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THE AMERICAN THYROID ASSOCIATION
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27 November 1989

Alan Roecklein, M.D.
Radiation Protection-Health Effects Branch
USNRC
5650 Nicholson Lane
Rockville, MD 20852

Dear Dr. Roecklein:

The American Thyroid Association has for some time monitored the problem of potential radioiodine contamination of the atmosphere in the event of a nuclear reactor core melt accident. There has been concern about the possibility of radioiodine in the fallout accumulating in the thyroid gland and irradiating it, with the potential of causing thyroid neoplasms and hypothyroidism.

Potassium iodide (KI), by blocking radioiodine uptake by the thyroid gland, has a radioprotective effect. However, there are a number of significant difficulties in using KI for this purpose.

The American Thyroid Association has re-examined the issues involved in stockpiling KI for use in the event of a reactor accident. The attached statement is an update of a previous published analysis of this complex situation (Journal of the American Medical Association, 1984; 252:659). It is hoped that this statement will generate renewed consideration of this complex problem.

Sincerely yours,

John F. Wilber, M.D.
President, A.T.A.

Leonard Wartofsky, M.D.
Secretary, A.T.A.

David S. Cooper, M.D.
Chairman, Public Health Committee
Johns Hopkins University

David Becker, M.D.
Cornell University

Statement on Potassium Iodide Stockpiling

American Thyroid Association

The recent reactor accident at Chernobyl in which large amounts of radioactive iodine were released into the atmosphere again raised questions about proposed methods of protecting those at risk of exposure. In a previous statement (JAMA 1984, 252:659), the American Thyroid Association (ATA) reviewed the scientific information available about the usefulness of potassium iodide (KI) as a blocking agent to prevent radioactive iodine from entering the thyroid gland of those exposed to fallout. It also reviewed available data about the possible effects on the thyroid of low level radiation from radioiodine as well as the potential toxic side effects of distribution of potassium iodide to large unsupervised populations.

It was concluded at that time that information necessary for the development of a suitable public health strategy required risk/benefit data (ratio of the risk of the hazards of radioiodine to those of stable iodine administration) but that such information was not then available. The ATA is aware of no new information altering the issues raised at that time.

It was concluded in that report that, although the general distribution of KI was not recommended except in special locations and under special circumstances, advanced planning for possible distribution was advisable and it urged that a national task force of specialists be convened to review the issues in KI distribution and to develop alternate national distribution strategies for consideration.

As best as can be determined at this time, no substantial stockpile of potassium iodide is available for public use. Despite the unlikely event of an emergency requiring its use, the ATA believes that the option of potassium iodide distribution should be available for consideration to those responsible for public health measures. To this end, the ATA believes that it would be prudent to have available at central locations a suitable stockpile of KI for possible distribution should its use be contemplated.

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The Use of Iodine as a Thyroidal Blocking Agent in the Event of a Reactor Accident

Report of the Environmental Hazards Committee of the American Thyroid Association

David V. Becker, MD; Lewis E. Braverman, MD; John T. Dunn, MD; Eduardo Gaitan, MD; Colum Gorman, MB; Harry Maxon, MD; Arthur B. Schneider, MD, PhD; Lester Van Middlesworth, MD, PhD; Jan Wolff, MD, PhD

• In the event of a nuclear reactor accident, radioactive materials could be released into the environment: radioisotopes of iodine could constitute a major component of such a release. Upon such exposure, radioiodines could enter the body and accumulate in an unprotected thyroid gland where they would remain for varying periods of time. A number of methods have been proposed to protect those at risk of exposure. Administration of thyroid-blocking agents (such as potassium iodide) to exposed populations could be effective, but their use has raised a number of questions since there are considerable gaps in the scientific information available about the possible effects of low-level radiation from radioiodine. In addition, there are only limited data available about potential toxic side effects of potassium iodide distributed widely to large, unsupervised populations. Concern about these issues led the American Thyroid Association to appoint a committee of its members with special interest and competence in these areas to review the problems in detail and develop an advisory statement on the questions at issue for those to whom this matter might be of concern.

