

### Risk of severe allergic reactions from the use of potassium iodide for radiation emergencies

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Potassium iodide (KI) may be prescribed for widespread use in the event of a radiation emergency to prevent the uptake of radioactive iodide by the thyroid gland. The available literature was reviewed and expert opinion sought among members of the Adverse Reactions to Foods and the Adverse Reactions to Drugs and Biologicals Committees of the Academy to assemble evidenced-based conclusions regarding the risks of an allergic reaction to this therapy. This article describes the information leading to the following conclusions: (1) anaphylactoid reactions to radiocontrast media should not be considered evidence of KI allergy, (2) allergic contact dermatitis from iodine-containing antibacterial preparations should not be considered evidence of IgE antibody-mediated KI allergy or sensitivity, (3) IgE antibody-mediated allergy to seafood should not be considered evidence of KI allergy or sensitivity, and (4) physicians should ensure that persons are not allergic to inactive ingredients or components of the KI formulation prescribed. (*J Allergy Clin Immunol* 2004;114:1395-7.)

**Key words:** Potassium iodide allergy, radiocontrast, shellfish allergy

Potassium iodide (KI) has been suggested for use to prevent the uptake of radioactive iodide by the thyroid gland in the event of exposure or potential exposure in radiation emergencies.<sup>1,2</sup> On the basis of data from natural disasters in which radioactive iodine was released into the atmosphere, the rate of thyroid cancers after exposure was

#### Abbreviations used

FDA: Food and Drug Administration  
KI: Potassium iodide  
RCM: Radiocontrast media

increased as much as 100-fold. The effectiveness of KI as a specific blocker of radioiodide uptake is well established, and when used for prophylaxis in Poland after the Chernobyl accident, it reduced the rate of expected thyroid cancers.<sup>3</sup> Recommendations have been made to provide KI to persons living in proximity of nuclear power plants both for risks of accidental discharge or terrorism. KI is the same compound used, in smaller quantities, to iodize table salt. The US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research provides a document entitled, "Guidance Document: Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies" that discusses the particular recommendations for use of KI.<sup>1</sup> Specific information about Food and Drug Administration (FDA)-approved KI products is available at <http://www.fda.gov/cder/ob/default.htm>.

Although the FDA considers KI to be a safe and effective and concludes that the risks of KI are far outweighed by the benefits for prevention of thyroid cancer in susceptible individuals, specific cautions are given as follows: "Short-term administration of KI at thyroid blocking doses is safe and, in general, more so in children than adults. The risks of stable iodine administration include sialadenitis (an inflammation of the salivary gland, of which no cases were reported in Poland among users after the Chernobyl accident), gastrointestinal disturbances, allergic reactions and minor rashes. In addition, persons with known iodine sensitivity should avoid KI, as should individuals with dermatitis herpetiformis and hypocomplementemic vasculitis, extremely rare conditions associated with an increased risk of iodine hypersensitivity."<sup>1</sup>

The purpose of this article is to discuss the risks of allergic reactions to oral administration of KI to persons with iodine sensitivity and allergic reactions to iodide. This report does not discuss additional issues of thyroidal and extrathyroidal adverse reactions. Several terms regarding

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adverse reactions to iodine and iodide are used in the literature, sometimes without precise definitions. The term *allergy* is typically used to describe a specific adverse immune response to (usually) a protein, more specifically an IgE antibody response. In a typical allergic reaction, the target protein binds to previously formed IgE antibodies specific to the protein. These IgE antibodies are bound to high-affinity IgE receptors on mast cells/basophils. This binding of protein to IgE results in aggregation of high-affinity IgE receptors, the transduction of cellular signals, and the release of mediators such as histamine that result in clinical symptoms (eg, anaphylaxis). *Anaphylactoid* reactions occur when similar mediators are released through mechanisms other than through IgE antibodies. There are no studies to demonstrate IgE antibodies to small molecules or salts such as iodine or iodide. *Sensitivity* is a term usually used to refer to nonimmunologic adverse events. *Hypersensitivity* is a term usually used to indicate a response that is abnormal and out of proportion with expected adverse reactions, and the term is sometimes used to imply an immune basis for the reaction (of a variety of types such as cell-mediated, IgG antibody-mediated).

