REVIEW ARTICLE

CURRENT CONCEPTS

Short-Term and Long-Term Health Risks of Nuclear-Power-Plant Accidents

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O N MARCH 11, 2011, A 9.0-MAGNITUDE EARTHQUAKE STRUCK THE EAST coast of Japan. The total number of people who died in the earthquake and the tsunami that it generated is still being assessed, but the official estimation already exceeds 14,000.[1] The natural disaster also caused substantial damage to the Fukushima Daiichi nuclear power plant, the consequences of which are still unclear. The purpose of this review is to put the emergency at the Japanese power plant, even as it is evolving, into the context of the extensive literature on nuclear-reactor accidents by analyzing the mechanisms and major short-term and long-term health risks of radiation exposure. In addition, we briefly discuss the accidents at Three Mile Island in Pennsylvania in 1979 and at Chernobyl in Ukraine in 1986 because they illustrate the broad range of potential outcomes.

MECHANISMS OF EXPOSURE

REACTOR ACCIDENTS AND THE RELEASE OF RADIOACTIVE MATERIALS

In a nuclear power plant, the fuel, an isotope of either uranium or plutonium, undergoes fission to produce the energy that is used to heat water and turn steam-driven turbine generators. In addition to the release of energy, the split fuel creates radioactive fission products. In the event of an accident, the primary concern is that the support structure (core) containing the fuel and the fission products may become damaged and allow radioactive elements to escape into the environment. One mechanism by which this can happen is failure of the core cooling system. In such a circumstance, the reactor core and even the fuel itself can partially or completely melt. Elevated temperatures and pressures can result in explosions within the reactor, dispersing radioactive material. In most plants, the potential effects of a cooling-system failure are minimized by surrounding the reactor core with a steel-walled vessel, which in turn is surrounded by an airtight, steel-reinforced concrete containment structure that is designed to contain the radioactive material indefinitely (Fig. 1). Of note, the explosions that have been seen in reactor accidents are not the same as those seen after the detonation of a nuclear weapon, since the latter requires highly enriched uranium or plutonium isotopes in concentrations and configurations that are not present in power plants.

In the partial meltdown at Three Mile Island, the plant's containment structure fulfilled its purpose, and a minimal amount of radiation was released.[2] However, there was no such containment structure in place at the Chernobyl reactor — the explosions and the subsequent fire sent a giant plume of radioactive material into the atmosphere. Although the Three Mile Island accident has not yet led to identifiable health effects,[3-5] the Chernobyl accident resulted in 28 deaths related to radiation exposure in the year after the accident.[6,7] The long-term effects of the
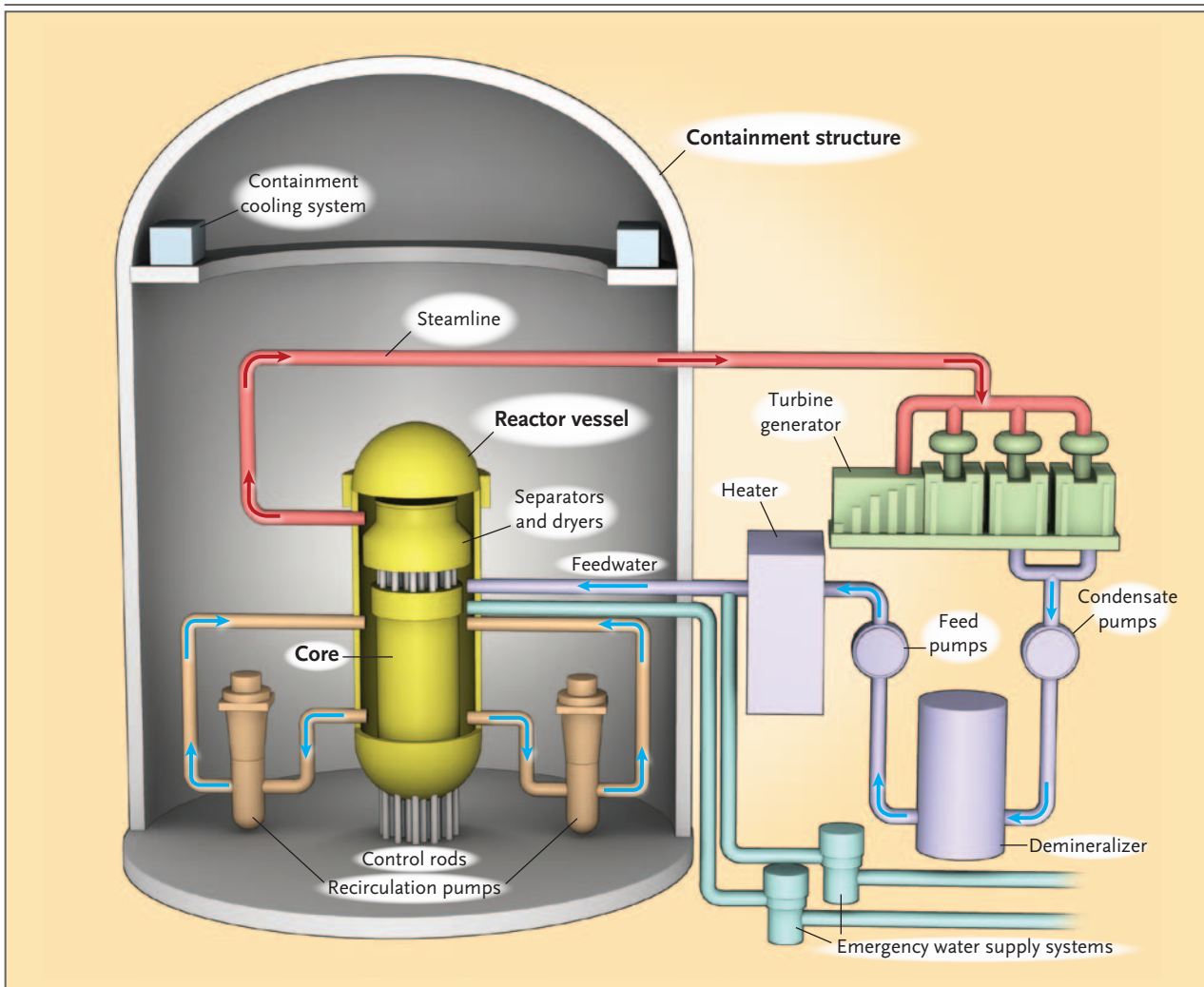
Figure 1. Key Components of a Nuclear Power Plant.