(*JAMA* 1984;252:659-661)

INDUCTION OF THYROID NEOPLASMS BY RADIATION

AT SOME level of exposure, radioactive iodine may be tumorigenic for the human thyroid gland,[1] and at higher levels it is ablative. It should be noted that radiation-induced thyroid neoplasms are usually benign or well-differentiated carcinomas with a good prognosis. The precise level of radioiodine incorporation into the thyroid that may be tumorigenic is unknown because most of the available data on low-dose (nonablative) radiation derive from x-ray studies[2] and relatively little from radioiodine studies.[3] There is considerable evidence that a rad of iodine 131 is substantially less tumorigenic than a rad of x-ray.[1,4,5] Estimates of the ratio of tumorigenic potential of ^{131}I as compared with x-ray vary from 1:1[1] to 1:5[6] to 1:20[1] and higher.[1] In persons exposed to accidental release of radioiodine from nuclear power plants, the ratio may vary depending on the mixture of isotopes released. Factors influencing the ratio include half-life of the radionuclides, dose rate, and distribution of the dose within the gland. Evidence from subjects exposed to relatively large amounts of diagnostic ^{131}I in Sweden who were carefully followed up suggested no increase in the incidence of thyroid tumor in populations exposed to about 100 rad (adults) or 159 rad (persons younger than 20 years).[7] For these reasons, projected thyroidal doses from radioiodine as high as 500 rad have recently been proposed as a realistic threshold for the institution of blocking countermeasures in the event of a reactor accident releasing radioiodines into the environment.[8]

PHARMACOLOGIC BLOCKADE OF THE THYROID WITH IODINE

Numerous studies have considered various protective measures against environmental contamination with radioiodine. Although other agents might be useful, it has been concluded that thyroid blockade by iodides is

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the most effective method. Thyroid radioiodine uptake can be reduced to less than 1% by the daily oral intake of 130 mg of potassium iodide (100 mg iodide).[8,9] Ingestion of stable e may also reduce the whole-body radiation burden from radioiodine.[2] Important factors in such protective treatment are as follows: (1) Sufficient dose—100 mg of iodide per day, although 30 mg of iodide per day is almost as effective.[9] (2) Early administration—since optimum effectiveness requires ingestion of iodides *before* exposure to radioiodine. (If contamination continues, treatment after initial exposure will still be helpful in reducing total radiation dose. This critical time element implies that protective responses involving the use of potassium iodide will have to be planned well in advance of accidents.) (3) Duration—blockade with a single 100-mg dose of iodide lasts between 24 and 48 hours, so daily administration is necessary. Unless exposure continues, treatment for no more than seven to 14 days is contemplated.

ADVERSE REACTIONS

any anecdotal reports of isolated ions to iodides have been published, but reliable incidence data do not exist.[10] It is reasonable to assume that obvious iodide reactions are rare in the United States where the diet is high in iodine content and where the population ingests more than 10⁷ potassium iodide tablets annually and povidone-iodine is widely used for local antisepsis.[11] When reactions do occur, they may be intrathyroidal or extrathyroidal.

Intrathyroidal Iodide Reactions

Low Doses (Usually Less Than 25 mg/Day).—Jodbasedow or iodide-induced thyrotoxicosis may occur.[12,13] This syndrome is uncommon in the United States,[9] but is more frequent in countries where there is iodine deficiency. It may occur after the administration of iodine in the treatment of endemic goiter or after the administration of iodine-containing drugs.

High Doses (50 to 500 mg/Day).—These may induce iodide goiter and/or hypothyroidism.[12,13] Iodide-induced hypothyroidism may also occur ng the administration of lower es of iodine but usually requires prolonged exposure to high doses of iodine and is generally not considered to be a danger during a seven- to 14-day treatment period. Subjects with underlying thyroid disease are at potentially greater risk. There appears to be a risk of neonatal goiter and hypothyroidism in newborns whose mothers were exposed to pharmacologic doses of iodine during pregnancy, although the dose and duration of iodine therapy are probably greater than those considered in this article. On the other hand, fetal thyroids are radiosensitive so they should be protected via the mother.

Very High Doses (More Than 1,000 mg/Day).—Thyroiditis rarely occurs and would not be a problem in a protective program where the recommended dose of iodine is much smaller.

Extrathyroidal Iodide Reactions

Low Doses.—Complications are extremely rare and include ioderma, periarteritis nodosalike syndromes, exacerbation of hypocomplementemic vasculitis,[8] dermatitis herpetiformis,[9] and allergies such as edema and nasal polyps.

High Doses.—Sialadenitis (iodide mumps) is perhaps the most common adverse reaction and occurs in the parotid and submaxillary glands. It is easily reversed by iodide withdrawal. Iodide fever is rare but should be considered when fever develops in patients receiving iodides.

Very High Doses.—Upper gastrointestinal tract symptoms may occur but would not be expected during a protective program.

