Polonium-210 in Bronchial Epithelium of Cigarette Smokers

The biologic significance of radioactive polonium in tobacco smoke has been widely debated since the original report by Radford and Hunt (*1*). Holtzman and Ilcewicz (*2*) have mentioned some seemingly conflicting evidence concerning radiation doses from this source to bronchial epithelium.

Their paper for the first time indicates that, in addition to ^{210}Po, tobacco smoke contains some of that isotope's grandparent, long-lived lead-210; and that, in rib bones and lung parenchyma, ^{210}Pb was higher in smokers than in nonsmokers of about the same age. We agree that this means of exposure to environmental ^{210}Pb is important, and results of a few studies of smoke in our laboratory roughly confirm theirs. Indeed ^{210}Pb in smoke may be more significant than their data imply.

Because Holtzman and Ilcewicz's mainstream smoke samples contained much lower amounts of ^{210}Po than we and others have found, their estimates for inhaled ^{210}Pb also may be low. As far as radiobiological implications are concerned, however, it is the amount of ^{210}Pb present in the bronchial epithelium of smokers that is of greatest interest; no evidence is yet available. The presence of ^{210}Po in "hot spots" that we have reported (*3*) at bifurcations of segmental bronchi may depend on the presence of ^{210}Pb, environmental sources of which may account for the ^{210}Po found in epithelia of nonsmokers.

In view of the potential importance of such hot spots in smokers' lungs, we wish to comment on the wide discrepancy between our estimates of radiation dose for small regions of the bronchial epithelium and those reported by Hill (*4*) and Rajewsky and Stahlhofen (*5*), which are mentioned without comment by Holtzman and Ilcewicz. We believe that the apparently 100-fold difference in estimates of dose largely results from differences in the techniques of measuring epithelial ^{210}Po concentrations, and that, if carefully analyzed, the results of all three studies are compatible.

Bronchial specimens may be divided into three components: bronchial wall and submucosa, bronchial epithelium, and superficial mucus. Our pertinent findings from detailed analysis of pulmonary tissues from 25 cigarette smokers (*3*) are summarized in Table 1.

Table 1. Average concentrations of ^{210}Po in various components of bronchial specimens from 25 cigarette smokers.

Location	^{210}Po in wet tissue (pc/g)
Bronchial wall and submucosa	0.004
Superficial mucus	.013
Bronchial epithelium:	
Trachea	.12
Lobar bronchi	.19
Segmental bifurcations	4.5

The ^{210}Po concentrations in bronchial wall and submucosa and in superficial mucus were very low. Most of the measured activity lay in the epithelium, yet the epithelium accounts for only 2 to 3 percent of a bronchial specimen by weight. Thus it is evident that the ^{210}Po concentration measured in a whole specimen of bronchus may appear low, but, as most of the activity is in the epithelium, the epithelial concentration may be higher by nearly two orders of magnitude. For this reason, the local radiation dose to the epithelium would be correspondingly higher than that incurred if the activity were distributed uniformly throughout the entire specimen.

Hill (*4*) analyzed whole bronchial specimens weighing 5 to 15 g and containing several secondary bifurcations; he found the average ^{210}Po concentration in smokers to be 0.007 pc per gram of tissue. Applying our average results (Table 1) to a large specimen similar to Hill's, of which 2 percent by weight was epithelium and 5 percent of the epithelial surface represented tips of segmental bifurcations, we would expect the average concentration in the whole specimen to be 0.012 pc/g—in reasonable agreement with Hill's measurements.

Rajewsky and Stahlhofen (*5*) have analyzed pooled samples of epithelium, separated from bronchial wall, taken from "the bifurcation, the secondary bifurcation and parts of the trachea." The anatomical sources, and relative amounts of epithelium from each site, of these samples are not stated, but the amount of tissue available from tips of bifurcations is much smaller than that obtainable from the trachea and adjacent bronchi. The average ^{210}Po content in these pooled epithelial samples was 8×10^{-4} pc per square centimeter of epithelial surface. If we assume that the average thickness of the epithelium is 40 μ, this content represents 0.20 pc per gram of epithelium, a concentration intermediate between those we have found in trachea and in segmental bifurcations (Table 1). In private conversation, Stahlhofen has concurred that the results in the two laboratories actually agree closely. Because of the high background in their counters, Rajewsky and Stahlhofen could not have measured the ^{210}Po concentration in epithelium from individual bifurcations, and thus estimated local radiation doses in these areas.