In a boiling water reactor — the type in use at Fukushima, Japan — water is boiled by the heat produced by nuclear fission. The resulting steam drives the turbines that generate electricity, while the condensed water is collected, cooled, and returned to the reactor vessel. The reactor core, which contains the fuel and radioactive fission products, is situated inside a thick-walled steel vessel that houses the cooling water. However, in the event of a failure of the cooling systems, the water can boil off, with the potential for the temperature to rise sufficiently for the core and the fuel itself to melt partially or completely. In most reactors, the effects of such meltdowns are minimized by surrounding this vessel in an airtight, steel-reinforced concrete containment structure, designed to contain the fuel and fission products indefinitely. Adapted from the Nuclear Regulatory Commission.

Chernobyl accident are still being characterized, as we discuss in more detail below. The situation at Fukushima, though still in daily flux, will probably end up ranking between these two historical accidents in terms of radiation releases and health consequences.

TYPES OF RADIATION EXPOSURE

Human radiation exposure as a result of reactor accidents is generally characterized in three ways: total or partial body exposure as a result of close proximity to a radiation source, external contamination, and internal contamination. All three types can affect a given person in a radiation accident. Total or partial body exposure occurs when an external source irradiates the body either superficially to the skin or deeply into internal organs, with the depth depending on the type and energy of the radiation involved. For example, beta radiation travels only a short distance in tissue, depending on its energy, and can be a significant source of dose to skin. High-energy

gamma radiation, however, can penetrate deeply. In previous reactor accidents, only plant workers and emergency personnel who were involved in the aftermath had substantial total or partial body exposure. Persons who have had total or partial body exposure but no contamination are not radioactive and therefore cannot expose their caregivers to radiation. External contamination occurs when the fission products settle on human beings, thereby exposing skin or internal organs. Populations living near a reactor accident may be advised to remain indoors for a period to minimize the risk of external contamination. Internal contamination occurs when fission products are ingested or inhaled or enter the body through open wounds. This is the primary mechanism through which large populations around a reactor accident can be exposed to radiation. After Chernobyl, approximately 5 million people in the region may have had excess radiation exposure, primarily through internal contamination.[7]

Reactor accidents can release a variety of radioisotopes into the environment. Table 1 lists the radioisotopes that were released during the Chernobyl accident.[8] The health threat from each radioisotope depends on an assortment of factors. Radioisotopes with a very short half-life (e.g., 67 hours for molybdenum-99) or a very long half-life (e.g., 24,400 years for plutonium-239), those that are gaseous (e.g., xenon-133), and those that are not released in substantial quantities (e.g., plutonium-238) do not cause substantial internal or external contamination in reactor accidents. In contrast, iodine-131 can be an important source of morbidity because of its prevalence in reactor discharges and its tendency to settle on the ground. When iodine-131 is released, it can be inhaled or consumed after it enters the food chain, primarily through contaminated fruits, vegetables, milk, and groundwater. Once it enters the body, iodine-131 rapidly accumulates in the thyroid gland, where it can be a source of substantial doses of beta radiation.