If general distribution of potassium iodide is contemplated, it should be accompanied by carefully prepared public information material. Persons potentially at risk for iodide side effects should be identified and alerted. These include particularly those persons with previously known iodide sensitivities, those with hypocomplementemic vasculitis, and those with goiters or autoimmune thyroid disease. Persons already taking thyroid hormone medication for replacement or suppression therapy need not take iodide to block their thyroids.

CONCLUSIONS AND RECOMMENDATIONS

The development of an appropriate strategy for proper protection against radioiodine contamination requires risk-benefit (risk ratio of radioiodine hazards to stable iodine hazards) and cost-benefit evaluations, but adequate data are not now available for either the numerator or the denominator.

The American Thyroid Association recommends that more vigorous attempts be made to obtain such essential data through funding by the appropriate governmental agencies such as the Nuclear Regulatory Commission, the Environmental Protection Agency, and the National Center for Devices and Radiological Health (NCDRH) of the Food and Drug Administration. For example, review and extension of the NCDRH radioiodine side-effects study of potential adverse effects following the use of diagnostic iodine would be very useful[2] and/or studies similar to the Swedish follow-up evaluation[7] of patients receiving tracer doses of $^{131}I could be instituted in the United States. Studies of the biologic effects of radioiodine on the thyroid should also be sponsored. It would seem reasonable to institute the following: (1) Establishment of a central registry of side effects from iodide ingestion. (2) A prospective study under the auspices of the National Institutes of Health, the Department of Defense, and/or the NCDRH in which volunteers would ingest potassium iodide in the form, dosage, and duration proposed. If new data provide the necessary information to define more precisely the risk of radioiodine exposure and the risk of short-term iodide therapy, then the necessary risk and cost-benefit analysis will be feasible. In the interim, the American Thyroid Association concludes that:

1. Potassium iodide in an appropriate dosage form (130-mg scored potassium iodide tablet or as an oral solution) should be manufactured in sufficient quantities to fill anticipated needs if its use is required.

2. The projected absorbed dose of 10 to 30 rad recommended by the National Commission on Radiation Protection and Measurement[4] as the threshold for the institution of iodine blockade in the event of a reactor accident is overly conservative. Based on available data, it seems unlikely that clinically significant thyroid disease would result from individual

thyroid exposure of less than 100 rad.

provide an added measure of protion for children and pregnant women, a radiation dose of 50 rad to the thyroid is suggested as a threshold for iodine blockade for this group.

3. Although distribution of potassium iodide is not recommended at this time, advance planning for possible distribution of potassium iodide may be advisable. Because of the complexity of the problems of distribution of medication to a large population, a national task force of appropriate specialists should be appointed to develop alternate distribution strategies for consideration.

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(DRAFT BY PETER CRANE)

MEMORANDUM FOR: The Commissioners

FROM: Hugh L. Thompson, Jr.
Deputy EDO

SUBJECT: DIFFERING PROFESSIONAL OPINION
ON STOCKPILING POTASSIUM IODIDE

As you know, the staff has under review a differing provessional opinion filed by Peter Crane of the Office of the General Counsel. That DPO made essentially two points: (1) that the cost-benefit analysis which the staff performed on KI in the early 1980's was flawed, and (2) that in 1983, there were inaccuracies in the information provided by the staff to the Commission and the public on the medical significance of radiation-caused thyroid abnormalities if and when they do occur.

I have had the opportunity to review the report of the panel convened to review Mr. Crane's DPO, as well as his comments on the report. My initial review indicates that the cost-benefit analysis relied upon by the Commission in the 1984 time frame did in fact contain flaws, and that it seriously overstated the ratio of costs to benefits of a KI program. It also appears that the information provided to the Commission and the public regarding the consequences of radiation-caused thyroid abnormalities was deficient in several respects.

The fact that the analysis performed in the early and mid-1980's may have been flawed does not, of course, mean that the result reached -- i.e., a recommendation that stockpiling of potassium iodide is not worthwhile -- is therefore necessarily incorrect. We are not yet in a position to make that judgment. However, we are conscious that the NRC is in the position of have provided information to states, localities, and other federal agencies -- information on which those entitites may well have relied for their own determinations on the desirability of stockpiling KI -- that may be deficient in important respects. The cost-benefit analysis is in fact referenced in the Federal Government's current Policy Statement on potassium iodide.

