At Los Alamos, some 100 men and women work with plutonium routinely in the only remaining plutonium-processing facility in the United States. As shown on these pages, from the moment they enter the facility, they follow rigid safety precautions. Protected by specially designed clothes, gloves, and goggles, these experts use glove boxes for their work with plutonium, handling even minute quantities with amazing dexterity. At the end of the day, their radiation levels are thoroughly monitored. Our people are well protected, but their work has its risks. Therefore, the Laboratory places the highest importance on providing more-accurate answers to the question of how dangerous plutonium is to human health. This article summarizes our findings over several decades.
Pictured here are Jason Lashley and Ramiro Pereyra, two of the contributors to this volume.
ever since its discovery in 1941, plutonium has been known as a very dangerous material. Because it is capable of sustaining a nuclear chain reaction, plutonium is used in atomic weapons. Indeed, the first atomic bomb detonated at Trinity Site on July 16, 1945, was made of plutonium. At Trinity, scientists experienced firsthand the awesome power of the metal they had made. And feelings were profoundly ambivalent—joy at a remarkable scientific achievement and horror at having created a deadly instrument of war. J. Robert Oppenheimer was reminded of words from the Hindu scripture, the Bhagavad-Gita, “Now I am become Death, the destroyer of worlds.”

But concerns about plutonium are only partly related to its use in atomic weapons. Because it is radioactive, plutonium is dangerous when it finds its way into the human body. Driven by knowledge of the possible harmful health effects of plutonium, scientists carefully warned the public about them and established procedures to protect the workers in plutonium-processing facilities. In fact, their care was so extreme that many believe it was the scientists themselves who promoted an overstated idea that became well known at the end of the 1940s: “Plutonium is the most toxic substance known to man.”

In this article, we will give a realistic assessment of the health risks of plutonium. We will also stress that, because these risks were immediately anticipated, protective measures were taken soon after macroscopic amounts of plutonium had been produced. Most of the article, however, will explore related topics on plutonium that are of much concern to the general public:

What are the health risks of plutonium? What is the likelihood of exposure to plutonium? What is the metabolism of plutonium once it enters the body?

### The Health Risks of Plutonium

**Background.** Much of our early understanding of the health risks of plutonium comes from knowledge of the effects of radium, a radioactive element discovered by Marie Curie in 1899. (An element is radioactive if its nucleus is unstable, decays, and emits radiation.) Having a half-life of 1620 years, radium-226 remains a relatively intense and constant source of radiation for hundreds of years. These features triggered its use in the treatment of cancer as early as 1906. Applicators that contained radium salts would be placed on the surface of tumors to shrink or eliminate them. When scientists later discovered that the radiation penetrating the applicators was primarily composed of gamma rays from the daughter nuclei of radium decay, other gamma-emitting radioisotopes replaced radium in this application. The new radioisotopes became available from nuclear reactors during the 1960s.

But the use of radium as a cure for cancer was so much publicized in the press at the time that people thought its healing powers had no limits. Radium became known as the elixir of life and a cure for every ailment. Even when stories surfaced about the dangers of radium’s “emanations,” people would still hail the new element as a “miracle.”

Radium-laced water, radium baths, or radium-containing facial creams were the latest fashion throughout Europe and the United States in the first decades of the 20th century. Thousands of people were exposed to this element before 1932. Whatever the merits of low doses of radium, the tragic effects of high-dose exposures became evident after only a few years.

Acute cases of radium poisoning ended in rapid death, whereas other cases followed a much slower course: Victims suffered from infections of the jaw bones, pathological bone fractures, or cancers of the bone. The stories of those who had been exposed to radium—the young radium-dial workers being best known among them—made a deep impression on the scientists and contributed to awakening the public to the dangers of radium. (See “Radium—The Benchmark of Alpha Emitters” in *Los Alamos Science* No. 23, 1995.)

Radium was considered so dangerous that the National Bureau of Standards formed a nine-member committee to come up with an occupational standard for radium. On May 2, 1941, the standard for radium-226 was adopted—only two months before the discovery of plutonium. The publicity regarding the new standard alerted scientists on the Manhattan Project to the potential hazards of plutonium, a radioisotope similar to radium. Gram for gram, plutonium would be roughly as dangerous as radium. By extrapolation, the scientists were able to draw conclusions about the risks of plutonium. Both radium and plutonium emit alpha particles, which are positively charged helium nuclei ejected during radioactive decay. Helium nuclei are doubly charged because they are composed of two protons and two neutrons.

Tunneled out of a nucleus with a kinetic energy of about 5 million electron volts (MeV), the alpha particles...
from plutonium-239 move at a speed of about $1.5 \times 10^7$ meters per second (5 percent of the speed of light). Because of their relatively low speed and their double charge, the alpha particles travel only a short distance, depositing their energy by ionization—they collide with molecules, break those molecules apart through electrical forces, and leave a trail of ion pairs in their wake.

The density of the ion pairs is essentially the same for most of the distance covered by the alphas but then increases sharply for an instant, as the particles seemingly “stumble” and dump—all at once—what is left of their energy. As shown in Figure 1(a), their travel has come to a halt. It has been much like the journey of a person running through sand—at first the run is smooth, progress then turns awkward, and the stop comes with a stumble. In air, alphas travel only 3 to 5 centimeters and in living tissue only about 30 micrometers (which is equal to 3 to 5 cell diameters) before they expend their energy and come to rest. The latter distance is less than the thinnest part of the epidermis (the dead layer of external skin cells). It is also less than the thickness of a standard piece of paper (about 100 micrometers). Fortunately, therefore, the penetration power of alpha particles is limited. A mere sheet of paper or the outer layers of our skin will block their passage—see Figure 1(b). To be harmful, alpha emitters have to be inside the body, but there are other types of radiation—x-rays, gamma rays, and beta particles—that are harmful by hitting the body from the outside. They deposit their energies by ionization as well. The amount of energy for external radiation depends on the particle. Energy ranges for x-rays vary from less than 30 kilo-electron-volts (keV) to 25 MeV; for gamma rays, from 1 keV to 10 MeV; and for beta particles, from 1 keV to 2 MeV. Unlike alpha particles, x-rays, gammas, and betas generally travel farther and leave a less-dense track of ion pairs in their wake. For all types of ionizing radiation, the effects depend on the dose. High radiation doses usually manifest their effects soon after a person has been exposed. These effects are deterministic, or predictable, and their severity increases with dose. External radiation may cause skin burns, a temporary decrease in the number of blood cells, cataracts, and even death—only a few possible health effects triggered by the severe dysfunction or death of large numbers of cells.