The release of radioactive water into the sea at the Fukushima plant has resulted in an additional route whereby the food chain may be affected, through contaminated seafood. Although the radioactivity in seawater close to the plant may be transiently higher than usual by several orders of magnitude, it diffuses rapidly with distance and decays over time, according to half-life, both before and after ingestion by marine life.

Table 1. Estimated Releases of Isotopes during the Chernobyl Accident.*

Isotope	Half-Life	Type of Radiation	Estimated Release during Accident†
			PBq
Neptunium-239	58 hr	Beta, gamma	95
Molybdenum-99	67 hr	Beta, gamma	>168
Tellurium-132	78 hr	Beta, gamma	1150
Xenon-133	5 days	Beta, gamma	6500
Iodine-131	8 days	Beta, gamma	1760
Barium-140	13 days	Beta, gamma	240
Cerium-141	33 days	Beta, gamma	196
Ruthenium-103	40 days	Beta, gamma	>168
Strontium-89	52 days	Beta	115
Zirconium-95	65 days	Beta, gamma	196
Curium-242	163 days	Alpha	0.9
Cerium-144	285 days	Beta, gamma	116
Ruthenium-106	1 yr	Beta, gamma	>73
Cesium-134	2 yr	Beta	54
Plutonium-241	13 yr	Beta	6
Strontium-90	28 yr	Beta	10
Cesium-137	30 yr	Beta, gamma	85
Plutonium-238	86 yr	Alpha	0.035
Plutonium-240	6,850 yr	Alpha, gamma	0.042
Plutonium-239	24,400 yr	Alpha, gamma	0.030

* Data are from the Nuclear Energy Agency.[8]
† A petabecquerel (PBq) equals 10^{15} becquerels (decays per second).

CLINICAL CONSEQUENCES OF RADIATION EXPOSURE

TYPE OF RADIATION AND DOSE RATES

At a molecular level, the primary consequence of radiation exposure is DNA damage. This damage will be fully repaired or innocuous or will result in dysfunction, carcinogenesis, or cell death. The clinical effect of radiation exposure will depend on numerous variables, including the type of exposure (total or partial body exposure vs. internal or external contamination), the type of tissue exposed (tissue that is sensitive to radiation vs. tissue that is insensitive), the type of radiation (e.g., gamma vs. beta), the depth of penetration of radiation in the body (low vs. high energy), the total absorbed dose, and the period over which the dose is absorbed (dose rate). The type of radiation and the dose rates that are involved in a reactor accident would typically be very different from those

seen in the detonation of a nuclear bomb, which is why the biologic consequences of these events may differ substantially.

The literature on radiation refers to dose in terms of both gray (Gy), the unit of measurement for the absorbed dose, and sievert (Sv), the unit of measurement for the effective dose, which is the absorbed dose multiplied by factors accounting for the biologic effect of different types of radiation and the radiation sensitivities of different tissues. For high-energy gamma radiation and whole-body exposures, 1 Gy equals 1 Sv. Table 2 shows estimated effective doses received during common medical and nonmedical activities and how these doses relate to those received by the populations around Three Mile Island and Chernobyl.[9-15]

Radiation exposure can potentially result in short-term and long-term effects in every organ system in the body. Comprehensive reviews of the literature on radiation exposure have been produced by the International Atomic Energy Agency and the World Health Organization.[7,15] In this review, we focus on the two potential outcomes of radiation exposure that have garnered much of the media attention in the wake of the ongoing crisis in Fukushima: acute radiation sickness and increased long-term cancer risks.

