Table 21–12. Excess cancer in 6158 ankylosing spondylitis patients given a single X-ray treatment as of the last follow-up

<table>
<thead>
<tr>
<th>Site</th>
<th>Obs</th>
<th>Estimated Exposure</th>
<th>Dose (Gy)</th>
<th>Lifetime (Risk Gy⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>31</td>
<td>6.5</td>
<td>2.9</td>
<td>0.0011</td>
</tr>
<tr>
<td>Lung*</td>
<td>101</td>
<td>69.5</td>
<td>1.8–6.8¹</td>
<td>0.0008–0.0028</td>
</tr>
<tr>
<td>Esophagus</td>
<td>28</td>
<td>12.7</td>
<td>4.2</td>
<td>0.0006</td>
</tr>
<tr>
<td>Breast</td>
<td>26</td>
<td>16.0</td>
<td>6.8²</td>
<td>0.0015²</td>
</tr>
</tbody>
</table>

* Lung cancer appearing less than five years after exposure is not included as this is less than the minimum latency for tumor expression.
† The dose to the pulmonary lung and main bronchi was estimated as 1.8 Gy and 6.8 Gy, respectively. The majority of lung cancer is bronchogenic and the dose estimates for the main bronchi are probably most pertinent.
‡ The dose to the breast is taken as the dose to the main bronchi.
† The number of women having one X-ray treatment was 1008.

*otoxic effects of Radiation and Radioactive Materials

ternal X or gamma radiation for persons under 18 years of age is about a factor of 10 lower than that reported by Ron and Modan in the tinea capitis irradiations. However, the tinea irradiations were given to children with mean age of about 7 years and in the Israeli study there is apparently an increased sensitivity due to ethnicity.

The effect of ethnicity and sex is also suggested by NCRP (1985) for thyroid cancer. The incidence rates of spontaneous thyroid cancer for persons of Jewish origin in Europe and North America is three to four times that for other racial groups. There is an obvious susceptibility of women for thyroid cancer and adenomas in both the NYU and Israeli tinea capitis studies.

Ankylosing Spondylitis

About 14,000 persons, mostly men, were treated with X rays for ankylosing spondylitis at 87 radiotherapy centers in Great Britain and Northern Ireland between 1935 and 1954. Court Brown and Doll (1957) were the first to report that these patients had a leukemia risk substantially in excess of that for the general population. Subsequent publications have developed the time pattern of appearance not only of leukemia but of solid tumors (Court Brown and Doll, 1959, 1965; Smith and Doll, 1978, 1982; Smith, 1984; Darby et al., 1985, 1987).

A group was selected consisting of 11,776 men and 2335 women all of whom had been treated with X rays either once or twice. About half of the total group received a second X-ray treatment or treatment with thorium. The reports on the ankylosing spondylitis patients attempt to consider health effects from only the first X-ray treatment. For this reason an individual receiving a second treatment is included in their follow-up only until 18 months after the second course (a short enough time so that any malignancies in this interval cannot be ascribed to the second X-ray treatment).

The appearance of excess leukemia is now well documented and solid tumors are also apparent in the population. The part of the body in the direct X-ray beam (spine) received the highest dose but it is thought that other sites received substantial radiation from scatter or from the beam itself.

The importance of this study is in the health effects of partial body exposure and in the temporal pattern of appearance of solid tumors in irradiated adults. Smith and Doll (1978, 1982) and Darby et al. (1985, 1987) in the most recent follow-up publications concerning these patients have shown that the excess risk for solid tumors is diminishing with time since exposure, with maximum appearance 5 to 20 years after exposure. This has significant implications for risk projection modeling. Many projection models assume a constant rate of appearance either as an absolute number of tumors per person per unit exposure (constant absolute risk) or as a fraction of the baseline age specific cancer mortality rate (constant relative risk). The emerging pattern is that constant risk models, either absolute or relative, are not correct for certain cancers such as lung cancer.

The dosimetry was redone in 1988 (Lewis et al., 1988) and, although better estimates of dose are now available, it is still the dose which is most uncertain for the cohort. No details of the X-ray machines used to deliver the exposures, such as output, kilovoltage, or half-value layer, are reported.

The excess cancers and the estimate of lifetime cancer risk at three sites in the ankylosing spondylitis cohort are shown in Table 21–12. For the purpose of calculating lifetime risks as of the time of follow-up, the number of persons used here as the individuals at risk is the number...
actually receiving only one X-ray treatment (6158). This assumes that those followed for 18 months subsequent to the second treatment do not contribute significantly to the malignancies.