If enough cells are involved, tissues may be affected or entire organs may be impaired. Early symptoms of acute external-radiation doses are fatigue, nausea, and vomiting. Radiation primarily affects systems that contain rapidly dividing cells, such as the blood-forming system (whose cells originate from the bone marrow) or the gastrointestinal system (the cells that line the small intestine). It also affects the central nervous system. For example, bone-marrow stem cells can die when they are irradiated. Their death diminishes or stops the resupply of circulating red and white blood cells and other blood constituents. After about three weeks, the reduction in blood cell supply leads to immune deficiencies, infections, fever, bleeding, and even death unless the bone marrow starts to regenerate.

At lower doses, acute radiation effects become less noticeable, and below certain levels of exposure, effects cannot be predicted. It is at these low levels of exposure that stochastic, or probabilistic, effects become apparent. Cancer is best known among them. Ionizing radiation of any kind can lead to alterations of a living cell’s genetic makeup, and sometimes those alterations trigger the uncontrolled growth and multiplication of that cell’s progeny, more commonly known as cancer. Stochastic effects occur randomly and are assumed to have no threshold dose. Their probability increases with dose. Their severity, however, does not. Moreover, there is

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**Figure 1. Emitters of α-Particles**

(a) The density of the ion pairs created as the alphas pass through a substance or through air is essentially the same for most of the distance covered by the alphas but then increases sharply as the particles dump, all at once, what is left of their energy. (b) Emitted with an energy of about 5 MeV, plutonium α-particles travel in air 3 to 5 cm and in living tissue about 30 µm before they expend their energy and come to rest. A mere sheet of paper (typically about 100 µm thick) or the outer layers of intact skin will block their passage. Therefore, when plutonium (or any other α-emitter) is external to the body, it is not a health hazard.  

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2 Cataracts are densities that form within the eye lens and do not allow the light to penetrate.
a substantial delay between the time of exposure and the appearance of the effect. If the effect is cancer, the delay ranges from several years for leukemia to decades for solid tumors.

**Plutonium Toxicity.** It is important to remember that, because their power of penetration is limited, alpha emitters are hazardous to human health only when they have found their way into the body. When inhaled, ingested, or passed into the blood stream through a wound, plutonium deposits in the lung, liver, or bones. Only about 10 percent of it is distributed to other organs. The plutonium atoms remain in the body for many decades, a fraction of them emitting alpha ionizing radiation and damaging the surrounding cells. The long radioactive half-lives of the plutonium isotopes and the amounts retained in the body make plutonium a long-term source of radiation to nearby cells and thus a biological hazard.

The half-life of plutonium-239 is 24,065 years. This half-life is short enough that 1 microgram of material will undergo more than 2000 decay events per second, but it is long enough to allow that microgram to decay at an approximately constant rate for thousands of years. If plutonium had uranium’s half-life of 4 billion years, there would be so few decays over the span of a human’s lifetime that the radiological toxicity of plutonium would be much less severe. However, that is not the case.

No humans have ever died from acute toxicity due to plutonium uptake. Nevertheless, lethal doses have been estimated from research on dogs, rats, and mice. Animal studies indicate that a few milligrams of plutonium per kilogram of tissue is a lethal dose. For example, the LD$_{50}(30)$ for dogs after intravenous injection of plutonium is about 0.32 milligram per kilogram of tissue. Assuming this animal dose also applies to humans, an LD$_{50}(30)$ by intravenous injection for an average human of 70 kilograms would be about 22 milligrams. By inhalation, the uptake would have to be about 4 times higher.

Because the levels of plutonium exposure have been kept extremely low, even cancer cannot be linked to such exposure with any certainty in epidemiological studies of workers in the United States. So far, only one plutonium worker in the United States has died of a rare bone cancer, which may have been caused by exposure to plutonium. But epidemiological studies are not very sensitive to low risks, especially because the number of plutonium workers is small. As a precaution in setting radiation standards, the International Commission on Radiation Protection (ICRP) assumes that some risk may be involved in any exposure.

Although dangerous, plutonium is not “the most toxic substance known to man.” On a weight-by-weight basis, plutonium is less toxic than the unforgiving bacterial toxins that cause botulism, tetanus, and anthrax. And yet, plutonium’s position is frighteningly high on the lethal ladder. A few milligrams of a gram (or a few micrograms) distributed through the lungs, liver, or bones may increase the risk for developing cancer in those organs. Airborne, soluble chemical compounds of plutonium are considered so dangerous by the Department of Energy (DOE) that the maximum permissible occupational concentration in air is an infinitesimal 32 trillionths of a gram per cubic meter! By comparison, the national standard for air concentrations of inorganic lead is 50 millionths of a gram per cubic meter, which suggests that inorganic lead is a million times less dangerous by weight than plutonium.

**The Plutonium Standard.** By 1945, when plutonium was being produced in kilogram quantities to enable the development of a plutonium-implosion bomb that would help put an end to the war, scientists had become sensitive to the risks of radiation, particularly through previous experience with radium, and were educating the workers about those risks.

Moreover, the experience with radium also provided a quantitative basis for the creation of a plutonium standard. Robert Stone, the head of the Plutonium Project Health Division at the Metallurgical Laboratory (Met Lab) in Chicago, made the earliest estimate of a permissible plutonium body burden—the total amount of plutonium that can be present in the body over a lifetime without causing ill effects—and those of their daughter nuclei and the difference in the average energy of their alpha particles. Results indicated that, gram for gram, plutonium was less toxic than radium by a factor of 50, and the permissible body burden was therefore set to 5 micrograms, or 0.3 microcurie. In July 1945, in the wake of disturbing animal experiments, which

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3 Uranium is also much more soluble than plutonium and leaves the body rapidly.