## IODINE ALLERGY AND RADIOCONTRAST MEDIA

Radiocontrast media (RCM) containing organic iodine may cause adverse reactions such as urticaria, angioedema, bronchospasm, laryngospasm, and shock. Several studies and a previous position statement indicate that these reactions are not attributable to specific immune responses (eg, IgE antibodies) to iodine, and although the exact mechanism is unknown, it is apparently related to the high osmolarity of these agents (lower-osmolar preparations are less likely to cause reactions).<sup>4-6</sup> Thus, such reactions are anaphylactoid in nature. Several studies indicate a higher risk of reactions to high-osmolar radiocontrast agents among persons with allergic disorders such as asthma, allergic rhinitis, and food allergy.<sup>6-8</sup> There is an apparent concern about seafood allergy in relation to an increased risk of reactions on the basis of the higher content of iodine in fish.<sup>9</sup> However, the risk of reactions to RCM was similarly elevated (approximately a 3-fold relative risk compared with average) for persons with allergy to egg, milk, or chocolate,<sup>6</sup> indicating that a general atopic disposition, rather than an iodine-specific reactivity, accounts for the increased incidence of reactions in this subgroup.<sup>6-8</sup> Thus, reactions to RCM should not be construed as an indication of an IgE antibody-mediated iodine allergy.

## IODINE SENSITIVITY AND TOPICAL ANTIBACTERIAL TREATMENTS

Topical antibacterial preparations containing iodine (povidone-iodine) sometimes cause allergic contact dermatitis or irritant reactions. Patients with allergic contact dermatitis appear to respond to the povidone-iodine

component but not to potassium iodide solution on patch testing.<sup>10</sup> There is 1 case report of anaphylaxis to povidone-iodine applied intravaginally,<sup>11</sup> but the component of the preparation that caused the reaction was not determined (eg, not necessarily a reaction to iodine). Thus, contact dermatitis caused by topically applied iodine-containing antibacterials does not indicate an allergy to iodine. Anaphylaxis to these preparations is exceedingly rare and not proven to be caused by iodine.

## IODINE IN RELATION TO SEAFOOD ALLERGY

As indicated, seafood may contain iodine. However, IgE antibody-mediated seafood allergy has never been attributed to iodine, but rather to specific proteins in fish and shellfish (eg, parvalbumin, tropomyosin) that also do not contain iodine.<sup>12</sup> Thus, fish or shellfish allergy does not indicate a sensitivity or allergy to iodine.

## OTHER POSSIBLE ADVERSE IMMUNOLOGIC REACTIONS FROM TREATMENT WITH KI

As indicated in statements from the FDA quoted previously, certain adverse effects that appear to have an immunological basis (though perhaps not directly related to an immune response to KI itself) have occurred in patients treated with KI preparations. Sialadenitis appears to be an idiosyncratic, possibly metabolic reaction, and no cases were observed during widespread use of KI in Poland (about 10.5 million children and 7 million adults treated).<sup>3</sup> Iododerma is a rare acneiform or proliferative/ulcerative eruption related to iodide ingestion that is reversible and appears to be more common among persons with renal insufficiency, multiple myeloma, lymphoma, polyarteritis nodosa, arthritis, and hypocomplementemic urticaria/vasculitis.<sup>13-17</sup> The mechanism for this reaction is unknown but is postulated to result from nonspecific immune stimulation.<sup>18</sup> No such cases were specifically reported in the experience in Poland, but 1% of children and 1.25% of adults had a rash that was minor.<sup>3</sup> The extrathyroidal side effects reported from Poland included headache (0.2% of children; 0.7% of adults) and shortness of breath (0.1% of children; 0.6 of adults) but no control incidence values were determined.<sup>3</sup> Two adults with chronic obstructive pulmonary disease and previous known iodine sensitivity (specific problem not listed) developed respiratory distress, a problem reported elsewhere.<sup>19</sup> No episodes of anaphylaxis were reported.

Current approved formulations of KI for prophylaxis of radiation emergencies are not known to contain allergens, but care should be taken to be sure that individuals with allergies are not known to be reactive to the inactive ingredients or components of the formulation prescribed.

## CONCLUSION

Anaphylactoid reactions to RCM should not be considered evidence of KI allergy. Allergic contact dermatitis

from iodine-containing antibacterial preparations should not be considered evidence of IgE antibody-mediated KI allergy or sensitivity. IgE antibody-mediated allergy to seafood should not be considered evidence of KI allergy or sensitivity. Physicians should ensure that persons are not allergic to inactive ingredients or components of the KI formulation prescribed.

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