

Nasopharyngeal Radium Irradiation (NRI) and Cancer: Fact Sheet

Key Points

- Nasopharyngeal radium irradiation, (NRI) was widely used from 1940 through 1970 to treat ear dysfunctions in children and military personnel. Use of NRI was stopped when concern arose about possible adverse effects, including cancer.
- The purpose of NRI was to shrink swollen tissue in the nasopharyngeal cavity—the opening behind the nose and mouth. The treatment involved inserting a radioactive compound through the nostril into the nasopharyngeal opening for short periods of time. Some radiation exposure to the salivary, thyroid, and pituitary glands, and to brain tissue also occurred during this process.
- NRI was used in several European countries, Canada, and the United States. In the United States, it is estimated that between 0.5 million and 2.5 million children and at least 8,000 military personnel were treated with NRI.
- Children are considered to be the most vulnerable to radiation-related cancers.
- At this time, worldwide studies have not confirmed a definite link between NRI exposure and any disease.

Background

Nasopharyngeal radium irradiation (NRI) was introduced in the United States in 1926 as a treatment to shrink swollen lymphoid tissue in the region of the head near the back of the nose, especially in children. Through the 1960s, NRI was considered good medical practice and effective treatment for a number of medical problems of the head and neck, such as hearing loss and chronic ear infections, and for reducing the size of tonsils and adenoids. Middle ear dysfunctions caused by changes in air pressure in aviators or submarine personnel were also treated with NRI.

NRI treatment consisted of inserting two cylinders of radioactive radium sulfate through the nostrils into the nasopharyngeal opening (the space behind the nose and mouth) for short lengths of time. Typically, each cylinder contained 25 milligrams of radium sulfate, and patients were exposed for three sessions of 8.5 minutes each.

The radium implant emitted three types of ionizing radiation—alpha particles, beta rays, and gamma rays. The alpha particles were blocked by the applicator and did not enter the tissue. The beta radiation, which travels short distances, targeted the nearby overgrown tissue in the nasopharynx. However, the gamma radiation, which penetrates further into the tissue than beta rays, was an unwanted by-product of the



radium implant, and may be the source of adverse health effects, including cancer. Low doses of gamma radiation were delivered to the pituitary, thyroid, and salivary glands, and to the brain.

Because of its proximity to the treatment area, the pituitary gland received a higher radiation dose than either the thyroid or brain (about six to seven times greater), but a lower dose than that delivered to the nasopharynx (25 times lower). Some scientists have speculated that damage to the pituitary gland from NRI treatment might affect circulating hormone levels, growth, and reproductive characteristics, such as fertility and early menopause. Such effects have been seen in children exposed to radiation doses much greater than that received from NRI.

By 1960, reports by both the National Academy of Sciences Committee on the Biological Effects of Atomic Radiation (1956 and 1960) and Britain's Medical Research Council (1960) raised general concerns that use of radiation therapy might have adverse, long-term effects, including increased cancer risk. In addition, effective antibiotic regimens and better surgical methods reduced the need for all types of radiation treatment for head and neck conditions. NRI treatments stopped in the early 1970s.

At least 8,000 military personnel and as many as 2.5 million civilians may have been treated with NRI in the United States. NRI therapy also was used in Canada and several European countries, including the Netherlands, where at least 24,500 patients were estimated to have been treated.

Evidence from an Early Observational Study

Several epidemiological studies have evaluated whether specific patient populations treated with NRI have an increased risk of cancer compared to untreated controls.

In one of the earliest studies, Hazen et al. (1966) compared the cancer risk of 417 children receiving NRI treatment, 971 children receiving X-ray treatment, and an untreated control group of 2,746. In follow-up periods averaging 14.6 years, no significantly increased cancer risk was observed among the treated groups compared to the controls.

Study of Military Personnel

World War II personnel such as pilots, divers, and submarine trainees (submariners) who were subject to differential air pressure between the middle ear and surrounding atmosphere commonly received NRI therapy for middle ear dysfunctions. In the first study of military personnel receiving NRI treatment, the Department of Veterans Affairs evaluated whether 1,214 NRI-exposed World War II submariners were at an increased risk of death compared to 3,176 untreated submariners (Kang et al, 2000).

The medical records revealed that the treated group had a higher probability of deaths due to all causes and all diseases of the circulatory system. Although researchers also found a small increased risk of death due to all cancers combined, as well as cancers of the head and neck, these findings were not statistically significant.

The higher death rate from circulatory disease was not expected. The authors speculated that the increased risk of circulatory and cancer-related deaths among treated veterans could be related to the fact that the treated veterans were recruited during wartime, whereas the untreated control group of veterans was recruited during the post-war period. The researchers postulated that the fitness eligibility requirements may have been less stringent during the war or that the soldiers smoked more during the war than did the post-war group. However, based on comparisons of deaths related to tobacco use (e.g., respiratory diseases, lung cancer, and emphysema), it appeared unlikely that there was a difference in tobacco use between the two groups. The study was limited by the lack of data on risk factors other than radium exposure.