4 Plutonium uptake is the amount of the metal retained by the body after some has been rapidly eliminated from the lungs and gastrointestinal tract, whereas plutonium intake is the total amount of plutonium that enters a person’s body.

5 The amount of material that causes death in 50 percent of the animals after $n$ days is known as the LD$_{50}(n)$, that is, the lethal dose 50 percent.

6 Epidemiology is the study of the number and distribution of health events in a given population.

7 In 1942, A. H. Compton consolidated the Plutonium Project at the University of Chicago under the cryptic name of Met Lab, which was to become one of the important sites of the Manhattan Project. The Met Lab’s goals were to demonstrate a nuclear chain reaction for plutonium-239 using natural uranium and to develop chemical procedures for isolating the plutonium that would be produced in the reactor fuel.

8 Radioactivity is the rate at which a radionuclide decays and emits radiation. That rate is expressed as a number of disintegrations per second and depends on the material’s half-life and on the amount of material present.

9 The quantity of plutonium present may be expressed either by weight (for example, in micrograms) or by radioactivity (for example, in microcuries). Because 5 micrograms of plutonium has a radioactivity of 0.3 microcurie, that quantity of plutonium may be expressed either way.
**Units of Radiation Dose**

To measure the absorbed dose of radiation from sources external to the body (for example, beta, gamma, or x-ray emissions), health physicists calculate the amount of energy absorbed per kilogram of tissue for specific organs or the whole body. The unit of energy used is the joule, and 1 joule = 10^6 ergs. The absorbed dose is called a gray,* and 1 gray is the deposition of 1 joule of energy per kilogram of tissue. An earlier conventional unit for this same measurement was the radiation absorbed dose (rad), and 100 rad = 1 gray.

The biological damage done by 1 gray of ionizing radiation depends on the type and energy of that radiation. The more energy carried by the radiation and deposited in the tissue, the more damage done to the cells. However, the different types of radiation are not equally effective at producing biological damage. For example, 1 gray of neutron radiation is 2 to over 20 times more damaging than 1 gray of gamma radiation. To account for biological effects, health physicists multiply the absorbed dose (given in gray) by appropriate weighting factors and obtain an adjusted dose that has the same biological effect for different types and energies of radiation. The unit for this adjusted dose is called a sievert. An earlier conventional unit was the roentgen equivalent man (rem), and 100 rem = 1 sievert.

Doses from radioactive sources inside the body depend on the amount of the radionuclide in the body. And that amount is inferred from the radionuclide’s activity, which is the number of decays per second. For external radiation sources (x-rays, gammas, or betas), the radioactivity is measured with dosimeters; for alpha emitters, it is inferred from measurements of the radioactivity of excreta, such as urine or fecal samples; and for gamma radiation coming from a person’s body, it is measured by whole-body counting. The person is placed in a shielded room whose background radiation is low. Gamma radiation penetrates a detection crystal, excites a scintillator, and gives a direct measure of the person’s internal gamma radioactivity. The unit of radioactivity is the becquerel, and 1 becquerel = 1 disintegrating atom per second. A historical unit for measuring the radioactivity in the body is the curie (1 curie = 37 × 10^9 becquerels).

To obtain doses from the amount of radionuclide in the body, health physicists use biokinetic models. These models take into account the radioactive half-life of the radionuclide, the type and energy of the radiation the radionuclide emits, the metabolism it undergoes once it is in the body, and the time it takes for half the amount of the radionuclide (or half time) to leave the body. Because internal doses to organs are often nonuniform, the composite health detriments from them are converted to a value that is equivalent to an equal health detriment from an external radiation dose to the whole body. This adjusted internal dose is called effective dose equivalent, or simply effective dose, and is distributed over the period in which the radionuclide is present in the body. And the sum of these doses over future years is called the committed dose. The committed dose generally spans 50 years for occupational exposures and 70 years for children and the general population.

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* All the modern radiation units described in this box were named after scientists in radiation research.

**Plutonium and Health**

indicated that plutonium was distributed in bones differently and more dangerously than radium, a group of scientists—among whom were Drs. H. Friedell, L. H. Hempelmann, J. W. Kennedy, and W. H. Langham—met at Los Alamos to discuss these results. The outcome of this meeting was that the 5-microgram standard was reduced by a factor of 5. The permissible body burden for plutonium was thus set to 1 microgram, or 0.06 microcurie. This limit was intended to better protect plutonium workers in the United States.

Later, however, discussions at the Chalk River Conferences in Ontario, Canada (1949 to 1953), led to further reductions in the plutonium standard, which was set at 0.65 microgram, or 0.04 microcurie, for a permissible lifetime body burden.

This standard remained unchanged for more than two decades. In 1977, however, the International Commission on Radiation Protection (ICRP) described a new radiation-protection concept (ICRP 26, 1977) based on plutonium dose rather than plutonium deposition. The guideline for a maximum occupational dose is based on a calculated effective whole-body dose equivalent, and because it uses weighting factors, it does take into account organ doses. The overall guideline is that the maximum occupational plutonium dose is not to exceed an effective whole-body dose equivalent of 0.05 sievert, or 5 rem, annually from all types of occupational radiation exposure—internal and external (see the box “Units of Radiation Dose”).

Published between 1979 and 1988, a series of reports known collectively as ICRP 30 contains the derived annual limits of radionuclide intake10 for the protection of workers. Although the conceptual basis for limiting exposure to plutonium has changed drastically, the limit on internal deposition has not.