We are aware that because of recent interest in the potassium iodide issue in other areas of the Federal Government, the Centers for Disease Control will shortly be coordination a new examination of the matter. The question now facing the Commission is the position that the NRC should take publicly in the interim. We recommend that the Commission be straightforward about the problems identified in the agency's past handling of the potassium iodide

question. Under this approach, a brief notice in the Federal Register would state that the Commission has become aware of deficiencies in its earlier analysis; is currently reexamining its position in light of new information; recommends that its earlier guidance on the potassium iodide issue be regarded as in abeyance pending further guidance from NRC; and urges interested parties to look to the forthcoming Centers for Disease Control Study for additional guidance on this issue.

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

APR 16 1990

MEMORANDUM FOR: Chairman Carr
Commissioner Roberts
Commissioner Rogers
Commissioner Curtiss
Commissioner Remick

FROM: James M. Taylor
Executive Director for Operations

SUBJECT: NRC POSITION ON POTASSIUM IODIDE: DIFFERING PROFESSIONAL OPINION

This memorandum provides the Commission with information on the status of the Differing Professional Opinion (DPO) regarding the stockpiling of potassium iodide as a protective measure for radiological emergency. The DPO addressed two basic points: 1) that the cost-benefit analysis contained flaws and omissions, and 2) that inaccurate information was provided to the public and the Commission on the significance of radiation-caused thyroid abnormalities. The DPO suggested prompt withdrawal of NUREG/CR-1433, "Examination of the Use of Potassium Iodide (KI) as an Emergency Protective Measure for Nuclear Reactor Accidents;" notification of States, localities, other federal agencies and the public of the flaws and omissions in the cost-benefit analysis; and affirmative steps be taken to ensure potassium iodide is stockpiled for possible emergencies.

After the DPO was filed on July 7, 1989, the DPO review panel met with the submittor, Mr. Peter Crane on June 24, 1989, to clarify points in the DPO. Subsequent to the meeting, the DPO review panel compiled additional information and prepared a simplified cost-benefit analysis incorporating the new information. The findings and recommendations of the DPO review panel were documented in a memorandum dated December 14, 1989. The results of the cost-benefit analysis differed from the results of the previous analysis in that the previous analysis overstated the ratio of costs to benefits of a potassium iodide program. However, the results still indicated stockpiling of potassium iodide is not cost beneficial. Additionally, the report indicated the panel's strong conviction that potassium iodide has a very limited efficacy as a public protective measure. The panel felt that this is not only due to the fact that it is useful for only one organ, one nuclide of interest and one exposure pathway, but also because its efficacy is dependent upon its being available either before or within a few hours after exposure. The DPO review panel recommended the current Federal guidance not be changed, and the information developed as a result of pursuing the DPO be transmitted to the States and other interested Federal agencies for their information.

By memorandum dated January 4, 1990, Mr. Crane responded to the DPO review panel report. Mr. Crane stated that although the panel performed a cost-benefit analysis, it was not the entire point of the DPO. The crux of the DPO was that the information on potassium iodide given to the Commission and the

public in 1983 (in part the basis for the Commission decision), was misleading and should be corrected by publishing the latest analysis. Additionally, Mr. Crane discussed other areas he felt were not addressed by the DPO review panel. Namely, that the 1983 report did not make clear that 4% of the accident-caused nodules would be fatal (as assumed in WASH-1400).

By memorandum of March 15, 1990, the responsible office director, Mr. Eric Beckjord, submitted his analysis of the DPO review panel report. As mentioned above, some aspects of the DPO were not resolved by the review panel. The staff is working on their resolution as suggested by Mr. Beckjord. In addition, Mr. Beckjord proposed to publish a supplement to NUREG/CR-1433 based on the new information complied by the DPO review panel.

We understand that the American Thyroid Association (ATA) asked the Federal Radiological Preparedness Coordinating Committee (FRPCC), of the Federal Emergency Management Agency (FEMA), to reexamine the issues in stockpiling KI. A Subcommittee of the FRPCC has been established to review the issue and is expected to begin review sometime this year. ATA made the same request to the Food and Drug Administration which conveyed the request to its Center for Disease Control (CDC) in Atlanta. CDC has agreed to evaluate the U.S. and foreign experience in KI stockpiling and distribution.

I have directed that NRR and AEOD, through their membership in the FRPCC, fully participate in this evaluation. I will keep the Commission informed. NRR will have the lead in reexamining whether it is warranted to stockpile KI in the vicinity of nuclear power plants. As part of the FRPCC Subcommittee, NRR will coordinate the NRC review with RES and AEOD on this issue.

Once all the above is completed, I will request that the Commission review the new analysis and decide whether the current policy should to be changed.

Original Signed By:
James M. Taylor

James M. Taylor
Executive Director
for Operations

cc: SECY
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OCA

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