ACUTE RADIATION SICKNESS AND ITS TREATMENT

When most or all of the human body is exposed to a single dose of more than 1 Gy of radiation, acute radiation sickness can occur. Much of our understanding of acute radiation sickness is based on the clinical experience of more than 800 patients who have been described in national and international registries of radiation accidents that have been predominantly medical in source.[16] Acute radiation sickness has not been seen in the general population in association with a nuclear-reactor accident. All 134 patients with confirmed acute radiation sickness at Chernobyl were either plant workers or members of the emergency response team.[6] No confirmed diagnoses of acute radiation sickness were noted in workers or in the general population at Three Mile Island.[17]

Much of the short-term morbidity and mortality associated with a high total or near-total body dose is due to hematologic, gastrointestinal, or cutaneous sequelae. In the Chernobyl accident, all 134 patients with acute radiation sickness had bone marrow depression, 19 had

widespread radiation dermatitis, and 15 had severe gastrointestinal complications.[18] Hematologic and gastrointestinal complications are common because bone marrow and intestinal epithelium are especially radiosensitive as a result of their high intrinsic replication rate. Cutaneous toxic effects are common because external low-energy gamma radiation and beta radiation are chiefly absorbed in the skin. In Chernobyl, estimated skin doses in some patients were 10 to 30 times the bone marrow doses.[18] If total body doses are extremely high (>20 Gy), severe acute neurovascular compromise can occur. At Chernobyl, the highest absorbed dose in a worker was 16 Gy.[19]

Acute radiation sickness can be categorized into three phases: prodrome, latency, and illness. Table 3 summarizes the constellation of hematologic, gastrointestinal, and neurologic symptoms, along with the time to onset and dose dependence, associated with each of these phases. Cutaneous manifestations of acute radiation injury include mild erythema and pruritus with limited skin doses (3 to 15 Gy) and blistering and ulceration with very high skin doses (>15 Gy).[6]

The first step in the care of any patient who is exposed to radiation is to manage immediate life-threatening injuries, such as those from trauma or burns. The next step is to address external and internal radiation contamination, if any. Decontamination protocols are available from several sources.[20,21] Once these issues have been addressed and acute radiation sickness is suspected, treatment is guided by the estimated total dose, which is determined on the basis of the initial clinical symptoms, lymphocyte depletion kinetics, and cytogenetic analyses, when available.[22,23]

Patients with modest whole-body doses (<2 Gy) may require only symptomatic support for nausea and vomiting. In patients with whole-body doses of more than 2 Gy, the treatment of the consequences of bone marrow depletion is paramount. Strategies include management of infections with antibiotics and antiviral and antifungal agents, the use of hematopoietic growth factors, and possibly bone marrow transplantation.[20] The use of bone marrow transplantation is controversial, since outcomes after radiation accidents have been poor. After Chernobyl, only 2 of the 13 patients who underwent bone marrow transplantation survived long term. Among the 11 patients who died, complications from

Table 2. Effective Doses of Radiation, According to Source of Exposure.

Exposure	Effective Dose	Estimated Duration of Equivalent Radiation Dose from Natural Background
	mSv	
Medical or nonmedical exposure		
One-way flight from New York to Tokyo[9]	0.07	7 days
Chest radiograph (posteroanterior and lateral)[10]	0.1	10 days
Average annual occupational exposure of crew on commercial airline[11]	2	6 mo
Computed tomography of the chest[10]	7	2 yr
Thallium cardiac stress test[12]	36	12 yr
Annual dose allowed for a U.S. radiation worker during occupational exposure[13]	50	17 yr
Risk of health effects that is either too small to be observed or nonexistent[14]	<100	<34 yr
Three Mile Island exposure[2]		
Average dose to residents within 10 miles of the plant	0.01	1 day
Maximum dose to a person at the plant boundary	1	3 mo
Chernobyl exposure[15]		
Residents in low-contamination areas from 1986 to 2005*	10–20	3–6 yr
Evacuated residents in 1986	>33	>11 yr
Residents in high-contamination areas from 1986 to 2005*	>50	>17 yr
Reactor-site clean-up workers in 1986 and 1987	>100	>34 yr

* This dose is in addition to the dose from natural background radiation.

transplantation appeared to be the primary cause of death in 2 patients.[24] Gastrointestinal radiation sequelae are managed with supportive care and possibly with the use of prophylactic probiotics.[25] Cutaneous radiation injuries may evolve over the course of weeks. Treatment of such lesions involves minimizing acute and chronic inflammation with topical glucocorticoids while avoiding secondary infections. Several organizations have developed detailed treatment algorithms for acute radiation sickness that are publicly available.[6,20,26,27]

INCREASED LONG-TERM CANCER RISKS

In the region around Chernobyl, more than 5 million people may have been exposed to excess radiation, mainly through contamination by iodine-131 and cesium isotopes.[7] Although exposure to nuclear-reactor fallout does not cause acute illness, it may elevate long-term cancer risks. Studies of the Japanese atomic-bomb survivors showed clearly elevated rates of leukemia and solid cancers, even at relatively low total body doses.[28,29] However, there are important differences between the type of radiation and

dose rate associated with atomic-bomb exposure and those associated with a reactor accident. These differences may explain why studies evaluating leukemia[30-36] and nonthyroid solid cancers[37-40] have not shown consistently elevated risks in the regions around Chernobyl. Alternatively, small increases in the risks of leukemia and nonthyroid solid cancers may become more apparent with improved cancer registries or longer follow-up. In the population around Three Mile Island, there was a notable temporary increase in cancer diagnoses in the years immediately after the accident, but this increase may have been the result of intensified cancer screening in the area. Long-term follow-up has shown no increases in cancer mortality.[4]