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10 The annual limit of intake is the activity of a radionuclide that, taken internally, would irradiate a person, organ, or tissue to the limit set by the ICRP for each year of occupational exposure.
The ICRP protection concept requires calculation of organ doses. For plutonium, these doses are uncertain because the internal distribution of plutonium varies greatly from one case to the next and the microdistribution of dose within organs is poorly understood. Therefore, the effective dose equivalent for plutonium is calculated with standard models, as recommended by ICRP 30 (see the box “Models Predicting Risk of Carcinogenesis”). This revised worker-protection guidance was placed into effect for DOE facilities at the beginning of 1989.

In the spring of 1991, the ICRP published new recommendations (ICRP 60) according to which the occupational exposure limit will be reduced to 0.02 sievert, or 2 rem, per year, which includes external and internal radiation doses. So far, the United States has not adopted this latest recommendation.

The Likelihood of Exposure to Plutonium

The largest amount of plutonium that has entered the environment is, by far, from radioactive fallout caused by aboveground nuclear weapons tests. From the Trinity Test in 1945 until atmospheric testing was banned in 1963, over 5 tons of plutonium were dispersed in the atmosphere in the form of small particles blown around the globe by the wind.

Most of this plutonium dust fell into the oceans, and approximately 96 percent of that amount simply sank as sediment onto the ocean floors because plutonium is not readily soluble in seawater. The fact that plutonium dissolves very slowly in water also explains why the plutonium concentration in our oceans is low and will continue to be so. The rest of the plutonium dust fell on land.

At present, surface soils everywhere contain minute quantities of plutonium. Plutonium attaches itself to...
Nuclear Accident at Chernobyl

On April 26, 1986, one of the four reactors at the Chernobyl nuclear power station in the Ukraine (formerly part of the Soviet Union) melted down and exposed millions of people to the single largest radiation event in world history. The facts leading up to the explosion are well known. Reactor 4 produced steam that drove generators to make electricity. On the night of the accident, operators were testing the generators to determine how long they could run without power. To this end, they reduced the power produced in reactor 4 and stopped the steam flow to the generators. But the RBMK-1000 design of reactor 4 has a flaw that makes its operation at low power unstable. Moreover, in violation of existing rules, the operators withdrew most control and safety rods from the core and switched off some important safety systems so that those should not interfere with test results. Ironically, the safety systems could have averted the destruction of the reactor’s core.

Power production in the reactor’s core surged to 100 times the maximum permissible level, temperature increased in a couple of seconds, and two explosions blew off the metal plate sealing the reactor’s top and destroyed the building housing the reactor. Within seconds, the explosions showered the environment with hot and highly radioactive gases. The gases contained aerosolized fuel and fission products, the radioactive nuclei created when uranium atoms split.

Early health consequences of this disaster were seen only in the firemen and power plant personnel exposed at the plant site. Of the 237 persons immediately hospitalized, 134 had clinical symptoms and signs attributable to radiation exposure. From among these 134 acute cases, 28 persons died as a result of exposure to high levels of radiation. The off-site environmental contamination levels were high enough to require, within about 10 days of the accident, that about 135,000 people leave their homes. Ten years after the accident, the area within 30 kilometers of the Chernobyl plant was largely uninhabited, and people in 60 settlements outside this zone had also been relocated (Shcherbak 1996).

Most of the reactor fuel was uranium. Mixed with it was plutonium (about 580 kilograms) created as a by-product of normal operations. And yet, in spite of the large quantity of plutonium present in the reactor, this metal has seldom been mentioned in accounts of the Chernobyl accident. Plutonium is not very volatile, and even the red hot meltdown of the Chernobyl reactor core did not disperse much of it. About 3.5 percent of the plutonium (or a volume equivalent of about 1 liter) in the reactor was released to the environment. Plutonium was detected with sensitive measurement techniques in contaminated areas, but the levels were below those that would cause health concerns.

Instead, the main radioisotopes that caused significant radiation doses during this accident were two uranium fission products: cesium-137 and iodine-131. About 50 to 60 percent of the iodine-131 and 20 to 40 percent of the cesium-137 were released to the environment. Because cesium-137 has a half-life of 30 years, scientists believe it will account for the largest radiation doses in the long run. Having a relatively short half-life (only 8 days), iodine-131 caused large radiation exposures in the weeks immediately after the accident. Ten years after the accident, health studies showed an increased incidence of thyroid cancer among infants who were in the most-contaminated off-site zones immediately after the accident. By the end of 1995, close to 800 children in Belarus, northern Ukraine, and Russia were reported to have thyroid cancer. Clinical experience indicates that 5 to 10 percent of these children will die of thyroid cancer, but only a handful have so far. No significant rise in leukemia has yet been detected among the inhabitants of those same zones or among the emergency workers and evacuees exposed to the highest initial doses of radiation.

Indeed, so far, the Chernobyl experience has not validated the opinions of either optimists or pessimists. The former predicted no long-term medical consequences from the explosion; the latter predicted well over 100,000 cancer cases. However, previous experience with long-term radiation effects at Hiroshima and Nagasaki suggests that the current toll will continue to rise and that the health effects triggered by this accident will be fully understood only a few decades into the future.

Interestingly, a gamut of psychosomatic disorders became widespread after the Chernobyl accident. The hushing up of the dangers from this accident in Soviet propaganda caused people to live in constant fear for their lives and the lives of their children. Indeed, a 10- to 15-fold increase has been observed in the incidence of psychosomatic disorders (Shcherbak 1996). Even in less-contaminated areas, there has been a large upswing in stress-related physical ailments. In the end, the morbidity* and mortality caused by psychosomatic disorders may become far reaching. Perhaps, they may even exceed the number of sicknesses and deaths caused by exposure to radiation.

* The ratio of the number of sick individuals to the total population of a community.
soil particles through ion-exchange processes—minerals in the soil can be exchanged for plutonium, which will stick to the soil and move only when the soil does. This chemical property of plutonium restricts its movement through soil and limits its uptake into most plants. For example, if soil were to contain 10,000 parts of plutonium, approximately 1 part would be taken up by a plant. The highest plutonium contamination on leafy vegetables or grains comes from wind-blown dust and rain splash.

