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## Radon in caves: clinical aspects

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### Abstract:

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Historical, experimental and clinical evidence is presented to suggest that radon constitutes a relatively small carcinogenic risk for casual visitors to caves. The risk is dependent on radon levels and the smoking of tobacco. Show cave guides, chronically exposed to radon, may be at increased risk for lung cancer due to the effects of radon, especially if they are smokers of tobacco.

**Keywords:** alpha particles, carcinogenesis, cave environment, lung cancer, radon, regulations, smoking, tobacco.

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### INTRODUCTION

Prof. Cigna's otherwise detailed review of the radon problem in caves (Cigna, 2005) gives insufficient attention to the confounding influence of radon on the aetiology of lung cancer, which is better known for being associated with tobacco rather than with radon. Although for ethical reasons a cause and effect relationship has not been and never will be proved, there is no physician who does not believe that smoking causes lung cancer. In every country the increase in incidence of, and mortality from, lung cancer coincides, after a latent period, with the rise in tobacco consumption. The risk of lung cancer increases with the number of pack years smoked. It is a rare disease in non-smokers (Spiro, 1996), and "predominant" among uranium miners who smoke (Archer et al., 1973). Despite solid evidence that radon is a carcinogen, and that the risk rises with time of exposure (usually many years) and increased concentrations of radon, expressed in Becquerel per cubic metre (Bq/m<sup>3</sup>) in confined spaces, such as homes and caves (Darby et al., 2005) the risk varies with climate and geographical location. Because of the short times that casual cavers are exposed to radon, the risk of developing a lung cancer for a non-smoking caver can be considered very small; the risk is compounded for smokers. All people are at some risk due to radon as there is a ubiquitous background concentration of radon at around 40 Bq/m<sup>3</sup> (USA), and about half that amount (United Kingdom), in the air.

### THE HISTORICAL EVIDENCE FOR RADON AS CARCINOGEN

Titus Lucretius Carus, cited by Cigna (2005), addressed the dangers of mining in three sentences: "... what stench Scaptensula breathes out underground? And what poison gold mines may exhale! How strange they make men's faces, how they change their colour! Have you not seen or heard how they are wont to die in a short time and how the powers of life fail those whom the strong force of necessity imprisons in such work?" (Bailey, 1972).

This merely tells us that ancient Greek gold miners had a short life expectancy, and hints that the cause was respiratory in origin.

Lucius Annaeus Seneca, also cited by Cigna (2005) is even more vague. He gives Asclepiodotus as the source of his information, and confirms the dangerous nature of mining without giving any detail thereof. His extravagant mention of, "... huge rivers and vast reservoirs of motionless water, equal to ours above ground ... but with a vast free space overhead" contributes nothing to discussion of the radon problem (Corcoran, 1972).

Georgius Agricola, who is misquoted and therefore misinterpreted by Cigna (2005), is a more reliable witness. He is well known in mining and metallurgical circles because of his textbook of mining, *De Re Metallica*, which was published posthumously in 1556. For the next 180 years it was the only available guide for miners and metallurgists, and was widely read. It has since become a very scarce collector's item, but the 1950 reprint of the 1912 English translation is more readily available.

Agricola was also a physician who trained in Italy. In 1527 he was appointed town physician at Joachimstal (now Jáchymov) on the Bohemian side of the metalliferous Erzgebirge. In about 1533 he crossed

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the mountains to be town physician at Chemnitz in Saxony. Agricola can therefore be expected to have attended the miners. His book indicates that he was familiar with the occupational diseases and hazards of mining. He described the effects of foul air, cold and wet conditions, heavy metal toxicity and accidents. He also recorded the respiratory diseases of miners, and attributed them to dust. It is worth quoting him verbatim:

“... penetrates into the windpipe and lungs, and produces difficulty in breathing, and the disease which the Greeks call ἀσθμα.”

“... it eats away the lungs, and plants consumption in the body” (Hoover & Hoover, 1950). Although Agricola made no claim to have performed autopsies on his patients, he must have done so, or he would not have discovered that whatever disease he was describing “eats away the lungs”.

The former description is compatible with silicosis and pneumoconiosis, the latter with tuberculosis – all traditional diseases of miners. No description is compatible with lung cancer, which is a macroscopically localised pulmonary disease which does not, “eat away the lungs”. Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* which causes liquefaction of lung tissue and subsequent cavities (Davies et al., 1996). In other words it, “eats away the lungs”.

