Letters

Potassium Iodide for Thyroid Protection

In her letter of 19 November (p. 743), Rosalyn Yalow continues her arguments against the Food and Drug Administration's (FDA's) recommendations (*1*) concerning the use of potassium iodide for thyroid blocking in the event of a major release of radioactive iodine from a nuclear reactor accident. Yalow also says I made "erroneous statements" in my letter of 1 October (p. 6), where I supported the FDA recommendations.

Specifically Yalow disputes my use of the thyroid radiation risk estimates published in the most recent review sponsored by the National Academy of Sciences (NAS) (*2*). She points out that these risk estimates are derived principally from populations which have been subject to external (x-ray) irradiation of the thyroid rather than the internal (beta ray) irradiation that would be involved after exposure to radioiodines. She dismisses the only recent animal experiment on the subject, in which it was found that x-rays and iodine-131 are equally effective, per rad, in producing thyroid carcinomas and adenomas in rats (*3*). And she argues that, if this were true for humans, the use of radioiodines for diagnostic and therapeutic purposes during the period 1948–1968 would have resulted in 120,000 extra thyroid cancers in the subsequent years, an increase which she states "simply did not occur."

The issue then is whether the FDA, in arriving at its thyroid protection recommendations, should have assumed that the carcinogenic effects of irradiating the thyroid with iodine-131 are comparable to or much less than those resulting from irradiation by x-rays.

The FDA's answer to this question was published along with its recommendations (*1*):

> [t]he paucity of human data relevant to the induction of radiation effects from [iodine-131], particularly relevant in children, have convinced the Food and Drug Administration that it is prudent to be conservative and to employ risk estimates from external irradiation studies in reaching the conclusions upon which this recommendation is based.

I agree with this decision. Yalow contends that it was too conservative.

An error is evident in Yalow's assumption that the incidence of excess thyroid carcinomas should scale linearly with dose from the relatively low dose region (tens to hundreds of rads), where thyroid cancers induced by x-rays have been observed, to the doses on the order of 10,000 rads that were used in the therapeutic treatment of hyperthyroidism. Yalow uses this assumption of linearity in combination with the NAS risk numbers (*2*) to obtain the estimate (which she then argues is in conflict with actual experience) that 100,000 thyroid cancer cases should have resulted from the use of iodine-131 for the treatment of hyperthyroidism during the period 1948–1968.

It is well known, however, that, while the incidence of radiation-induced cancers increases (sometimes linearly) as a function of dose at low and intermediate doses, it plateaus and then falls at very high doses due to "cell-killing" effects (*2*). Dead cells do not produce carcinomas. The iodine-131 doses used for the treatment of hyperthyroidism were intentionally in the cell-killing dose region because their purpose was to reduce the activity of the thyroid.

The fact that the incidence of thyroid cancers after iodine-131 irradiations of about 10,000 rads is much lower than would be predicted by a linear extrapolation with dose of the incidence observed following much lower doses of x-ray irradiation is therefore not evidence, as Yalow states, of the lower carcinogenic effect of iodine-131 irradiation, but rather is largely and may even be entirely due to the incorrectness of her linear extrapolation. This same mistake was made in one of the references (*4*) cited by Yalow and has continued to propagate (*5*), despite the fact that it had already been flagged in the NAS review of 1972 (*2*).

What then about Yalow's other estimate that, if iodine-131 irradiation were as carcinogenic as x-rays, 20,000 extra thyroid cancer cases should have resulted among the 2 million individuals whom she says received thyroid doses of approximately 100 rads as a result of the use of iodine-131 for diagnostic purposes during the period 1948–1968?

Here the situation is still not resolved. Only one (Swedish) study of the incidence of thyroid cancers following the use of iodine-131 in diagnostic tests, that by Holm *et al.* (*6*), is cited in the FDA review (*1*). That study found no excess thyroid cancers beyond an expected number of six to eight, whereas about 75 would have been expected using the NAS risk coefficients. However, more than 95 percent of the population examined by Holm *et al.* were over age 20 at the time of exposure, while the NAS risk estimates are based primarily on populations who received their thyroidal x-ray doses as children. Holm *et al.* suggest, therefore, that their results may indicate that the thyroids of adults are much less susceptible to radiation-induced cancer than those of children. If this is true, it would also be necessary to reduce greatly the estimate of 20,000 thyroid cancer cases which Yalow projects by applying the NAS dose-risk coefficients to the mostly adult U.S. population which received diagnostic iodine-131 doses during the period 1948–1968.

Thus it appears that there are good reasons to reduce dramatically Yalow's estimate that 120,000 extra U.S. thyroid cancers resulting from iodine-131 irradiation should be expected if thyroid irradiation by iodine-131 were just as carcinogenic as x-ray irradiation. The annual U.S. incidence of diagnosed thyroid cancers is currently about 10,000 per year (*7*) and appears to have risen about fivefold since 1940 (*8*). A few thousand thyroid cancers induced by iodine-131 spread over the past 20 years may or may not have contributed to that increase. Resolution of that question awaits an epidemiologic study with carefully chosen controls.

Finally I would like to comment on the resolution opposing the stockpiling of potassium iodide for thyroid protection that was passed by the Committee on Public Health of the New York Academy of Medicine. Before other state governments follow this recommendation, as Yalow suggests, I suggest they study the brief report in which the committee documented the basis for its conclusion (*9*). They will find that the committee relied heavily on a statement by the Electric Power Research Institute that very little radioactive iodine would be released in any future nuclear reactor accidents. This assertion led the Nuclear Regulatory Commission to sponsor a major review of the subject, which concluded

that some important types of nuclear reactor accidents could result in huge releases of radioiodines to the atmosphere (*10*).

It appears, therefore, that potentially serious nuclear reactor accidents could occur and that thyroid blocking would offer one of the few practicable strategies for mitigating their consequences. The FDA has determined that potassium iodide is safe and effective for this purpose. The task now is to develop recommendations for the states concerning distribution schemes that would make potassium iodide available to the population downwind from a major release of radioactive iodine when needed. Thus far no federal agency has been willing to undertake that task. That is why Representative Edward Markey (D–Mass.) held the congressional hearing which originally sparked this exchange of letters (News and Comment, 19 Mar., p. 1485).

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References and Notes

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4. H. R. Maxon, S. R. Thomas, E. L. Saenger, C. R. Buncher, J. G. Kereiakes, *Am. J. Med.* **63**, 937 (1977).
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9. Committee on Public Health, New York Academy of Medicine, *Bull. N.Y. Acad. Med.* **57**, 395 (1981).
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ACS Electioneering

With respect to Eliot Marshall's article "Acid electioneering at ACS" (News and Comment, 29 Oct., p. 455), I think it would be well to clarify a bit what was said or implied in the article. The "grass roots group" does not want the American Chemical Society (ACS) to abandon any of its admirable educational and scientific efforts but to add to those a strong professional activity. This stance is supported not only by industrial chemists (65 percent of the ACS) but also by many academic chemists and for many good reasons. One is that in the last decade the median salary of chemists has decreased 18 percent in terms of constant dollars, with a loss of at least $2 billion to the membership. On 1 July 1980, the California Section Executive Committee of the ACS passed a resolution calling on the board of directors to take steps to rectify this situation to the greatest extent possible. In spite of this, and subsequent urging, the ACS has done little to deal with this problem or to show any real interest.

Finally, petition electioneering can cut both ways. Last year two prominent industrial chemists were regularly nominated, and friends of Fred Basolo of Northwestern University petitioned to get him on the ballot; he won narrowly.

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