People are exposed to plutonium mainly when they inhale small particles from the top soil kicked up by the wind or by some human activity. Measurements of the plutonium uptake have been derived from autopsy tissues, and scientific data indicate that the levels of plutonium in the general population of the United States are very small. On average, the committed effective dose from the plutonium content of a person living in the northern hemisphere is an insignificant 0.00006 sievert compared with the background radiation dose, which can be as high as 0.21 sievert. The committed effective dose is the estimated amount of radiation a person in the general population receives from a given source, in this case plutonium, over a 70-year period. Involved in this study were primarily people who lived in the 1950s and 1960s, decades during which radioactive fallout was being generated from atmospheric weapons testing.

But fallout from weapons testing is not the only possible source of plutonium dust in the environment. Nuclear accidents, such as the 1986 Chernobyl accident, may cause plutonium dust to enter the environment. And yet, although the meltdown of the Chernobyl reactor was a potentially large source of plutonium dust, scientific data indicate that cesium-137 and iodine-131, rather than plutonium, were the major sources of hazard following that accident (see the box “Nuclear Accident at Chernobyl”).

Scientists who work with plutonium and are familiar with its properties will

Figure 2. Plutonium Entry Routes into the Body

(a) Inhalation is the most likely and dangerous entry route for plutonium particles. Approximately 5% to 25% of the inhaled particles are retained by the body. Depending on particle size (the smaller the particle, the higher its risk to be retained) and chemical form (soluble forms are more easily absorbed by the blood), inhaled plutonium will remain lodged in the lung or lymph system, or it will be absorbed by the blood and delivered mainly to the liver or bones.

(b) Ingestion of plutonium is the least likely entry route for plutonium particles. In adults, only about 0.05% of the ingested soluble plutonium compounds and a mere 0.001% of the ingested insoluble ones enter the bloodstream. The rest passes through the gastrointestinal tract and is excreted.

(c) Absorption of plutonium through skin cuts is a serious risk but mainly for workers who handle highly contaminated items in glove boxes. Up to 100% of the plutonium absorbed in this way will be retained by the body.

argue that, although highly dangerous, plutonium is handled safely. In occupational terms, therefore, plutonium is no more of a hazard than other industrial toxins. In terms of the general public, barring serious accidents and nuclear war, another way in which people in the United States or elsewhere could possibly increase their levels of plutonium would be by eating dirt! And there are people who suffer from an eating disorder called pica, or the compulsive ingestion of large quantities of dirt. While eating dirt, these people will ingest greater than normal plutonium quantities. However, even then, they are significantly protected because the human gastrointestinal tract absorbs only about 1 part of plutonium out of 5000 to 10,000 parts swallowed.

And yet, none of the above should detract from the fact that
plutonium is a very hazardous material. Great attention is paid to providing safe workplaces and work practices for plutonium operations. More than 50 years have passed since plutonium was discovered, and experience with this dangerous metal proves that people can be protected.

**Data from Plutonium Exposures**

Suppose for a moment that, in spite of safe standards and handling procedures for plutonium, one is accidentally exposed to low levels of plutonium. What is the risk for developing cancer or suffering any other detectable effects, such as chromosomal instabilities or cell dysfunctions? To answer that question, we shall first have to discuss plutonium metabolism, once this metal enters the body.

**Plutonium Metabolism.** The ease with which plutonium is absorbed in the body depends significantly on two factors—the means of entry and the type of plutonium compound that has entered the body. In general, soluble forms such as nitrates, citrates, and certain oxides are absorbed more readily by the body’s fluids than insoluble forms. Figure 2 summarizes the plutonium entry routes into the body.

Absorption of plutonium through intact skin is very low. But puncture wounds, cuts, and to a lesser extent, skin burns contaminated with plutonium favor deposition of the element into tissues within and below the skin. The amount of plutonium picked up in the blood circulation depends on the chemical form of the plutonium. Soluble forms start being distributed throughout the body within minutes or hours of the uptake. Some of the plutonium may be transferred to lymph nodes near the wound, where it may stay for years. Even some insoluble forms of plutonium are taken up into the blood circulation quickly, but most remain at the site and are slowly mobilized over weeks and months. The plutonium absorbed in the blood circulation is called the systemic burden because it gets redistributed throughout the body. About 90 percent of the systemic burden gets deposited in the liver and bones. Urine, produced in the kidneys, reflects the concentration of the plutonium circulating in the blood. Plutonium measurements from urine are therefore the major source of data about the overall systemic plutonium deposition in the body over time.

Ingesting plutonium is perhaps the least likely means for plutonium to enter the body. But even if plutonium is ingested, the gastrointestinal tract provides a natural barrier, and in adults only about 0.05 percent of the soluble plutonium compounds and a mere 0.001 percent of the insoluble ones enter the bloodstream. The rest of the plutonium simply moves out of the body in feces. In babies under 1 year of age, however, the plutonium uptake may be as much as 10 times greater than in adults.

It is the inhalation of plutonium dust that is the most likely way for plutonium to enter the body. The size of the inhaled particles affects the ease with which plutonium is absorbed: the smaller the particle, the higher its likelihood to be retained. Most particles over 10 micrometers in diameter (considered large) are filtered out in the nose and upper respiratory region, then swallowed, and eventually passed out of the gastrointestinal tract in feces. Particles less than 10 micrometers in diameter are called respirable particles. When inhaled, some of them are deposited on the mucus layer of the bronchial tubes, whose lining contains numerous hair-like structures called cilia.

The natural wave motion of the cilia transports the mucus layer and its dust particles up to the throat. This process, known as lung clearance, removes much of the foreign material deposited in the bronchial tubes. Even smaller particles, especially those under 1 micrometer in diameter, or about one-tenth the thickness of a typical human hair, are carried down into the tiniest airways of the lung and into alveoli (also known as air sacs). Because all these structures have no cilia on their surfaces and no effective lung-clearance mechanisms, scavenger cells called phagocytes move in on the inhaled plutonium particles, engulf them, and transport them into lymph nodes or into lung tissues, which are sites of longer-term retention (see Figure 3). The plutonium particles
retained in lung tissues might increase a person’s risk for developing lung cancer.