Pneumoconiosis is a chronic fibrotic lung disease caused by inhalation of coal-mine dust. Silicosis is a chronic fibrotic lung disease caused by inhalation of silicon dioxide dust, and has been recognised in metal miners and stone masons for centuries (Seaton, 1996). Ancient miners, using hammers and chisels, raised much less dust than do their mechanised modern counterparts, but they were working in enclosed spaces and would have inhaled significant quantities of dust. By comparison stone masons work in the open air, using hammers and chisels. Despite the absence of confinement they suffered, and continue to suffer, from silicosis.

The Erzgebirge mines contain radioactive pitchblende, from which radium was first extracted by Marie Curie (Curie, 1898; Curie & Bémont, 1898). Radium decays through, *inter alia*, radon to lead (Mark et al, 1982). Gaseous radon and its microparticulate daughters readily enter the lungs. They therefore irradiate the trachea and bronchi.

The Erzgebirge miners formed the population in which lung cancer was first described in 1879, and in which a 20 year exposure to mine conditions was required for the cancer to develop. Three quarters of these patients had died of pulmonary malignancy. The authors of this detailed investigation into the “bergkrankheit” were aware that it had previously been misdiagnosed as pulmonary tuberculosis. They enquired at the distant mining communities of Modum in Sweden and Dobschau in Hungary, and ascertained that no lung cancer had been reported there (Härting & Hesse, 1897a, 1897b & 1897c). If it were assumed that the miners commenced their hazardous occupation while still in their teens, they

could be expected to have developed their lung cancers by the age of 35 years or shortly thereafter.

Agricola made no distinction between the occupational diseases of the Erzgebirge miners and those of miners elsewhere. It is therefore questionable whether at that tobacco-free time the incidence of lung cancer in European miners differed from that in non-miners. It must then have been a very rare disease. Tobacco was introduced to Europe in 1556 (Encyclopaedia Britannica, 1968), too late to have confounded Agricola’s observations on miners’ occupational diseases.

The failure of Agricola to report any respiratory disease peculiar to the Erzgebirge miners, and which was compatible with lung cancer, suggests that radon is only a minor factor in the causation of lung cancer. It is probably the synergistic effect of the radon on tobacco smoke that is responsible for the lung cancer of workers in radio-active mines. An alternative explanation may be that the 16th. century Erzgebirge miners did not live long enough to develop lung cancer. One twentieth century case report describes a patient with the bergkrankheit at 51 years of age, and whose father died of the same disease at 42 years (Löwy, 1929). Thereafter a historian of Europe misinterpreted this as indicating a life expectancy of 42 – 43 years (Wiskemann, 1938).

More recently, Saccomanno et al.(1996) found that smokers who are also miners have a 9.3% higher incidence of lung cancers than non-mining smokers and that lung cancer was increased in cigarette smoking miners and non-miners, but that the proportion of lung cancers in the “central zone” was significantly greater in miners than in non-miners. The higher percentage of central tumours in the miners was primarily due to the distribution of a greater proportion of squamous cell and small-cell tumours. In the mining cohort, there were ten times as many small-cell tumours in the central area as in the middle and peripheral regions versus only five times as many centrally located tumours as middle and peripheral tumours in the non-miners. The authors conclude that inhaled dust, **radon** and cigarette smoke combine to form large particles that deposit in the central bronchial tree, but that filtered smoke free of dust form smaller particles that deposit more peripherally. Obviously, the non-miners were exposed to only home or free-air radon levels, and the distribution of the cancers in miners and non-miners clearly differed. The alpha dose distribution determined by aerosol deposition and clearance may preferentially cause tumours at different sites, i.e. a larger dose proximally may affect tall columnar goblet cells or metaplastic squamous epithelium cells, while a smaller dose distally may affect bronchiolar, Clara or Type II cells.

Fifty eight per cent of miners were smokers compared with 35% of non-miners. Of the total cohort of 476 miners with lung cancer, only 24 were non-smokers. The overall exposure of miners to radon decay products was known and revealed that 54% of smokers and 66% of non-smokers had exposures

greater than 1000 WLM. Smokers therefore had an excess of cancers 19.8 times that of non-smokers despite the higher exposure of non-smokers.

### EPIDEMIOLOGICAL STUDIES: THE RISK FOR LUNG CANCER DUE TO EXPOSURE TO SMOKING

The epidemiological data relating lung cancer risk to smoking were summarised in a report from the United States Office on Smoking and Health (Koop, 1982) and by Wynder and Hoffman (1994).