However, there is strong evidence of an increased rate of secondary thyroid cancers among children who have ingested iodine-131. Careful studies of children living near the Chernobyl plant (which included estimates of the thyroid radiation dose) suggest that the risk of thyroid cancer increased by a factor of 2 to 5 per 1 Gy of thyroid dose.[41-43] Although this relative increase in incidence is large, the baseline incidence of

Table 3. Signs and Symptoms of Acute Radiation Sickness in the Three Phases after Exposure.*

Prodrome, According to Exposure Level	Latency†	Illness‡
Mild (1 to 2 Gy)		
Vomiting; onset, 2 hr	Duration, 21–35 days; lymphocyte count, 800–1500/mm³	Fatigue, weakness; mortality, 0%
Moderate (2 to 4 Gy)		
Vomiting, mild headache; onset, 1–2 hr	Duration, 18–35 days; lymphocyte count, 500–800/mm³	Fever, infections, bleeding, weakness, epilation; mortality, ≤50%
Severe (4 to 6 Gy)		
Vomiting, mild diarrhea, moderate headache, fever; onset, <1 hr	Duration, 8–18 days; lymphocyte count, 300 to 500/mm³	High fever, infections, bleeding, epilation; mortality, 20–70%
Very severe (6 to 8 Gy)		
Vomiting, severe diarrhea, severe headache, high fever, altered consciousness; onset, <30 min	Duration, ≤7 days; lymphocyte count, 100 to 300/mm³	High fever, diarrhea, vomiting, dizziness, disorientation, hypotension; mortality, 50–100%
Lethal (>8 Gy)		
Vomiting, severe diarrhea, severe headache, high fever, unconsciousness; onset, <10 min	No latency; lymphocyte count, 0 to 100/mm³	High fever, diarrhea, unconsciousness; mortality, 100%

* Data are adapted from the International Atomic Energy Agency.[20]
† Lymphocyte counts in the latency phase represent the range of values that may be seen 3 to 6 days after radiation exposure.
‡ Mortality estimates are for patients who do not receive medical intervention.

thyroid cancer in children is low (<1 case per 100,000 children). Factors that increase the carcinogenic effect of iodine-131 include a young age and iodine deficiency at the time of exposure. Among children in regions with endemic iodine deficiency, the risk of thyroid cancer per 1 Gy of thyroid dose was two to three times that among children in regions in which iodine intake was normal.[44,45] Moreover, the risk of thyroid cancer among children who were given stable iodine after the Chernobyl accident was one third that among children who did not receive iodine.[45] Studies of the effect of thyroid exposure to radiation in utero[46,47] and in adulthood[48-50] have been inconclusive.

In accidents in which iodine-131 is released, persons in affected areas should attempt to minimize their consumption of locally grown produce and groundwater. However, since the half-life of iodine-131 is only 8 days, these local resources should not contain substantial amounts of iodine-131 after 2 to 3 months. On the advice of public health officials, area residents may take potassium iodide to block the uptake of iodine-131 in the thyroid. To be most effective, prophylactic administration of potassium iodide should occur before or within a few hours after iodine-131 exposure. The adminis-

tration of the drug more than a day after exposure probably has limited effect, unless additional or continuing exposure is expected.[51] Although potassium iodide can have toxic effects, the Polish experience with en masse administration of the drug after Chernobyl was reassuring. More than 10 million children and adolescents in Poland were given a single dose of prophylactic potassium iodide, with very limited morbidity.[52] The Food and Drug Administration has issued guidelines for the administration of potassium iodide according to age and expected radiation exposure.[53]

CONCLUSIONS

Because nuclear-reactor accidents are very rare events, few medical practitioners have direct experience in treating patients who have been exposed to radiation or in the overall public health response. Organizations that could be involved in either activity — because of their proximity to a power plant or their role in the health system — must put detailed algorithmic response plans in place and practice them regularly. A critical component of the response, with respect to both treatment of individual patients and interaction with the community, is clear communication

about exposure levels and corresponding risk, with an eye toward widespread public apprehension about acute radiation sickness and long-term cancer risks.

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