The relatively low risk for leukemia (compared with atom bomb survivors) has been suggested to be due to cell sterilization at the high dose delivered. It is also possible that the low risk is due to partial irradiation of the skeletal red marrow. The volume of bone marrow irradiated in the spine, rib, and pelvis is much less than 50 percent of that in whole body irradiation.

The deaths due to causes other than neoplasms in the total cohort is about 30 percent higher than expected. This higher total mortality is of significance in risk modeling as the premature deaths due to competing causes decreases the observed fractional cancer mortality. Thus, the lifetime risk in this population probably underestimates the risk when projecting the effects of exposure in a healthy population.

**Uranium Miners**

Radon is ubiquitous on earth. It is found outdoors and in all dwellings as a result of the decay of the parent $^{226}$Ra which is present in all of earth’s minerals.

Although the lung cancer risk from radon exposure in underground miners is firmly documented, and quantitative risk estimates are available, the current interest lies in whether this risk carries over into environmental situations. Radon levels in homes that are comparable to those in mines surely confer risks to the residents. The question remains, can the risks in mines for exposures at higher concentrations over short time periods be used to model risks at lower environmental levels over a lifetime?

**Underground Mines.** There are four large studies of underground miners exposed to high concentrations of radon and radon daughters and the documentation of excess lung cancer is convincing. The carcinogen in the case of radon is actually the alpha emitting short-lived daughters of radon, $^{218}$Po and $^{214}$Po. The decay scheme for the entire uranium series, including radon and the daughter species, is shown in Figure 21–6. The daughters are solids and deposit on the bronchial airways during inhalation and exhalation according to the laws of diffusion. As the airway lining (bronchial epithelium) is only 40 $\mu$m thick, the alpha particles emitted are able to reach and transfer a significant amount of energy to all of the cells implicated in lung cancer induction. Although the daughters are the carcinogen, the term radon will be used interchangeably for radon daughters as without the parent radon the daughters could not exist for longer than a few hours.

The measurements in mines were usually of the daughter species rather than radon and the term working level (WL) was defined for occupational exposure. It indicated the total potential energy content in one liter of air for complete decay of the short-lived daughters. The exposure attributed to miners was developed in working level months (WLM) which is the numerical value of WL times the time exposed in multiples of the working month of 170 hours (Holday et al., 1957).

The follow-up studies from four large underground mining cohorts in Canada, Czechoslovakia, Sweden, and the United States have all produced data to show that the excess lung cancer risk from exposure to radon is about two to three per 10,000 persons per WLM exposure (Radford and Renard, 1984; Hornung and Meinhardt, 1987; Sevc et al., 1988; Muller et al., 1989). Expressed in another way, radon exposure increases the normal age specific lung cancer risk by about 1 percent for each WLM exposure. The latter way of expressing risk brings in the thought that many epidemiologists prefer, that the lung cancer risk is proportional to the normal baseline risk. This means, for example, that the lifetime excess lung cancer risk from radon would be different for smokers and nonsmokers (NAS, 1988).

The actual data from the underground studies are not clear cut with regard to the effect of smoking and it is apparent from more recent data that radon exposure does not simply multiply the baseline risks of the population by a constant factor. This is discussed in the section on risk.

The excess lung cancer risk in each of the exposure cohorts for the four major mining populations as of the date of the last published follow-up are summarized in Figure 21–4 (Harley, 1989). It can be seen in this figure that the range of risks for the same exposure varies by about a factor of six among the different studies. The highest values of excess lung cancer shown are in the Czechoslovakian mines and the lowest in the U.S. Colorado mines.

The differences are probably accounted for by errors in measuring and estimating total exposure. However, the Czech mine atmosphere is reported to contain arsenic as well as radon and the arsenic may contribute to the excess lung cancers observed.

A maximum value of 50 percent lung cancer

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* One working level is any combination of short-lived daughters in one liter of air that will result in $1.3 \times 10^5$ MeV of alpha energy when complete decay occurs. One working level is approximately equal to concentrations of 7400 Bq m$^{-3}$ (200 pCi/liter) of radon in a home and 11000 Bq m$^{-3}$ (300 pCi/liter) in a mine.
risk is indicated in Figure 21-4. This is the highest value ever observed in a mining population and was reported in the mines in Saxony at the turn of the century (Muller, 1989). These mines are thought to have had about 100,000 Bq m⁻³ of radon. It is noteworthy that concentrations this high have been reported in a few homes in the United States.

In Figure 21-4, the lowest exposures were in the Ontario mines and a mean exposure of 35 WLM has given an excess lung cancer risk of about 0.4 percent to date.