The rate of absorption from the lung into the blood is directly determined by the plutonium compound’s solubility. An oxide produced at high temperatures is not very soluble and remains for very long periods in the lung tissue or the lymph nodes, the filter system around the lung. In tissue samples taken during autopsy from three plutonium workers known to have inhaled plutonium dust, 35 to 60 percent of the plutonium in the body at the time of death was in the lung or the tracheobronchial lymph nodes. The plutonium remained there for about 40 years after inhalation.

Soluble forms of plutonium in wounds or lungs dissolve into surrounding tissue fluids, are picked up in the bloodstream, and will then be circulated around the body. About 90 percent of the plutonium picked up from the lung is deposited about equally into the liver and bones. The remaining 10 percent or so is quite uniformly deposited in soft tissues, and a small fraction of it is excreted in urine and feces.

Autopsy studies reveal that, initially, plutonium is not deposited throughout bone tissues. Instead, it is mostly deposited on the bone surfaces and, in particular, on the interlaced surfaces of the so-called trabecular bone (see Figure 4). Less than 5 percent of the plutonium is typically found within the bone marrow, the soft material that is the site of the blood-forming cells (the hematopoietic stem cells). Given this pattern of deposition, the primary carcinogenic risk from plutonium in the skeleton is bone cancer. There is no conclusive evidence that plutonium increases the risk for leukemia, which is the unchecked proliferation of certain blood cells produced in the bone marrow.

Once sequestered in the bone, plutonium remains there for a very long time. Normal remodeling of the bone structure results in plutonium being gradually redistributed more uniformly throughout the bone. Current models throughout the bone. Current models gradually redistributed more uniformly structure results in plutonium being time. Normal remodeling of the bone

...
also be considered when interpreting epidemiological data. We shall stop to look at only two of them: bias and confounding factors.

Bias is any trend in the collection, analysis, interpretation, publication, or review of data that can lead to conclusions systematically different from the truth. Often encountered is the “healthy-worker effect,” a bias that results from comparing employed people with persons in the general population. Employed people should be healthy enough to be in the workforce, whereas the general population will include some persons who are disabled or ill. Thus, unless it experiences strong, detrimental effects from exposures, the employed group generally looks healthier by statistical analysis than the general population.

A confounding factor is any risk factor, other than the risk under study, that influences the outcome. Smoking, for example, is a strong confounding factor because it increases the chance for cardiovascular diseases and the incidence of and mortality rate from lung and other cancers. Unless data are available and adjustments are made for differences in smoking between different populations, smoking may account for the differences in the observed frequency of smoking-related diseases rather than other factors such as exposure to radiation. So, interpreting epidemiological data is complex and potentially controversial. Although it may establish a statistical association between some agent or activity and health effects, this finding does not, by itself, establish causation. Causation decisions are judgments made on the strength of the data, confirmation by other studies, and biological credibility.

To date, there have been only few epidemiological studies of workers exposed to plutonium. Studies of workers at Los Alamos National Laboratory (Wiggs et al. 1994) and Rocky Flats (Wilkinson et al. 1987) are the only ones in the United States to have used quantitative measurements of plutonium exposures, but they involved few workers: 303 at Los Alamos and 1450 at Rocky Flats. These two studies showed no evidence of statistically increased rates of lung, liver, and bone cancers, which are shown in animal experiments to be the highest-risk cancers due to plutonium exposure. A study by Reyes et al. (1984) indicates that an increased brain-cancer rate in Rocky Flats workers was not caused by plutonium exposure or external radiation.

Over the years, there have been a few other studies on Los Alamos workers exposed to plutonium, but most of them are smaller in scope. Published in 1983, one such study by Voelz et al. was conducted on 224 males exposed to plutonium between 1944 and 1974. Their plutonium deposition was greater than 0.16 microgram, or 0.01 microcurie. None of the people involved in this study developed bone or liver cancer, and by 1980, the final year of the study, only one person had died of lung cancer. This study did not confirm earlier opinions of some nuclear-industry critics who predicted a very high risk for lung cancer at low plutonium doses.

Another study involved 26 chemists, metallurgists, and technicians at Los Alamos, who were accidentally exposed to plutonium between 1944 and 1946. The plutonium body burdens of these men were from 5 to more than 360 times the current annual limit of intake set by DOE. By weight, the corresponding body burdens, 50 years after exposure, ranged from 0.02 to 1.4 micrograms and were estimated by analysis of the men’s urine. Estimates are that the men took up about twice this amount at the time of exposure. Wright Langham, the originator of this ongoing study, roguishly called this tiny cohort of men the UPPU (or U-P-Pu!) club, a name by which they have been known since.

It is important to note that the mortality rate of the club members has been lower than that of the population in general. In 1996, the most recent year of our data analysis, 19 members were still alive. To this day, their health is being monitored periodically by Los Alamos physicians. Overall, it is typical of men their age.

Of the individuals in this club who are no longer alive, one man died of lung cancer in 1989, at the age of 66. Two men died of prostate cancer and congestive heart failure, respectively, but both had lung cancer at the time of death. All three men were very heavy smokers. Significantly, three cases of lung cancer are consistent with the national cancer incidence rate, over the same period, in U.S. white males of the same age. The national cancer incidence rate is the rate at which new cases of lung cancer emerge.

Another club member, who had an estimated plutonium deposition of 0.245 microgram, developed a rare bone cancer 43 years after exposure and died in 1990. This last finding is statistically significant for a small group like the UPPU club. But in the 1994 Los Alamos study (Wiggs et al.) of 303 workers, this same individual remained the only one to have developed bone cancer. Statistical analysis indicates that one death caused by bone cancer in this larger group may well be due to chance and is not statistically significant.

Finally, three more club members died of causes unrelated to cancer: one of a heart attack, another of viral pneumonia, and a third in a car accident. As shown in Table I, according to the national mortality rate, one would have expected 19.8 deaths in the UPPU club at the time of the latest data analysis. In this table, we did not include the pneumonia and car accident deaths in the breakdown on causes of death because plutonium clearly played no part in those deaths. We did, however, include the death from a heart attack because, as shown later, cardiovascular illnesses are significantly low for this small group.