**The major etiological factor** in the causation of lung cancer is the smoking of tobacco, mainly cigarettes. Bronchogenic carcinoma is without doubt the greatest neoplastic killer in industrialised countries; it accounts for 35% of the cancer deaths in the United States. Since 1985, lung cancer also surpassed breast cancer in females. This is in sharp contrast to most other cancers, the incidence of which either stayed constant or declined slightly. The major cause of lung cancer has long been recognised to be cigarette smoking; male cigarette smokers are 10 to 20 times more likely to die of lung cancer than non-smokers. Statistically, there is a linear correlation between the frequency of lung cancer and the pack-years of smoking (Frank, 1982). About 80% of lung cancers occur in current smokers.

Evidence for the relationship between smoking and lung cancer is derived from clinical, epidemiological and experimental studies.

#### Pathogenesis

The clinical (pathology based) evidence relates to the progressive changes in the epithelium of the respiratory tract of habitual cigarette smokers. Firstly, there is a loss of the cilia, followed by typical squamous metaplasia, replacing the mucous goblet cells and pseudo-stratified columnar cells. This is followed by dysplasia and eventually abnormalities approaching carcinoma *in situ*, followed by frankly invasive bronchial (lung) carcinoma (Auerbach, 1979).

It should also be kept in mind that not only smoking, but also chronic bronchitis, can lead to squamous metaplasia, so that not only smokers are exposed to this thinning and potentially pre-cancerous lesion (Geneser, 1986).

#### Histogenesis of lung cancer

Which is the target cell in terms of carcinogenesis, and can an alpha particle reach these cells?

Most of the evidence suggests that proliferating cells of the mucosa give rise to lung tumours. Two cell types proliferating in the mucosa are the secretory (goblet) cells and the basal cells. Both of these cell types are within 50 micrometres of the airway surface and may be reachable by the alpha particles. (McDowell et al. 1978 and 1993). In the peripheral airways, Clara cells or Type II pneumocytes are implicated as precursor cells for the non-mucosal subtype of bronchiolo-alveolar tumours. Endocrine (APUD) cells (Krause &

Cutts, 1981; Geneser, 1986) are other occupants of the epithelium. Small cell carcinomas, 20 to 25% of the common lung cancers, may have the neuro-endocrine or APUD cells as cell of origin (Robbins and Kumar, 1987; Saccomanno, 1988) and are strongly associated with smoking and radon exposure (Darby 2005). These data suggest that the basal cells are towards the limit of the range of alpha particles or just out of range. The epithelium, changed after metaplasia and dysplasia, will not be "horny" like skin, but rather soft like moist epithelium, such as may be encountered in the vagina. The basal cells of the altered epithelium here should be in easy reach of alpha particles.

At the **bottom** of the epithelium are the basal cells, stem cells that replace worn-out ciliated and goblet cells (Moran & Rowley, 1988). This epithelium covers the trachea and bronchi, and seems to have a thickness on histological preparations of about 90 to 100 microns. The *in vivo* thickness of the epithelium may be thicker because with histological slide preparation there is a degree of shrinkage, and the mucus layer may be washed off.

#### Experimental studies

Cigarette smoking could be shown to induce DNA single strand breaks in human cells (Nakayama, 1985). Furthermore, it is well recognised that environmental and other factors can enhance the carcinogenicity of cigarette smoke, for instance the increased incidence in miners due to, not only radioactive materials, but also to asbestos, arsenic, chromium, uranium and nickel (Robbins & Kumar, 1987).

The radioactive material under suspicion is mostly radon gas emanating from uranium and radium in rocks, and the radioactive non-gaseous "daughters", all emitting alpha particles. Uranium and radium found in granite rocks disintegrate slowly with the emission of radon which decays by alpha particle emission to leave behind the radon daughters, which are nongaseous micro-particles which may be captured in the lung, continuously emitting alpha particles. Alpha particles end up after electron capture as helium. Eventually the mother molecules of uranium and radium end up as stable lead. An alpha particle has two neutrons and two protons, each of the two protons carrying a unit of positive charge; and both alpha particles as well as the negatively charged daughters can be attracted electro-statically to dust particles.

#### Radiobiological considerations

Alpha particles have contradictory qualities as a candidate carcinogen in the lung. On the one hand a very short range – about 45 to just less than 100 microns in a watery medium – an alpha particle cannot penetrate a sheet of paper, or the horny layer of the skin. For 5.5 MeV alpha particles, for instance, the range in air (density 1.2 mg/cm<sup>3</sup>, is about 3.7 centimetres, in paper (density 0.89 g/cm<sup>3</sup>) 53 micrometres and in water (density 1.0 g/cm<sup>3</sup>) the range of an alpha particle is 45 micrometres.

