (Sv).

• The **committed dose**, as a result of internal exposure, is the cumulated dose received in fifty years (for workers and adults) or until age 70 (for those aged below 20) after the year of **incorporation** of the radionuclide, unless it has disappeared by physical shedding or biological elimination.

• The **collective dose** is the dose received by a population, defined as the product of the number of individuals (e.g., those working in a nuclear plant, where it is a useful parameter in the optimisation and application of the ALARA system) and the average equivalent or effective dose received by that population, or as the sum of the individual effective doses received. It is expressed in man-sieverts (man.Sv). It should be used only for groups that are relatively homogeneous as regards the nature of their exposure.

D Radiological and chemical toxicity

The chemical toxics linked to the nuclear industry include **uranium** (U), **cobalt** (Co), **boron** (B), used for its neutron-absorbing properties in the heat-exchange fluids of nuclear power plants, **beryllium** (Be), used to slow neutrons, and **cadmium** (Cd), used to capture them. Boron is essential for the growth of plants. Cadmium, like lead (Pb), produces toxic effects on the central nervous system. When the toxicity of an element can be both radiological and chemical, for example that of plutonium (Pu), uranium, neptunium, technetium or cobalt, it is necessary whenever possible to determine what toxic effects are radiological, what are chemical, and what can be either radiological or chemical (see *Limits of the comparison between radiological and chemical hazards*).

For **radioactive** elements with long physical **half lives**, the chemical toxicity is a much greater hazard than the radiological toxicity, as exemplified by rubidium (Rb) and natural uranium. Thus the chemical toxicity of uranium, which is more important than its radiological toxicity, has led the French regulators to set the **ingested** and **inhaled** mass limits for uranium in chemical compounds at 150 mg and 2.5 mg per day respectively, regardless of the **isotopic** composition of the element.

Certain metals or **metalloids** that are non-toxic at low concentrations can become toxic at high concentrations or in their radioactive form. This is the case for cobalt, which can be **genotoxic**, selenium (Se) (naturally incorporated in **proteins** or **RNA**), technetium (Tc) and iodine (I).

Cyrille Dupont/CEA

Two-dimensional gel electrophoresis image analysis carried out in the course of nuclear toxicology work at CEA Marcoule Centre in the Rhone Valley.