The table gives standardized mortality ratios, which compare the mortality rates of the exposed group with those of an unexposed group. Both groups were composed of U.S. white males. Should the mortality rates
of the exposed and the comparison groups be identical, the standardized mortality ratio will have a value of 1. A value of 0.37, as shown in the first line of the table, for example, indicates that the mortality rate in the workers exposed to plutonium is 37 percent that of the white male population of the United States. The potential error associated with this rate is given by the 95 percent confidence intervals. These intervals have a 95 percent statistical probability of including the true value of the standardized mortality ratio. And the probability values, or p-values for short, shown in the far-right column of the table are the probability that a particular finding—in this case, the mortality rate—has occurred by chance. A p-value of less than 0.05 has therefore less than a 5 percent chance of having been caused by random events and is considered statistically significant. With less than a probability of 1 percent to have been caused by chance, a p-value of less than 0.01 is considered very significant. In Table I, there are three such values. The first (0.0009) indicates that a generally low mortality rate among the 26 workers exposed to plutonium is not due to chance. But that outcome may have been influenced by the healthy lifestyles of the people who were still alive—less smoking, plenty of exercise, and good food. The second statistically significant finding is a p-value of 0.01 for one death from bone cancer. Because bone cancer was also present in experimental animals exposed to plutonium, this finding has biological credibility. However, no other bone tumors have been reported in U.S. plutonium workers. The third significant p-value (0.006) indicates a very low rate of cardiovascular deaths in this small group of people, which was probably caused by a confounding factor—most likely smoking. A higher percentage of white males in the United States tend to smoke than in the small UPPU club. The rate of expected cardiovascular deaths in this small population is therefore high.

Overall, data from the several studies of persons exposed to low levels of plutonium radiation in the United States do not show a relationship between dose and effect. They merely indicate that such a relationship does not exist or cannot be confirmed. If plutonium is harmful at these low levels, its health risks are so small that, given the small number of workers involved, epidemiological methods cannot differentiate between effects triggered by plutonium radiation and variations in a group of people unexposed to such radiation.

We need to stress that cancer risk from low doses of radiation and low-dose rates is not known precisely. When an individual who has had a history of radiation exposures—occupational and or medical—plus other possible additive and synergistic insults is diagnosed with cancer, no specific cause is readily attributable. In case of litigation, the medical testimony will rest on opinions about the probability that the occupational radiation dose may or may not have been a major cause. In the future, when radiation risk coefficients for low doses are better defined, it may be easier to form these medical opinions.

Although studies conducted on plutonium workers in the United States did not yield data that demonstrate the risk from plutonium radiation, there are such data from much higher doses to which Russian plutonium workers have been exposed.

**High-Level Exposures.** Russian scientists have recently published two studies (Tokarskaya et al. 1997, Koskhunikova et al. 1998) of workers who had been exposed to plutonium at the Mayak Plant, the first nuclear facility in the former Soviet Union. The authors demonstrate that an increased risk for lung cancer is associated with higher exposures. Although both studies investigate this risk on many of the same workers, their conclusions about the relationship between dose and risk are different (see Figure 5).

Koshurnikova et al. analyzed data from a cohort of 1479 workers who had been exposed to high doses of various types of radiation, including plutonium radiation, between 1948 and 1993. The control group was composed of 3333 other workers at Mayak who had also been exposed to radiation but within occupational limits. As illustrated in Figure 5(a), the authors found a linear relationship between lung doses from 0.5 to 30 sieverts (or 50 to 3000 rem) and standardized mortality ratios. This result means that no threshold was found; that is, no dose value

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**Table I. Number of Deaths and Mortality Rates among 26 Plutonium Workers* in the United States**

<table>
<thead>
<tr>
<th>Causes of Death</th>
<th>Observed Deaths</th>
<th>Expected Deaths</th>
<th>Standardized Mortality Ratios</th>
<th>95% Confidence Intervals</th>
<th>p-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>7</td>
<td>19.8</td>
<td>0.37</td>
<td>0.15–0.77</td>
<td>0.0009*</td>
</tr>
<tr>
<td>Cancer</td>
<td>3</td>
<td>4.6</td>
<td>0.65</td>
<td>0.13–1.9</td>
<td>0.326</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
<td>0.60</td>
<td>0.01–3.4</td>
<td>0.509</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>1</td>
<td>2.7</td>
<td>0.04–15</td>
<td>0.309</td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>1</td>
<td>90</td>
<td>1.18–502</td>
<td>0.01*</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular illness</td>
<td>2</td>
<td>9.1</td>
<td>0.22</td>
<td>0.02–0.80</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

*Analyses of results through 1996

*Significant p-values
Figure 5. Plutonium Dose vs Lung Cancer Risk at Mayak—Two Results

(a) Results of an epidemiological cohort study at the Mayak Plant in Russia (Koshurnikova et al. 1998) show standardized mortality ratios—the ratio of the observed to the expected deaths adjusted for age distributions and calendar years of death—as a function of lung doses of up to 30 sieverts (Sv). The horizontal dotted line marks a mortality rate of 1, which indicates that no increase in lung cancer risk was observed. The mortality rate appears to increase linearly with dose and, at a dose of about 25 Sv, has risen to 11 times the normal rate. The statistical bars here and in (b) show the 95% confidence intervals. In other words, the true mortality rate has a 95% probability of falling within that interval.

