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Workers exposed to low-dose radiation face increased leukemia mortality risk

Blettner M. *Lancet Haematol.* 2015;doi:10.1016/S2352-3026(15)00113-1.
Leuraud K, et al. *Lancet Haematol.* 2015;doi:10.1016/S2352-3026(15)00094-0.

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Nuclear workers' prolonged exposure to low-dose radiation corresponded with increased risk for death from leukemia, according to study results.

"The primary basis for estimating cancer risks from ionizing radiation exposures are epidemiological studies of Japanese survivors of the atomic bombings of Hiroshima and Nagasaki," **Klervi Leuraud, PhD,** of the Institute for Radiological Protection and Nuclear Safety, and colleagues wrote. "Within a few years of the bombings there was evidence of an excess of leukemia, predominantly myeloid subtypes, among the survivors. These findings helped to establish that ionizing radiation causes leukemia. However, this evidence mostly relates to acute high-dose exposure. The risks associated with protracted or repeated low-dose exposures are more relevant to the public and health practitioners."

Leuraud and colleagues conducted The International Nuclear WORKers Study (INWORKS) to observe the influence of prolonged low-dose radiation exposure typical of leukemia, lymphoma and myeloma risk among radiation-monitored workers.

The analysis included data from 308,297 radiation-monitored workers in the U.S., the U.K. and France. All study participants worked for the Atomic Energy Commission, AREVA Nuclear Cycle or the National Electric Company (in France); the Departments of Energy and Defense (in the U.S.); and nuclear industry employers listed in the National Registry for Radiation workers (in the U.K.) for at least 1 year.

The researchers followed the cohort for a total of 8.22 million person-years and ascertained deaths caused by leukemia, lymphoma and multiple myeloma.

Mean follow-up was 27 years (standard deviation [SD], 12) and approximately 22% of the cohort died by the end of follow-up.

The researchers observed a mean yearly radiation dose of 1.1 mGy (SD, 2.6), and a mean cumulative dose of 16 mGy.

Five hundred thirty-one deaths occurred due to leukemias other than chronic lymphocytic leukemia, — for which the researchers were not able to estimate an excess relative risk (ERR) — 814 deaths were caused by lymphoma and 293 deaths were caused by multiple myeloma.

Researchers calculated ERRs for mortality based on 2-year lagged cumulative radiation doses.

Fifty-three percent (n = 281) of deaths from leukemia — excluding CLL — occurred in people who accrued less than 5 mGy (ERR = 2.96 per Gy; 90% CI, 1.17-5.21).

Notably, the researchers observed an association between radiation dose and mortality from chronic myeloid leukemia (excess RR = 10.45 per Gy; 90% CI, 4.48-19.65).

"Associations also were positive but highly imprecise for Hodgkin's lymphoma, non-Hodgkin's lymphoma and multiple myeloma, with CIs that spanned zero," the researchers wrote. "The association between radiation dose and CLL morbidity was negative."

The researchers acknowledged measurement errors in occupational radiation dose estimates and exposure misclassification as study limitations.

"This study provides strong evidence of an association between protracted low-dose radiation exposure and leukemia mortality," Leuraud and colleagues concluded. "At present, radiation protection systems are based on a model derived from acute exposures, and assumes that the risk of leukemia per unit dose progressively diminishes at lower doses and dose rates. Our results provide direct estimates of risk per unit of protracted dose in ranges typical of environmental, diagnostic medical, and occupational exposure."

Heterogeneity between countries evaluated, errors in the outcome variable, and confounding by socioeconomic status and other life style factors are known challenges of pooled analyses of nuclear workers, **Maria Blettner, PhD,** of the Institute of Medical Biostatistics, Epidemiology and Informatics in Mainz, Germany, wrote in an accompanying editorial.

"To properly understand the mechanisms and effects of low-dose radiation, we need new data collected by comparable methods for all participants: excellent dosimetry for internal and external exposure, including organ doses, data for exposure to ionizing radiation from other sources such as medical and background exposure, data on other known occupational risk factors, lifestyle factors, biological material, genetic markers and medical history, including information on screening and medical history," Blettner wrote. "We need longitudinal (prospective) data (as we have from atomic-bomb survivors in Japan) to help us understand the dose–response relationship, interaction and

confounding, and outcome pathways. We also need more sophisticated statistical analyses: not only for dose measurement errors, but also to deal with confounding, with errors in the outcome variable, with heterogeneity, multiple testing, and to model the dose-response relationship." – *by Cameron Kelsall*

Disclosure: The researchers and Blettner report no relevant financial disclosures.