On the other hand, the short range is compensated for by the fact that an alpha particle is densely ionising

and therefore very capable of causing profound damage to a cell if the nucleus should be traversed. In its short path it strips many electrons off nearby molecules in contrast to X- or gamma rays (photons) which on the other hand are very penetrating, but sparsely ionising. Alpha particles will lose about 80 to 150 keV per micrometre in cells, as opposed to beta particles, which will yield about 0.1 to 3 keV per micron and even less for photons.

Densely ionising radiation causes many double strand breaks that are difficult for the damaged cell to repair. The single strand breaks usually caused by sparsely ionising radiation, like photons, are much easier for the cell to repair (Hall, 1988a & 1988b).

Cancer is more likely to arise in damaged DNA, but not so damaged that the cell is reproductively dead. In this regard, it has been shown that in **isolated** cells alpha particles are very effective cell killers and damagers of chromosomes. Many studies over the past 30 years agree that the cell survival curve can be represented accurately from a single straight line in the conventional exponential plot with a  $D_0$  of 0.6 for human cells exposed to alpha particle irradiation. Simmons et al. (1996) found that on average only three alpha particles must traverse the nucleus for a mean lethal dose for a human lung cell, representing an energy exchange of only 1.0 MeV. The rate of chromosome aberration induction can also be described by straight lines with slopes of 0.3 and 0.6 respectively for V79 and human lung cells.

However, newer evidence that alpha particles may not have the nucleus as the only target is emerging. Evidence for a so-called "bystander effect" is mounting. The alpha particles will generate chemical radicals if the cytoplasm alone is hit. These chemical radicals may cause indirect damage at a short distance from the ionisation locus (Hall, 1988a & 1988b). In this regard, there is supporting evidence for an extra-nuclear target for alpha particle irradiation. Deshpande et al. (1996) investigated the relationship between nuclear hits and the subsequent occurrence in sister chromatid exchange in normal human lung fibroblasts. This may result in accumulations of the cell cycle regulating protein p53 in immortalised rat lung epithelial cells in a higher percentage of the exposed population than expected. These findings point to the possibility that the DNA effects of alpha radiation may not be initiated exclusively in a cell's nuclear compartment, and may imply that a direct hit on a cell is not needed to induce malignant transformation in a cell. This work has been elegantly corroborated by Wu et al. (1999) who showed that selective irradiation of the cytoplasm could be mutagenic, and that this mutagenicity was due to the generation of oxygen species and is accomplished by little or no killing of the target cells leaving, in principle, the cells enough time to undergo malignant transformation.

Similar findings were recorded by Zhou et al. (2000 & 2001). The latter paper provides clear evidence that alpha-irradiated cells can induce a bystander mutagenic response in neighbouring cells not directly traversed by alpha particles, and that a cell-cell

communication process may play a critical role in mediating the bystander phenomenon. This implies some signal transduction at distances longer than the range of, for instance, hydroxyl radicals with a range of only about 4 nano-metres (Wu, 1999).

## RECENT EPIDEMIOLOGICAL STUDIES

### Radon alone as a causative factor for lung cancer

The Iowa Radon Lung Cancer Study (Field et al., 2000) studied 1000 housewives exposed for 20 years to relatively high values of radon in their homes in order to assess radon as a factor in causing lung cancer. Sixty per cent of the homes exceeded, for cases and controls, the action level of 4 pCi/L (148 Bq/m<sup>3</sup>). Risk estimates were adjusted for age, active smoking and education. The results suggested that cumulative exposure to radon is a significant factor for lung cancer in women. For all lung cancer subtypes there was a positive categorical trend ( $p=0.05$ ). The study estimated excess odds of average 0.5, for radon levels approximately equivalent to a 15 year exposure at an average radon level of 4 pCi/L (148 Bq/m<sup>3</sup>). The conclusion was that radon is a significant risk factor for developing lung cancer.

### Meta-analysis of epidemiological studies

A study that will probably stand as a landmark is a meta-analysis of the role of radon in homes with regard to the development of lung cancer (Darby et al., 2005). It is presented here in some detail.

