that there was a higher success rate where the subject was male, young (less than 50 years), had been in hospital for a short time, and when the request was made between six and 24 hours after death.

We also found that some clinical units were more successful than others; the necropsy rates varied from one unit to another from 50% to 92%. Apparently the nature of the approach made is of greater importance than reluctance on the part of relatives.

Consideration of this would be essential in any attempt to introduce the partial audit. That the answer lies with the clinicians is indicated by comments we have had from some of our consultant colleagues: "We put less pressure on relatives than we used to" and "pressure is brought to bear on the reluctant, because I believe the necropsy is of fundamental importance."⁴

We gratefully acknowledge the willing collaboration of the clinical consultants and their staffs that made this study possible. We thank

Mrs B A Wilson and Mrs C M Curlewis for their invaluable help and the pathologists who cheerfully undertook the additional necropsies. This study was supported by a grant from the Scottish Home and Health Department.

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Scientifically Speaking

Iodide

WALLACE K WATERFALL

Washington, DC—The legacy of the nuclear power plant accident at Three Mile Island is more than huge clean-up costs, tighter government regulations, and regional psychological stress. That mishap in the spring of 1979, although not yet proved to have injured anyone, has inspired a clinical debate of apparently growing proportions. The question is whether potassium iodide should be distributed to people living in the neighbourhood—in order to reduce thyroid uptake of radioactive iodine-131—after a nuclear reactor leaks appreciable amounts of its fission products.

The topic was the basis for an entire evening's symposium at the recent annual meeting of the Endocrine Society here. "We're willing to stay 'til midnight," said Joseph E Rall in his chairman's introduction to the session. Scientific director of the National Institute of Arthritis, Metabolism, and Digestive Diseases, Dr Rall said the debate had never before been aired in a "public forum," which in this case consisted of several hundred of the society's members, followers, and spouses. Although the discussion did not run to an hour when anyone's taxi was threatened with becoming a pumpkin, it generated some clear-cut differences of opinion.

The format of the evening gave Dr Rall the task of describing how much of a carcinogenic problem radioiodine is, followed by

Herbert J C Kouts, chairman of the division of nuclear energy at Brookhaven National Laboratory, telling of the pertinent physical aspects of reactor accidents. They established a context for an exchange of views between Jan Wolff, medical director in the endocrinology branch of the arthritis institute, who sees a distinct place for prophylactic potassium iodide, and Rosalyn S Yalow, Nobel Laureate for the radioimmunoassay and sceptic about the worth of potassium iodide as weighed against the potential for adverse reactions to it.

Potassium iodide prophylaxis

Concern about the effects of ionising radiation on the thyroid has created a considerable body of scientific published reports over the years, but it is only since the Three Mile Island event that there has been cause for much dispute about potassium iodide prophylaxis. Government actions in sending hundreds of thousands of doses of potassium iodide to Pennsylvania storage facilities around the fulminating reactor called new attention to the potential for mass pretreatment. The doses were never distributed, but their preliminary deployment was widely noted in news reports.

No one on the Endocrine Society programme was questioning the efficacy of potassium iodide to block thyroid uptake of radioiodine, or was denying the existence of circumstances in which such blockage could be desirable. The question is, as Rosalyn Yalow put it, "the advisability of general distribution of potassium iodide to a population which is alarmed by fear of radiation at any level and is poorly informed concerning the potential hazards of taking or not taking the drug."

As it turns out, that is not the only question. There seems to be considerable uncertainty about the thyroid consequences of

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various types of ionising radiation. X rays, for instance, may be regarded as a greater influence on the eventual development of thyroid carcinoma than radioiodine is. Or x rays may be a lesser threat than radioiodine for thyroid cancer if they damage the gland sufficiently to prevent cellular proliferation. Joseph Rall said that several surveys seem incontestably to establish a link between ionising radiation and thyroid adenoma nodules or carcinoma. Nevertheless, he said, there is also strong evidence that the development of thyroid cancer after exposure to ionising radiation is strongly related to the age at which a person was exposed—younger is worse.

The radioiodine of concern in a reactor accident is principally ^{131}I , with a half-life of eight days. Nuclear reactors generate a range of iodine isotopes—129 and 131 to 135—Herbert Kouts said, but within about six hours after a reactor is shut down only ^{131}I is present in threatening quantity, the rest having largely decayed. A fully operational reactor has hundreds of millions of curies of radioiodine in the core, "available for release," he said. Availability in that quantity is what prompted one government-sponsored study group to estimate that the worst type of reactor accident—a "core melt"—would produce 8000 thyroid nodules a year in an exposed population of 10 000 000 during the peak years of nodule incidence. But only about one-third of those nodules would prove to be malignant, the study report projected, and 10% of those would lead to death of the patient.