The estimate of a maximum dose of approximately 200 rem/25 yr to the bronchial epithelium of lower-lobe bifurcations of smokers in our series (*3*) is based solely on the measured concentration of ^{210}Po in epithelial samples. This highly localized dose should not be compared with the dose to the whole lung, as calculated by Ferri and Baratta (*6*); nor does it take into account radiation arising from ^{210}Po in the mucous layer, as is included in the theoretical model of Radford and Hunt (*1*) and used as the basis for the doses estimated by Rajewsky and Stahlhofen (*5*). On the basis of our measurements in superficial mucus, we feel that this latter component is very small compared to radiation received from the isotope deposited within the epithelium.

Another problem in any analysis of bronchial epithelium is the rapidity of postmortem changes in this tissue. Histologic sections obtained within even a few hours of death often show loss of considerable areas of epithelium; therefore we have used only specimens obtained directly from the autopsy table when autopsy quickly followed death and when histological controls showed the epithelium to be reasonably intact. Hill and Rajewsky and Stahlhofen made no mention of this point.

We hope that future investigations and estimates of doses, particularly those evaluating the importance of ^{210}Pb in the bronchial epithelium of smokers, will allow for these factors.

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References

1. E. P. Radford, Jr., and V. R. Hunt, *Science* **143**, 247 (1964).
2. R. B. Holtzman and F. H. Ilcewicz, *ibid.* **153**, 1259 (1966).
3. J. B. Little, E. P. Radford, Jr., H. L. McCombs, V. R. Hunt, *New Engl. J. Med.* **273**, 1343 (1965).

4. C. R. Hill, *Nature* **208**, 423 (1965).
5. B. Rajewsky and W. Stahlhofen, *ibid.* **209**, 1312 (1966).
6. E. S. Ferri and E. J. Baratta, *Public Health Rept. U.S.* **81**, 121 (1966).

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Little and Radford's demonstration that their data and conclusions (*1*), showing the existence of areas of relatively high levels of ^{210}Po in human lung tissue, do not disagree (despite appearances to the contrary) with those of Hill (*2*) and Rajewsky and Stahlhofen (*3*) is significant. One should note, however, that the discrepancies are still not fully resolved either in the light of existing data or regarding some theoretical considerations.

First, the autoradiographic measurements by Hill (*2*) on specimens of vacuum-dried epithelium, from bronchial bifurcations taken from smokers, showed an upper limit of α-activity of 0.01 pc/cm^2, equivalent to a concentration of less than 2 pc/g. This upper limit is thus quite a little lower than the average value of 4.5 pc per gram of wet tissue determined from similar specimens by Little *et al.* (*1*). Second, this latter specific activity of epithelium is higher than that of dried smoke, 2 pc/g, as shown by Kelley (*4*) and Hill (*2*) and confirmed by us; it could be explained by preferential retention of the nuclide in the tissue over other components of the smoke, but this point is not established.

Finally, the origin of the high levels of ^{210}Po (up to 7 pc/g) (*1*), especially in nonsmokers, is of interest since the location at the bifurcations indicates that it is acquired by precipitation of that nuclide itself, or of its parent ^{210}Pb, from inhaled air. Thus these tissues, if they weigh 0.1 g and the concentration is 4 pc/g, might contain a total of 0.4 pc, a quantity representing the total weekly intake of ^{210}Po or 1 day's intake of ^{210}Pb. Considering that only a small fraction of the activity, say 5 percent, precipitates in these areas, the rate of build-up of ^{210}Po would approach the rate of its physical half-life, 138 days. Clearance processes operating on the deposited materials would make this build-up still more unlikely. On the other hand, build-up of ^{210}Pb presents these difficulties to a lesser extent, not only because of the higher concentrations in the atmosphere (0.02 pc of ^{210}Pb per cubic meter compared to about 0.002 pc of ^{210}Po), but also because of the much longer half-life of the parent, 21 years. Lead, however, may be more mobile in soft tissues.