Radon 222 and its decay products are responsible for probably half of the background, non-medical, exposure to radiation in many countries. The authors stress that air pollution by radon is ubiquitous. Concentrations are low outdoors, but can build up indoors, like in homes (and caves). The highest concentrations occur underground, especially in uranium mines. This collaborative study included 13 case control studies in 9 European countries each of which registered over 150 people with lung cancer and 150 or more controls, and which included data about radon levels over 15 years or more of observation. The available radon measurements covered a mean of 23 years. The analysis included 7148 people with lung cancer and 14,208 controls. For cases of lung cancer, the mean measured radon concentration was 104 Bq/m<sup>3</sup> while for controls the weighted average of the study specific means was 97 Bq/m<sup>3</sup>. The risk of lung cancer versus the radon concentrations (after stratification for study, age, gender, region of residence and smoking) was found to be increased by 8% per 100 Bq/m<sup>3</sup> increase in radon concentration. The authors distinguished between measured radon and "usual radon" which is the radon level after correction for the dilution of radon data caused by uncertainties in measuring radon concentrations. For "usual radon" concentration, the risk for developing lung cancer is said to be 16% per 100 Bq/m<sup>3</sup> increase in radon concentration. The dose response relationship was linear even down to levels of >200 Bq/m<sup>3</sup> (the so-called "action level").

If smoking had been omitted from the stratification of cases, the risk of lung cancer would only have increased by 2.3% per 100 Bq/m<sup>3</sup> increase in measured radon.

The authors concluded that the lifelong risk of lung cancer by age 75 would be 0.41%, 0.47%, 0.67% and 0.93% for lifelong non-smokers, versus 10.1%, 11.6%, 16.0% and 21.6% in cigarette smokers, for levels of 0, 100, 400 and 800 Bq/m<sup>3</sup> respectively. Furthermore, that if the proportionate increases in risk per unit exposure are approximately independent of smoking history, then as lung cancer is much commoner in cigarette smokers than in lifelong non-smokers, radon poses a much greater absolute hazard to cigarette smokers, and to recent ex-smokers, than to lifelong non-smokers. Table 1 shows the results.

For lifelong non-smokers, they found that the increase in risk per 100 Bq/m<sup>3</sup> was 10.6%. The average radon concentration in dwellings in Europe is about 59 Bq/m<sup>3</sup> which implies a risk to people spending much time in their homes of about a 9% risk of developing lung cancer, or about 2% of all cancers.

### RISK ESTIMATES FOR CAVERS EXPOSED TO RADON

From an internet derived article on "Caving in Ireland" <http://www.cavingireland.org/safety/radon.htm> the authors estimated the recreational caver spending 50 hours per year caving to have a lifetime risk of 1 in 12500 or 0.00008. For professional cavers, the lifetime risk is estimated, assuming 600 hours per year caving, for premature death from lung cancer, to be 1 in 1000.

No distinction is made between the risk to smokers and non-smokers. Against this background, the estimated risk of death due to accidents during a single caving trip is 1/40,000 or for 50 trips, 0.00125, that is, again, 1.25 deaths per 1000 cavers per year. The authors estimate the risk of a fatal lung cancer developing as a result of a single 4 hour exposure to 7000 Bq/m<sup>3</sup> as about 1/3 to 1/4 of the estimated risk due to an accident. This article cites the ICRP recommendation of the adoption of a risk factor of 0.0001 for developing lung cancer to chronic exposure of radon gas concentration of 1 Bq/m<sup>3</sup>. The risk to the general UK population therefore should be 40 x 0.0001 or 0.004. The above risk estimates are based on this recommendation.

Hyland and Gunn (1994) found levels of radon in British caves varying from 484 Bq/m<sup>3</sup> to 8868 Bq/m<sup>3</sup>. The mean concentrations for integrated (dose measured over several days and averaged) fall in the range 2,300 Bq/m<sup>3</sup> to 3,300 Bq/m<sup>3</sup> but the means from spot measurements vary much more due to diurnal variations in radon concentration. For example, a spot measurement from Giant's Hole in Derbyshire showed a radon concentration of 155,000 Bq/m<sup>3</sup>. Radon gas concentrations (Bq/m<sup>3</sup>) have been converted to effective dose equivalents (mSv). The average annual background concentration of radon in the UK is 20 Bq/m<sup>3</sup>, which translates to a dose of 1.25 mSv per

year. A single 4 hour trip in a cave could reach this level of exposure. Fifteen mSv could be reached in 33h to 3,333h depending on the cave and region. This is a more than a 100 fold variation in concentration.