WASH-1400

That study, formally known as the Reactor Safety Study but more commonly called the Rasmussen Report, for study director Norman C Rasmussen of the Massachusetts Institute of Technology, or WASH-1400, which was the report number assigned by the sponsoring Nuclear Regulatory Commission, has often been accused of viewing nuclear power plants in too rosy a light. Completed in 1975, it was the first large-scale effort at probabilistic risk assessment for truly big accidents. The technique employed a "logic tree" of events from the initiation of trouble in a nuclear reactor (a valve opened by mistake, for instance) to the final event (core melt). Each of many possible initiating events was tracked through the maze of consequent possibilities to determine its probability of causing a core melt. Then the many different probabilities were combined to obtain a total probability of melting a core.

By these methods, WASH-1400 came up with an estimate that the chance for a core melt was one in 20 000 per reactor a year. Projecting that the USA would probably have 100 power reactors in operation in 1980, the study duly called attention to the arithmetic that made the chance for a melt-down anywhere in the USA one in 200 a year.

But the report, particularly in its summary, compared many core melt consequences with other natural and man-caused mishaps. The effect was to cast a scrim of relative innocuousness over nuclear plant accidents as compared with risks of death in motor vehicle accidents, air travel, hurricanes, and earthquakes. The only curve that fell as low on the chart for fatality risk as nuclear accidents was the probability of being killed by a falling meteor. It was those comparisons for which WASH-1400 was most criticised, but Herbert Kouts, who was a member of a committee that reviewed the report, says he continues to think it is the best such study done. The one matter for which WASH-1400 may have made estimates too grave, he said, are the consequences of radioiodine release. He said it could be "a substantial overstatement of risk from ^{131}I ."

Jan Wolff, in his turn at the Endocrine Society lectern, said that all the relevant reports on the subject recommended the use of potassium iodide to block thyroid uptake of ^{131}I . But successful prophylaxis "demands fast action," he said, which probably means storage of potassium iodide in the neighbourhood of every nuclear reactor. The agent must be swallowed at least 30 minutes before exposure to radioiodine, according to Dr Wolff, and 130 mg will serve to suppress ^{131}I uptake for about 24 hours.

The published reports also identify conditions that seem to predispose to potassium iodide sensitivity, he said, such as hypocomplementemic vasculitis, but Americans have taken millions of 300-mg doses of potassium iodide with "few reactions."

Report 55

Rosalyn Yalow blamed a publication of the National Commission on Radiation Protection for spreading the idea that potassium iodide is a fairly benign drug. Issued in 1976, NCRP report 55, "Protection of the thyroid gland in the event of releases of radioiodine," took the yearly US production of potassium iodide and the reported reactions to it and came up with 24 reactions per 48 million doses, she said. But if one figures that the recommended dose for treatment with potassium iodide is three to six pills a day every day, the reaction rate becomes five per 10 000 persons, which she called "hardly negligible if potassium iodide were to be administered to millions of people." Moreover, the number of reactions is taken from reports to the Food and Drug Administration, but "most reactions to a drug such as potassium iodide are not reported to the FDA." She finds it not unrealistic to believe that report 55 underestimated the reaction problem "by a factor of at least a thousand and we simply do not know how much greater."

Dr Yalow found a "multiplicity of papers describing acute reactions following a short period of even small doses of iodides." Many such reactions were dermatological, she said, and one study of drug-induced skin problems placed potassium iodide second only to the penicillins as an induction agent—about 20% incidence for the antibiotic and 1% for potassium iodide.

Possibilities for a life-threatening reaction to potassium iodide are not remote, according to Dr Yalow. One study's finding of particular sensitivity to potassium iodide among patients with hypocomplementemic vasculitis indicates that as many as six in 10 000 people could have a severe reaction to potassium iodide—if that study's incidence of hypocomplementemic vasculitis in 2-3% of sufferers from rheumatoid arthritis were broadly representative.

Even with its risk, potassium iodide prophylaxis could perhaps be considered if the hazard of exposure to ^{131}I were great. But studies of populations subject to nuclear bomb fallout has not indicated a thyroid threat except perhaps to children, said Dr Yalow. More to the point, millions of people have received ^{131}I tracer doses which, in her experience, expose the thyroid to an average 100 rads of energy. Using the WASH-1400 estimates of thyroid cancers, she said, the diagnostic use of ^{131}I in the USA from 1948 to 1978 should have produced almost 70 000 cancers of the thyroid. "In the presence of the usual thyroid cancer death rate of 1000 per year, such an epidemic should not have escaped notice." To her, the only explanation is that ^{131}I carcinogenicity, at least in adults, has been "greatly exaggerated."

Hardly had the debate ended at the Endocrine Society when a report appeared in the *New England Journal of Medicine*¹ supporting Dr Yalow's belief. Lars-Erick Holm and associates at the Radiumhemmet in Stockholm reviewed the cases of nearly 3000 adult patients at a mean of 13 years after they had received treatment with ^{131}I and found no increased incidence of malignant thyroid tumours. The finding, however, does nothing to ease the apprehension about children and ^{131}I . An editorial in the same issue of the journal points out that there are simply too few patients treated with ^{131}I as young children to provide evidence of relative harmlessness to the thyroid.

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No reprints of this article will be available from the author.