Study in Washington County, Md.

In another study involving NRI exposure in children, researchers at Johns Hopkins University in Baltimore, Md., assessed whether 904 NRI-exposed individuals had a greater risk of developing tumors of the head and neck than 2,021 non-irradiated patients (Yeh et al, 2001). The patients were treated at a hearing clinic in Washington County, Md., from 1943 to 1960. The median age of the study participants was 46 years at the time of the study.

Researchers found an elevated but statistically non-significant risk of developing brain cancer: three malignant tumors were identified in the treated group vs. none in the non-irradiated group. Four benign tumors were also reported in the exposed group vs. none in the controls. Additionally, a non-significant excess risk of thyroid cancer was detected: two cases in the exposed group and one case in the non-exposed group.

The researchers also found that the rates for cancers of the breast, endometrium, ovary, and prostate were lower in the exposed population than in the non-exposed population. None of these findings was statistically significant. Nevertheless, these results, along with findings from other studies, led to speculation that irradiating the pituitary gland might induce hormone alterations leading to lower cancer rates of hormone-sensitive organs.

Dutch Patients

Another well-studied population is a group of children who were treated with NRI at nine ear, nose and throat clinics in the Netherlands from 1945 through 1981.

Investigators assessed whether cancer mortality of the Netherlands cohort was higher among 5,358 NRI-exposed individuals compared to 5,265 non-exposed patients (Ronckers et al, 2001). At the time of the study, they had been followed for an average of 31.6 years. The investigators found no increased risk of death from cancers of the head and neck, nor from brain tumors. They did, however, find evidence of a marginally statistically significant increase in death from non-Hodgkin lymphoma. (Lymphomas are cancers of the lymphatic system, which is involved in fighting infections and other diseases.) The authors noted that this increased risk had not been observed in other studies of NRI-exposed patients and might have been a chance occurrence. They concluded that their study did not indicate that NRI-exposure in childhood was associated with an increased risk of cancer mortality.

In an analysis of the cancer incidence among 4,339 NRI-treated Dutch patients in the same Netherlands cohort (Ronckers et al, 2002b), the investigators found no elevated risk of cancer in general, nor of tumors of the head and neck in particular, compared to the 4,109 untreated participants. The study did not confirm the findings from the Washington County study (Yeh et al, 2001) that NRI leads to decreased risk of breast or other hormone-related cancers. The authors did report a three-fold increased risk of thyroid cancer (four cases in the exposed group vs. one in the non-exposed group). This compares to a four-fold increased risk in thyroid cancer in the Washington County study (two thyroid cancer cases in the exposed group vs. one in the control group), where the patients received about a six-fold higher dose of radiation to the thyroid. The thyroid findings in Washington County and the Netherlands are not statistically significant, but together may suggest a possible effect.

Recently, the same researchers (Ronckers et al, 2002a) evaluated the occurrence of nonmelanoma skin cancer, benign tumors, and hormonal disorders in the same Dutch cohort. They found that the exposed population (3,440 patients) was not at increased risk of thyroid disorders or benign head and neck tumors, including pituitary adenomas and salivary gland tumors. Although the exposed population did appear to have a marginally statistically significant increased risk of basal cell carcinoma (BCC) of the skin of the head and neck area, the authors believe that the results may reflect, instead, an unusually low rate of BCC among the untreated group. They also found a marginally statistically significant increased risk of infertility in exposed men compared to the unexposed men.

Comparison of the Groups Treated as Children

The majority of study participants who were treated in childhood (Hazen study, Washington County, and the Dutch cohort) have now been followed for cancer risk into young adulthood. The numbers of cancer cases and deaths in these study groups are still too small, in most cases, for the results to reach statistical significance. Those that are marginally statistically significant may not represent a true increased risk. However, in 10 to 15 years when most of

the NRI-exposed subjects reach 40 to 60 years of age, when cancer rates tend to increase, analyses of the cancer patterns will allow the researchers to make more definite conclusions.

Although each of these three studies identifies possible associations between NRI treatment and subsequent disease, the findings are not consistent across studies. A clear link between NRI exposure and cancer risk, therefore, has not been established.

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 6.37, *Head and Neck Cancer: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Sites-Types/head-and-neck>)
- *Chemotherapy and You: Support for People With Cancer* (<http://www.cancer.gov/cancertopics/chemotherapy-and-you>)
- *Radiation Therapy and You: Support for People With Cancer* (<http://www.cancer.gov/cancertopics/radiation-therapy-and-you>)
- Throat (Laryngeal and Pharyngeal) Cancer Home Page (<http://www.cancer.gov/cancertopics/types/throat>)
- *What You Need To Know About™ Cancer of the Larynx* (<http://www.cancer.gov/cancertopics/wyntk/larynx>)

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