The records of the other four subjects were similar, showing continuous nystagmus in conditions (i) and (ii), nystagmus during 50 to 90 percent of the tracings in condition (iii), and no nystagmus during condition (iv).

It is well known that volunteer subjects in hypnosis studies are highly motivated to meet the experimental expectations of the investigator (*6*), and additional control procedures were therefore required before valid inferences could be drawn from these experiments. For this reason 30 additional subjects were obtained who were unaware that experiments to demonstrate hypnotically induced hallucinations were in progress. These subjects were asked to feign nystagmus under various conditions to ascertain that the response was not obtainable in the waking state. None of the subjects showed nystagmus in the absence of the actual rotating drum. It was later found that 16 of these subjects could be hypnotized. The three subjects who reported seeing the rotating drum when it was suggested to them developed nystagmus under this condition. All remained unable to do so in the waking state.

The findings of these experiments have several implications. First, they demonstrate that an external visual stimulus is not necessary for eliciting optokinetic nystagmus. Second, they offer evidence that hypnotically induced visual hallucinations are "real" in the sense that they are capable of eliciting an involuntary reaction. Third, they suggest a means of studying hallucinatory phenomena, since a means is provided for verifying a subject's report that he is experiencing a visual hallucination.

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Polonium-210 in Cigarette Smokers

Radford and Hunt's report [*Science* **143**, 247 (1964)] considered the bronchial epithelium as the critical organ in calculating the minimum dose from inhaled Po^{210} contained on particles of cigarette smoke. The mathematical model and assumptions used to make this calculation were not entirely evident in the report. The minimum dose estimate of 36 rem to bronchial epithelium as a result of smoking two packs of cigarettes per day over a period of 25 years far exceeds the dose of 1.1 rem to the entire lung as calculated from their data and the recommendations of the International Council for Radiation Protection [*Health Physics* **3**, 1 (1960)]. Because of the large difference in the minimum dose estimates, a comparison between Radford's assumptions and mathematical model and those of the ICRP is warranted.

Reference 16 of Radford and Hunt's report reads, "Dose [was] calculated on the basis of retention of 3.3×10^4 pc of Po^{210} in 25 years, a volume of the bronchial epithelium of 3 ml, and a mean transit time of the mucus sheet of 36 hours." This statement is confusing. Personal communication with Radford revealed that "retention" refers to the total quantity of Po^{210} deposited in the lung and not to the total quantity present at steady state. The value of 3.3×10^4 pc can be calculated from the product of the Po^{210} concentration in the main stream smoke, the number of cigarettes smoked in 25 years, and 75 percent deposition, with no correction for decay or biological elimination. The smoke particles are assumed to be deposited on the alveolar epithelium, from which they are phagocytosed and carried up the bronchial tree. In Radford and Hunt's calculation the bronchial epithelium is considered a single uniform sheet over which all the Po^{210} deposited in the alveoli passes with a mean residence time of 36 hours. However portions of the bronchial epithelium would in fact receive only that Po^{210} originating from alveoli connected to them. Mean exposure times and total quantity of Po^{210} passing over different segments of bronchial epithelium will be quite different and difficult, if not impossible, to calculate.

The ICRP recommends relative distributions of insoluble particles in the lung quite different from Radford and Hunt's. It is assumed that only 12½ percent of the total number of particles inhaled are removed from the lower respiratory passages in a short period of time. The ICRP recommendations indicate, therefore, that Radford and Hunt's dose estimate to bronchial epithelium might be too high by a factor of 8. The facts that a considerable quantity of smoke is exhaled and that many particles deposited in the alveoli remain there for a long period of time, as evidenced by the considerable amount of dust and soot found in the lung parenchyma of adults compared to the lungs of a new born child, indicate that Radford and Hunt's assumptions tend to overestimate the total quantity of Po^{210} passing over the bronchial epithelium, and hence to overestimate the dose. In reality probably neither Radford and Hunt's model and assumptions nor those of the ICRP actually describe the situation in the lung. However, it is important that present standards, such as those proposed by the ICRP, reflect not only our present state of knowledge but also safety factors where knowledge is lacking. Radford and Hunt's report indicates that there is Po^{210} in cigarette smoke and that there could be a harmful effect.

The report also implies that the recommendations of the ICRP with regard to distribution and fate of insoluble particles need revision. It is hoped that additional studies will be conducted to clarify this and many other points, so that the recommendations of the ICRP can be continued to be made on the basis of best knowledge available.