When radon gas decays to the solid daughter products, some 8 to 15 percent of the ²¹⁸Po does not attach to the normal aerosol particles and this ultrafine species is deposited with 100 percent efficiency on the upper bronchial airways. The rest of the daughters attach to the aerosol of about 100 μm average diameter (George and Breslin, 1980) and only a few percent of this aerosol deposits on these airways.

Measurements in mines have mostly been of the short-lived radon daughters as these are the easiest to measure rapidly. The alpha dose from radon gas itself is very low in comparison with that from the daughters as the daughters deposit and accumulate on the airway surfaces.

The first few branching airways of the bronchial tree are the region where almost all the lung cancers appear. This is true in general and not only for miners exposed to radon daughters. The alpha dose from radon daughters must therefore be calculated in these airways and not in the pulmonary or gas exchange regions. Although the dose to the pulmonary region should not be neglected it is about one-fifth that to the airways.

Several calculations regarding the absorbed alpha dose exist for radon daughters (NCRP, 1984; ICRP, 1987; Harley, 1987, 1989; James, 1987). The authors make different assumptions about the atmospheric and biologic parameters that go into the dose calculation, yet the results are comparable. The most significant variable is the particle size of the ambient aerosol. Very small particles deposit more efficiently in the airways so if small particles, such as from open flame burning (Tu and Knutson, 1988), contribute to the atmosphere, then the dose delivered to the bronchial epithelium can be higher per unit WLM exposure than the dose predicted from an average particle size. Conversely a hygroscopic particle can increase in size in the humid environment of the bronchial airways and deposition will be diminished. The particle size of the aerosol in mines is somewhat larger than that for environmental conditions (200 versus 100 nm; George et al., 1975). Figure 21-5 shows the alpha dose per unit exposure as it is related to the variables (particle size, unattached fraction, nasal deposition) known to affect dose.

As carcinogenesis is related to absorbed alpha dose, Figure 21-5 shows that particle size is an important determinant of risk. The average dose per unit exposure in WLM for miners is also indicated in Figure 21-5 to show that it is somewhat smaller than that for average environmental conditions.

Radon can deliver more or less carcinogenic potential by about a factor of 2 over the range of realistic indoor conditions (average particle size ranging from 80 to 300 nm). The allowable effective dose equivalent for continuous exposure of the population in the United States is 1 mSv/year (100 mrem/yr, NCRP, 1984, 1987). This limit would be delivered by exposure to 20 Bq m⁻³ of radon or
one-half the actual average measured indoor concentration in most countries where measurements have been made. Thus, the guidelines for exposure cannot be set in the usual way from dosimetric considerations.

**Lifetime Environmental Lung Cancer Risk Projections.** There are at present three sets of publications that provide the risk projection calculations for exposure to radon daughters. The following sections describe each in detail.

**National Council on Radiation Protection and Measurements.** In 1984, the U.S. National Council on Radiation Protection and Measurements (NCRP, 1984) developed a model to project the risk derived from the miner studies to whole life risk in the environment. It is a modified absolute risk model that reduces the risk subsequent to exposure with a half-life of 20 years. Risk is not accumulated until after age 40, the time when lung cancer normally appears in the population. There is no indication that early exposure produces any significant shift to younger ages, even for young miners exposed at significantly higher concentrations.

**National Academy of Sciences.** The U.S. National Academy of Sciences report in 1988 (BEIR IV) developed a model based on examination of the raw data from five mining cohorts (NAS, 1988). It was indicated that the highest risk appears from 5 to 15 years following exposure. After 15 years, the risk is one-half that of the 5- to 15-year risk (per unit exposure) and persists to the end of life. Again, no significant risk appears before 40, the usual age for the appearance of lung cancer. The NAS model also has a correction for attained age (at age >65 the risk is 0.4 of that for ages 55 to 64). The BEIR IV Committee assumed a relative risk model (risk is a fraction of the normal age-specific lung cancer risk per unit radon exposure with risk dependent on time from exposure. This means that the risk for smokers and nonsmokers differs because of their different baseline lung cancer values. Although the miner epidemiology did not support this strictly multiplicative relationship, the NAS chose the relative risk model as a conservative one. Their analysis supports the risk reduction subsequent to exposure.

**ICRP.** The International Commission on Radiation Protection (ICRP, 1987) developed two risk projection models, one based on a constant relative risk and the other a constant absolute risk model. Although neither the constant relative or constant absolute risk model is correct, because of the temporal reduction pattern of lung cancer subsequent to cessation of exposure, the numerical values obtained for the lifetime risk of lung cancer from radon exposure are not significantly different from other models.