It appears from these speculations that more evidence is necessary because of the high concentrations of ^{210}Po with the consequently high radiation level. Detailed and careful analyses, similar to those of Little *et al.* (*1*), and autoradiographic studies of the distribution of ^{210}Pb in the lung could perhaps establish the existence of high localized concentrations of ^{210}Po. Such studies might also provide insight into the origin and metabolism of ^{210}Pb and ^{210}Po.

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References

1. J. B. Little, E. P. Radford, Jr., H. L. McCombs, V. R. Hunt, *New Engl. J. Med.* **273**, 1343 (1965).
2. C. R. Hill, *Nature* **208**, 423 (1965).
3. B. Rajewsky and W. Stahlhofen, *ibid.* **209**, 1312 (1966).
4. T. F. Kelley, *Science* **149**, 537 (1965).

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Infrared Absorption of Carbonate Apatite

Termine and Posner (*1*) have concluded that the inorganic component of rat bone is composed of a two-phase mixture of crystalline and amorphous (noncrystalline) calcium phosphate. This they have done through consideration of a "splitting fraction measurement for the 600 cm^{-1} phosphate ion antisymmetric bending frequency in the calcium phosphates." They state that they "found a straight line correlation between the degree of this infrared splitting and percentage crystallinity (weight fraction of crystalline apatite) in synthetic samples containing these two phases." They refer to these synthetic substances as hydroxyapatite even though the substance of bone is not hydroxyapatite (*2*) and state that carbonate apatites were excluded from their investigation. Their basis for excluding the carbonate apatites is related to the size of individual crystallites in rat bone. There is no fundamental theory that will permit one to deduce the chemical composition of a crystalline phase from a knowledge of the size of the crystals, as Termine and Posner have done.

Elsewhere Posner *et al.* (*3*) have attempted to determine the "degree of crystallinity" of bone mineral by measuring line broadening of x-ray diffraction maxima, but incipient line splitting cannot, in general, be distinguished from line broadening (*4*).

The interpretation of their infrared absorption data is also erroneous. Coles (*5*) has pointed out: "The synthetic carbonate apatites have infrared spectra very different from those of other apatites. Distinguishing features are the strong carbonate band at about 1450 cm^{-1} and lack of resolution of the main PO_4^{-3} band into a doublet." By "main PO_4^{-3} band," Coles apparently means the pronounced absorption at about 1050 cm^{-1}. A similar lack of resolution has been observed in the absorption band at about 600 cm^{-1}, and was described by Zapanta-LeGeros *et al.* (*6*): "This band [635 cm^{-1}] is only very weakly present or even absent in the spectra of synthetic carbonate apatite, staffelite (carbonate-F-apatite), and biological apatite. This absence is believed due to the presence of the carbonate ion."

It is this reduction of resolution (absence of splitting) that Termine and Posner (*1*) used as a criterion to indicate the presence of an amorphous phase in rat bone, although the same reduction of resolution occurs for a holocrystalline, mineralogical carbonate apatite (*6*). Furthermore, although bone has been examined by both electron microscopy and electron diffraction by several investigators, no one has presented direct evidence of the existence of an amorphous inorganic phase, either phosphate or carbonate.

Thus, Termine and Posner have wrongly assumed that rat bone is a simple hydroxyapatite (instead of a carbonate hydroxyapatite) and have used a measurement that is spurious when carbonate apatite is present. They have furnished no evidence that an amorphous phase is present in bone.

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References

1. J. D. Termine and A. S. Posner, *Science* **153**, 1523 (1966).
2. D. McConnell, *ibid.* **136**, 241 (1962); *Clin. Orthop.* **23**, 253 (1962); *Amer. Mineral.* **45**, 209 (1960).
3. A. S. Posner, E. D. Eanes, R. A. Harper, I. Zipkin, *Arch. Oral Biol.* **8**, 549 (1963).
4. D. McConnell, *ibid.* **10**, 421 (1965).
5. J. L. Coles, thesis, University of Utah (1963).
6. R. Zapanta-LeGeros, J. P. LeGeros, E. Kline, O. R. Trautz, *J. Dent. Res.* **43**, 750 (1964).

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In our original report (*1*), we did not assign either structural or chemical identity to the poorly crystallized, apatitic fraction of bone mineral, since the exact nature of bone apatite is a matter of considerable debate (*2*). In