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We concur with the statement of Skrable, Haughey, and Alexander that the radiation dose to the lung parenchyma from polonium in cigarette smoke is negligible in comparison with the dose to bronchial epithelium. This difference between lung tissue and bronchi applies particularly to any insoluble aerosol containing a radioelement giving rise to an energetic alpha particle and having a physical half-life similar to or longer than the mean residence time of particles in the lungs. When one takes into account the direct deposition or absorption of an alpha-emitter into localized regions of bronchial epithelium, the radiation dose in these areas may easily be 100 to 1000 times the average lung dose. For these reasons the bronchial epithelium is the critical organ for inhaled insoluble aerosols containing alpha-emitters. In our opinion the International Committee on Radiation Protection has not given adequate attention to this fact in setting the maximum permissible concentration of the relatively long-lived alpha-emitting elements.

We are now in the process of measuring concentration of Po^{210} in bronchial epithelium of smokers in order to permit better estimates of doses in "hot spots" with a minimum of assumptions. As we pointed out in our original report, these doses from polonium within the epithelium are probably more important biologically than the "minimum dose" from polonium in transit questioned by Skrable *et al.*

We do not think that the ICRP model applies to cigarette smoke because cigarette smoke particles are nearly all smaller than 0.4 micron (*1*). For particles of this size the principal mechanisms of deposition in pulmonary tissue are diffusion and, to a lesser extent, gravitational settling. Table 10 of the ICRP recommendations, cited by Skrable *et al.*, states that retention of particles depends on many factors, but that the distribution in the table may be used "when specific data are lacking." In the case of cigarette smoke, specific data are available on particle size and fraction exhaled by "average" smokers (*1*). For particles deposited by diffusion the critical datum is the surface area of pulmonary tissue exposed to smoke. Since the surface area of the alveoli of a normal adult is more than 100 times greater than the surface area of the ciliated bronchi, our assumption that all of the smoke deposited [75 percent of inhaled smoke; see (*1*)] is initially on the alveolar surface seems reasonable.

Skrable, Haughey, and Alexander have correctly summarized the way we calculated the dose from polonium carried over the bronchial epithelium in the mucus sheet, and we agree that our use of the word "retention" was ambiguous. The estimate of 36 rem is calculated as the dose arising from all polonium deposited in the lungs and cleared via the bronchial tree, irradiation occurring only when the polonium is in transit. This dose may be too low or too high for many reasons other than the question of initial deposition raised by Skrable *et al.* For example, the transit time for ciliary clearance may be slowed considerably by the ciliostatic effect of chronic smoking, leading to a higher dose estimate. On the other hand, smoking may thicken the epithelium and lead to a lower dose to the basal cells if they are beyond the range of alpha particles from polonium on the surface. For these reasons, and also because of inhomogeneous deposition or clearance from alveolar tissue, estimates of the radiation dose from this source are indeed uncertain. We still believe the ciliostatic effect of smoke is the most important modifying factor, and therefore our "minimum dose" estimates are conservative for polonium carried out in the mucus sheet. The "in-transit" dose, however, is probably of minor significance compared to the dose from polonium absorbed in the epithelium.

We agree that better data are needed, and to this end we have suggested (*2*) that polonium from cigarette smoke may be a useful tracer of the movement of smoke particles in human lungs. The ICRP model for insoluble particles is based on the assumption that 12½ percent of inhaled particles are cleared from the lungs by absorption directly into the blood. We have measured polonium in blood, urine, and bronchial lymph nodes of smokers and conclude that less than 5 percent of deposited polonium is cleared directly into the blood. Our measurements in lung parenchyma of smokers support the conclusion that most polonium is cleared by way of the bronchi with a relatively short half-life of a few days. The fact that the lung parenchyma of adults contains carbon really tells little about dynamics of lung clearance of inhaled particles.

The subject of possible biological effects of cigarette smoking is one on which most scientists now have a bias in one direction or another; this bias often depends on whether one is a smoker or has some connection with the tobacco industry. From correspondence with Alexander, it is apparent that he is skeptical of the role of polonium in production of bronchial cancer. Skepticism is a proper scientific approach, and in this case, it is shared by us. Our skepticism is not dependent so much on uncertainty of the radiation dose to smokers as it is on the question of whether these doses can contribute to cancer production.

Whatever the effect of polonium in cigarette smoke proves to be, we believe that a conclusion of great importance will be reached with regard to human radiation exposures. If polonium in smoke is found *not* to be involved in bronchial carcinogenesis, this will greatly strengthen the view that exposure to chronic low doses of radiation, particularly to local groups of cells, is not hazardous. On the other hand, proof that chronic radiation exposure from polonium *is* involved in production of cancer would have obvious significance. Aside from our belief that polonium is a good suspect, we do not take a strong stand either way. Whatever the final result, knowledge of the actual radiation dose received by smokers will be very important, and inevitably a significant by-product of work toward such knowledge should be a better understanding of the way that inhaled smoke particles are deposited in and cleared from human lungs.

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