### Calculation of risk to speleologists due to radon based on the data supplied by Darby et. al. (2005)

Radon Level (Bq/m <sup>3</sup> )	0	100	400	800
Risk to non-smokers%	0.41	0.47	0.67	0.93
Risk increase% per 100 Bq/m <sup>3</sup>		14.6	14.2	9.7
Risk to smokers%	10.1	11.6	16.0	21.6
Risk increase% per 100 Bq/m <sup>3</sup>		14.9	28.7	8.75
Smoker/non-smokers	24.6	24.6	23.9	23.2

Table 1. Lifelong cumulative absolute risk of death due to lung cancer at age 75 years for individuals exposed to escalating levels of radon in homes (Expanded from Darby et. al. 2005)

Table 1 shows a virtually constant excess risk of about 25 times the risk for smokers to develop lung cancer compared to non-smokers. In non-smokers exposed to 800 Bq/m<sup>3</sup>, only about 9 out of 1000 people at age 75 can expect to die from lung cancer, whereas about 216 smokers per 1000 of the population can expect to meet this fate. Of the 9, a significant proportion of the public will be exposed to the natural concentration of radon in the free air, or about 20 Bq/m<sup>3</sup> (UK) or about 40 Bq/m<sup>3</sup> in the USA. "Action levels" are advised at ten times this level, or 200 Bq/m<sup>3</sup> in the UK. The authors quote an increased risk of lung cancer of 16% per 100 Bq/m<sup>3</sup> of radon. A smoker with risk x, will therefore have a risk of x + 16% at 100 Bq/m<sup>3</sup>, x + 32% at 200 Bq/m<sup>3</sup>, x + 48% at 300 Bq/m<sup>3</sup>, and x + 112% at 700 Bq/m<sup>3</sup>. The table also suggests a "saturation effect" in the sense that the increase in risk at 800 Bq/m<sup>3</sup> is 9.7% versus 14.6% and 14.2% at 100 and 400 Bq/m<sup>3</sup> respectively for non-smokers, and 8.75% at 800 Bq/m<sup>3</sup> for smokers but 14.9% and 28.7% for smokers, although the relative risk remains at about 24 times the risk for smokers versus non-smokers. The risk estimates at levels above 400 Bq/m<sup>3</sup> may therefore be too high if the risk is plot as a straight line function. However, risk may not disappear at very low levels of radon. Since there seems to be a linear relationship between level of exposure and risk then additional columns can be added to table 1 to produce table 2, to consider the effects when the data are extrapolated to include radon levels as high as 7000 Bq/m<sup>3</sup>.

Miners exposed to 1000 WLMs (see Saccomanno et al. 1996 above) = 7.4 x 10<sup>3</sup> Bequerel per cubic metre = 74 multiples of 100 Bq per cubic metre. The risk

to smoking miners (ignoring the effects of dust etc., must therefore be, ignoring “saturation dose effects” 74 x 1.4 or 103.6 times that of the general population, and for non-smokers 74 x 0.06 = 4.4 times the risk to the general population, using the risk estimates from Darby et al. (2005), table 2.

Radon Level (Bq/m <sup>3</sup> )	0	100	400	800	7000
Risk to non-smokers%	0.41	0.47	0.67	0.93	<b>3.72</b>
Risk % per 100 Bq/m <sup>3</sup>	0.06	0.066	0.065	0.6	
Risk to smokers%	10.1	11.6	16.0	21.6	<b>86.8</b>
Risk % per 100 Bq/m <sup>3</sup>	1.5	1.46	1.4	14	
Smoker/non-smokers	24.6	24.6	23.9	23.2	<b>23.3</b>
Risk% to non-smokers exposed for 50 hours p.a to 7000 B/m <sup>3</sup>					<b>0.00028</b>
Risk% to smokers exposed for 50 hours p.a.					<b>0.0066</b>

Table 2. Lifelong cumulative absolute risk of death due to lung cancer at age 75 years for individuals exposed to escalating levels of radon in homes (Expanded from Darby et al. 2005). Risk levels for speleologists are extrapolated from these data for exposure to 7000 Bq/m<sup>3</sup> for 50 hours per annum.

#### Calculation of the risk to speleologists on the basis of the above data

The hours in 75y are (75 x 365.25 x 24) = 657450 hours. Therefore the risk of developing lung cancer for an exposure, for non-smokers, to 50 hours in a cave with 7000 Bq/m<sup>3</sup> would be 0.00028%. Darby's extensive data are based on 7148 cases of lung cancer and 14208 controls.

For non-smokers spending 50 hours annually in caves with radon levels of 7000 Bq/m<sup>3</sup>, the risk of lung cancer per 1000 speleologists visiting caves at that level of radon will be 0.28 cases per year, and for smokers 6.6 cases.

The mean levels in caves according to Hyland and Gunn (1994) in Britain is between 2,300 Bq/m<sup>3</sup> and 3,300 Bq/m<sup>3</sup>. The “average” risk to cavers in Britain, using Darby's data should then, for every 1000 cavers spending 50 hours per year in caves, be 2200/7000 or 3300/7000, i.e. 0.088 cases per year to 0.13 cases per year for non-smokers, and 2.07 cases and 3.11 cases per 1000 speleologists who are also smokers, respectively per year, based on averaged concentrations. Concentrations may vary a hundredfold, however.