(b) In the case-control study by Tokarskaya et al. (1997), increased lung-cancer risk from plutonium radiation is shown to exhibit a threshold effect. The odds ratios for lung cancer are shown as a function of lung doses up to 30 Sv. The odds ratio is the exposed group’s probability divided by the control group’s probability of developing cancer. Up to a dose of about 7 Sv, the curve shows odds ratios less than 1—that is, no increased risk from plutonium radiation. Above 7 Sv, however, the curve begins to turn up, and at 16 Sv there is a threshold above which the risk increases rapidly. Some scientists have speculated that the dip below a value of 1 at low doses may be due to the adaptive response described in the box “Models Predicting Risk of Carcinogenesis” on page 80.
was found within the given range below which cancer risk from plutonium radiation would be completely eliminated. To obtain the mortality rates, the authors calculated the ratio of the observed to the expected deaths and then adjusted the result for age distributions and calendar years of death. The observed deaths (105) are those of workers who had been exposed to total lung doses of up to 30 sieverts. The expected deaths (40.67) are from the control group whose lung doses totaled only about 0.5 sievert. According to the data, in the dose range between 0.5 and 30 sieverts, lifetime risk from lung cancer increases by 1.2 percent for each additional sievert in that range, which is about double the lifetime risk quoted by the ICRP (ICRP 60, 1991). Shown in this graph are also 95 percent confidence intervals. The lowest values of these intervals for the first four sets of data points are less than 1. Below a mean dose of about 5 sieverts, therefore, the observed mortality rates in exposed workers have a reasonable likelihood of having been caused by chance. Nevertheless, the trend of increasing rates with increasing dose is impressive.

But Tokarskaya et al. (1997) found a nonlinear threshold relationship between dose and lung cancer risk. Their results are shown in Figure 5(b). This is a case-control study devoted to 162 plutonium workers who developed lung cancer between 1966 and 1991 and a control group of 338 Mayak workers who, during the same period, did not. As mentioned before, there was much overlap of workers between the two Russian studies because those people worked at the same Mayak Plant. Tokarskaya and her colleagues analyzed three risk factors for lung cancer: smoking (most of these workers were heavy smokers), plutonium radiation, and external gamma radiation. They determined relative risks by using a different methodology, namely, odds ratios. They calculated the ratio of the probability that lung cancer was the result of exposure to plutonium by juxtaposing the exposed and control groups. The authors found no lung-cancer risk up to a threshold dose of 16 sieverts, which corresponds to a deposition of about 1.6 micrograms of plutonium. Above this threshold value, however, the risk rises rapidly. The initial portion of the curve, up to a lung dose of at least 7 sieverts, has odds ratio values of less than 1. This finding suggests that there is no increased risk from plutonium radiation and that a possible beneficial effect cannot be ruled out. Above 7 sieverts, however, the curve begins to turn up, and above 16 sieverts, the risk rises dramatically. The 95 percent confidence intervals reveal that the lower and upper values of those intervals encompass the value 1 for all mean doses under 30 sieverts. This result indicates that slight variations in odds ratios, such as the initial dip below 1 and even the later increase to 2 may simply have been caused by chance.

The two curves based on Russian data are very different in shape. However, differences notwithstanding, the Mayak data demonstrate that lung cancer risk does indeed increase with higher doses. No studies have yet been published on the Mayak workers’ risk for developing bone or liver cancer.

Summary

It has been almost six decades since plutonium was first made, and people’s fears about this material are still strong today. No doubt, the dangers of plutonium are real. The fact that the defense and nuclear power industries have been able to limit the extent of exposures is a direct result of the foresight and careful planning on the part of the physicists and chemists who first isolated and produced plutonium. Almost from the moment plutonium was isolated, scientists worried about the possible health effects of this radioactive substance. Since then, plutonium has been handled in different chemical forms, fabricated as a metal, machined, and used successfully in many applications primarily because standards and procedures were soon established to prevent people from being exposed. There has been no instance of acute death from plutonium radiation except for external-radiation deaths resulting from criticality accidents. That is a remarkable achievement.

Precisely because it is conservative in its assumptions, the linear nonthreshold model for risk from low levels of plutonium radiation is at the basis of permissible plutonium occupational doses. Workers in the United States are well protected, but accidents can happen. From our extensive experience with plutonium and other radioactive materials, we know that effective communication with persons involved in radiation accidents is very important. Indeed, open communication with the general population is equally important.

Los Alamos has been leading the way in providing the world with facts about plutonium. Does the population at large need to be concerned about being exposed to plutonium radiation? Exposures to high levels of plutonium radiation can happen only during accidents. Should they occur, such exposures are dangerous as they can induce cancer in humans. Exposures to low levels of plutonium radiation are a real possibility for plutonium workers. Epidemiological studies, however, have not yielded data that would allow us to establish a clear relationship between plutonium dose and its possible health effects. And this kernel of uncertainty is the very reason for radiation protection measures to stay conservative—perhaps more conservative than is actually needed. Barring an act of sabotage, nuclear war, or a nuclear accident more severe than Chernobyl, the general public is not likely to be significantly exposed to plutonium. Plutonium is around only in negligible amounts. Hopefully, this excellent track record will continue indefinitely.
Further Reading


George Voelz, a native of Wisconsin, received his M.D. degree from the University of Wisconsin Medical School in 1950 and then did an internship at the University of Oregon Medical School Hospital and Clinics. After having completed an Atomic Energy Commission fellowship in occupational medicine at the Kettering Laboratory of the University of Cincinnati in 1951, George completed another fellowship at the Los Alamos Scientific Laboratory in 1952. From 1957 to 1970, George worked at the National Reactor Testing Station for the U.S. Atomic Energy Commission, Idaho Operations Office, where he organized and became director of the Health Services Laboratory in 1967. George returned to Los Alamos in 1970 to serve as leader of the Health Division until 1982. For the next five years, he was Health Division deputy leader, working primarily in the administration of research programs. From 1987 to 1990, George led the epidemiology section of the Occupational Medicine Group at Los Alamos. In 1990, he retired from the Laboratory. Since then, he has actively continued his research as a Laboratory associate, studying the health of nuclear industry workers. His special interest has been the effects of plutonium exposure on human health. George has been certified as a diplomat of the American Board of Preventive Medicine since 1959 and has served on numerous committees. He is a lifetime honorary member of the National Council on Radiation Protection and Measurements. He also served as a committee member for the International Commission on Radiological Protection and, in 1994, as a team member of the Los Alamos Human Study Project.