Later follow-up of the Czechoslovakian underground uranium miners presented by Kunz and Sevc (1988) indicates that the excess lung cancer risk may actually reduce to zero 35 years after exposure. If this factor were included in the NAS model (zero risk after 35 years) it would reduce their values by about a factor of 2.

The risk values obtained from the three models are shown in Table 21-13.

**Environmental Epidemiology.** There are at least 22 published studies attempting to define or detect the effect of radon exposure in the environment. These have been summarized by Borak and Johnson (1988), and by Neuberger (1989). The most recent study was performed in 1989 by the New Jersey Department of Health (NJDOH) in the United States (Schoenberg and Klotz, 1989). This is the most rigorous to date and is a case-control study with 433 lung cancer patients...
Table 21-13. Lung Cancer Risk for Continuous Exposure to 1 WLM
yr⁻¹ (150 Bq m⁻³ or 4 pCi liter⁻³) as Predicted by Various Models

<table>
<thead>
<tr>
<th></th>
<th>Lifetime Risk (%)</th>
<th>Model Type</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCRP</td>
<td>0.9</td>
<td>Modified absolute</td>
<td>Risk decreases with time from exposure</td>
</tr>
<tr>
<td>ICRP</td>
<td>1.6</td>
<td>Constant relative</td>
<td>No reduction in risk with time from exposure for either model</td>
</tr>
<tr>
<td></td>
<td>1.1</td>
<td>Constant absolute</td>
<td></td>
</tr>
<tr>
<td>BEIR IV</td>
<td>3.4 (2.2)* men</td>
<td>Modified relative</td>
<td>Risk decreases with time from exposure</td>
</tr>
<tr>
<td></td>
<td>1.4 (0.9)* women</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Beir IV values modified to express risk for 35 years after exposure rather than entire lifetime.

cases and 402 controls with year-long measurements of radon in the homes where individuals lived for 10 or more years. This study devoted a considerable effort to quality control concerning the exposure measurements. The results of this study are slightly positive, suggesting an association of radon and lung cancer, even at concentrations of 80 Bq m⁻³, but the results are not statistically significant.

Of the total studies, 13 are ecologic and 9 are case control. Ecologic studies depend on relating the disease response of a population to some measure of a suspected causative agent. There are usually insufficient data on all of the variables involved in the disease to infer any reliable associations. Ecologic studies are the weakest type of epidemiologic exploration.

Unless a biologic marker for radon-induced lung cancer is found, it is unlikely that environmental epidemiology will be effective. The effects of radon in the environment are subtle compared with the overwhelming lung cancer mortality from smoking.

Four concepts emerge from the radon research so far, however, and these are:

1. The mining epidemiology indicates that short exposure to high levels of radon and daughters produce a clear excess of lung cancer.
2. Particle size can change the actual dose delivered by radon to bronchial tissue with small sized particles giving a substantially higher dose per unit exposure. Passive tobacco smoke and open flames indoors produce a higher dose.
3. Smokers are at higher risk from radon per unit exposure than nonsmokers.
4. Urban areas almost universally have low radon and apartment dwellers removed from the ground source have particularly low radon exposure at home.

The miner data show clearly that there is a risk of lung cancer from exposure to high concentrations of radon delivered over short time periods. Comparable exposures delivered over a lifetime in the home have not produced statistically significant increases in lung cancer mortality. The risk can still exist, but the confounding effect of other carcinogens such as smoking and urbanization make it impossible to extract the more subtle impact of radon in existing studies.

Natural Radioactivity and Radiation Background

The occupational, accidental, and wartime experiences detailed in the preceding sections have provided the bases for all of the current radiation risk estimates. For many years, the radioisotopes deposited internally were compared with ²²⁶Ra in order to evaluate the maximum permissible body burden for a particular emitter. The present limits for external and internal radiation are based on dose estimates which in turn can now be related to cancer risks. One standard of comparison has always been the exposure from natural background and this source is assessed here.

Background radiation from all sources is described in detail in NCRP report 94 (1987) and some of the information is summarized here.

The risk estimates in the previous sections must be placed in context with the radiation dose received by all humans from natural background radiation. There is a substantial dose received annually from cosmic radiation and from external terrestrial radiation present from uranium, thorium, and potassium in the earth’s crust. Internal emitters are present in the body as a consequence of dietary consumption and inhalation. For example, potassium is a necessary element in the body and is homeostatically controlled. Radioactive ⁴⁰K is a constant fraction of all natural potassium. Potassium delivers the largest internal dose from diet of 0.15 mSv per year. However, the data are scant on the dietary intake of other radionuclides in the United States population. Given the usual distribution of intakes across a large population, it is probable that