#### DISCUSSION

Risk estimates from data are represented in this paper, from a 1/12500 (0.00008) lifetime risk of

premature death from lung cancer risk for casual cavers spending 50 hours per week in caves with an average concentration of 7000 Bq/m<sup>3</sup>, to a lifetime risk to die of excess cancer of 1 in 1000 for professional cavers spending 600 hours per year (50 hours per month) in caves. (<http://www.cavingireland.org/safety/radon.htm>).

We calculated risk for cavers spending 50 hours a year in caves based on the data from Darby et al. (2005). These risk estimates distinguish between smokers and non-smokers. These calculations give risk estimates of 0.00028 per cent, or 0.0000028 per individual for non-smokers, and a risk for smokers spending 50 hours per year in caves as 0.0066% for smokers or 0.000066 lifetime risk per individual.

With radon being such a strong carcinogen in the laboratory, and classed as a “class 1 carcinogen” why do we not see more cases lung cancer than we do?

We have a hypothesis that evolutionary forces help to protect the healthy respiratory system as natural selection would have tended to favour epithelia that would engender a survival advantage to members of a species with better developed epithelia, less vulnerable to radiation damage, in the airways. Ideally such an epithelium would have radio-resistant cells, or cells out of range of alpha particles, or cells readily affected by programmed cell death (apoptosis) if hit, or capable of activating tumour suppressor genes when genetic damage occurred.

Effective cilia that would remove offending particles rapidly would obviously constitute a benefit not limited to obnoxious radioactive particles. Smoking is, relatively speaking, a very recent habit and exposure to such a concentrated cocktail of carcinogens would leave the resultant metaplastic epithelium largely defenceless - loss of cilia, metaplasia etc.

Mining is also a relatively recent activity in evolutionary terms, and the evidence mentioned above (Saccomanno et al., 1996) is that mining dust and smoking create the opportunity for the formation of larger particles that will tend to deposit centrally and cause inter alia, squamous metaplasia. Our hypothesis of evolutionary protection against radon therefore is based on, firstly, the thickness of the pseudo-stratified ciliated columnar epithelium. Simply stated, the path length of the alpha particles (about 45 microns) may not be long enough to reach the nuclear DNA of the target cells, or many if not most of them will be out of range.

The basal cells are likely to be present for the duration of the individual's life, whereas the other cells (goblet cells and pseudo-stratified columnar epithelial cells etc.), may be replaced regularly and should be at a reduced risk for malignant transformation.

As far as the “bystander effect” is concerned, it depends how far the oxygen radicals or hydroxyl radicals can reach. The range is only about 4 nanometres for the hydroxyl radicals, but cell to cell communication by chemical mediators may extend to nearby cells and explain part of the mutagenic potential of radon in vivo.

The possible effects of chronic bronchitis in non-

smokers was not considered in the article by Darby et al. (2005). It is an aspect that may need research, as the basis of our hypothesis implies a normal, healthy epithelium of the respiratory tract. The attributable risk of radon in never-smokers without a history of asthma or chronic bronchitis may well prove to be lower still than the incidence in never-smokers.

It is of interest that Terzaghi-Howe (1994 & 1996; Terzaghi-Howe & Ford, 1994) studied the carcinogenic potential of alpha particles in the trachea of rats (intact trachea and cell cultures) whose respiratory epithelium closely resembles human respiratory epithelium, and whose habits may expose them naturally to larger doses of radon. She found that it is very difficult to transform cells with alpha radiation alone, and suspects that it is necessary for malignant transformation to have the effects of other factors, such as the chemicals in tobacco smoke, also present.

The United Nations Scientific Committee on the Effects of Atomic Radiation (2000) estimated that the mean radon concentrations in dwellings for 51 countries with a population weighted concentration is 39 Bq/m<sup>3</sup>. If this is correct, then if the excess risk of lung cancer is about 16% per 100 Bq/m<sup>3</sup> radon in homes should account for about 9% of the deaths due to lung cancer, and hence 2% of all cancer deaths in Europe. Clearly, the study by Darby et al. (2005) indicates that the risk level for never-smokers is very much lower than this figure, and that radon probably is not nearly as dangerous as is generally stated, provided that the respiratory epithelium is healthy and not compromised by disease or smoking. A certain percentage of the mining and general population may also have been cured of tuberculosis, which could also have damaged the larynx, trachea or bronchi. It may be a good study to compare carefully the epithelial thickness in healthy subjects (including the thickness of the mucous layer and cilia) to the range of alpha particles in this medium relative to the position of the nuclei of the cells most readily transformed. The effect of other respiratory diseases that can harm the bronchial epithelium should be taken into account in future epidemiological studies.

The failure of the authorities in Modum and Dobschau to report lung cancer in 1879 does not disprove our hypothesis. It must be remembered that at that time lung cancer had not been described in the medical literature. It is well known in medical circles that if we do not think of a certain diagnosis, we do not make that diagnosis. The doctors in those towns had probably never previously heard of lung cancer, and would not have considered it in the differential diagnosis of their miner patients with chronic lung disease.

There is a huge world literature on the subject of radon, smoking and lung cancer written by epidemiologists, environmentalists, radiation physicists, pathologists, clinicians and public health officers. Some of it is controversial (e.g. Cohen, 2004), and may reflect the training, interests, remit and subconscious bias of the authors. Good examples of the tunnel vision of authors are two reports of the

International Commission on Radiation Protection (ICRP) (Anon., 1987; Jacobi, 1993). They concentrated on ionizing radiation, and failed to assess adequately the contribution of tobacco smoke. A subsequent report of the ICRP cautioned that the effect of smoking on radon exposed miners is debatable. There may be other, unknown, carcinogens in the mines; and the smoking habits of the non-miner controls may differ from those of the miners (Masse & Cross, 1994). Care must be taken when extrapolating the results of *in vivo* and *in vitro* experiments, and epidemiological work done on miners, to cave visitors and employees.

This short paper does not attempt to summarise the literature. It serves to expand Cigna's (2005) paper from the point of view of clinicians. We have the above good reasons to believe that radon *per se*, in the low concentrations found in caves (Ford, 1991), does not pose a high risk for non-smokers. Cigna (1987) himself has come to the same conclusion using different arguments. The International Commission on Radiological Protection (Anon., 1987) has considered the radon problem in mines and homes. It initially confused the cause and effect relationship, and referred to the, "possible synergistic influence of cigarette smoking". It later again gave insufficient attention to the probable confounding effect on tobacco smoke, and dismissed this important matter in the penultimate paragraph. Nevertheless it later concluded that in workplaces where public occupancy is low, such as libraries, offices and theatres, no special regulation and treatment is necessary (Jacobi, 1993). Caves can be considered to fall into this category.

We further believe that it is the co-carcinogenic effect of radon on tobacco smoke (not the other way round) which is the risk factor for miners' lung cancer. We confirm Cigna's (2005) opinion that cave tourists and cave explorers spend insufficient time in caves for them to be at significant extra risk. However, show cave guides spend much of their working day in caves. It would therefore be prudent for tobacco smokers not to be employed as cave guides and in cave mouth buildings (Craven, 1997).

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## APPENDIX

### A note about units.

- Activity is expressed in Bequerels (Bq).  
 A Bequerel is defined as one disintegration per second.  
 A Curie (Ci, an older unit) is equal to  $3.7 \times 10^{10}$  Bq.  
 A Working Level (WL) = 200 pCi per litre (7400 Bq/m<sup>3</sup>) at 50% equilibrium of radon with its daughters.  
 One Working Level Month (WLM) = 170 hours of exposure in a workplace with one WL (or 170 hours of exposure to 7400 Bq/m<sup>3</sup>).  
 One WLM = (occupational) exposure for 12 months (8 h/d, 5 d/week) = 12 WLM/year, but at home with higher than 8 hours occupation (12 h/d, 7 d/w) therefore 1 WL (home) = 25.8 WLM/year.  
 One WLM/year = 74 Bq/m<sup>3</sup> (for <sup>222</sup>Rn series).  
 At complete equilibrium, one pCi/litre results in an exposure equal to 0.01 working levels, but it is assumed that inside buildings the radon decay product/radon equilibrium is only 50%. Thus inside buildings, one pCi/l = 0.005 working levels, or 1 WL = 200 pCi/l, and where 1 pCi/l = 37 Bq/m<sup>3</sup>.  
 One WL is therefore equivalent to 7400 Bq/m<sup>3</sup>, one WLM = 1,258,000 or 1.258 megabequerel/l, and 1 WLY = 15.1 MBq/l.  
 A count of 155,000 Bq/m<sup>3</sup> = 0.155 Mbq or about 0.12 WLM.

### Background radiation

The total background radiation due to cosmic rays, radon, medical exposure etc. is given as an Effective Dose (ED) of 360 millirem per year. Of this, radon is said to contribute 200 millirem, as against 63 millirem total for artificial sources.