Safe Handling of Radioiodinated Solutions

Barbara Y. Howard

University of Virginia, Charlottesville, Virginia

An incident of personnel contamination with radioiodine prompted a re-examination of procedures for handling radioiodinated solutions. Previous experiences with the handling of radioiodine and a summary of the chemical behavior of iodine are provided and are used to formulate recommendations for the safe handling of radioiodinated materials.

Radioiodinated compounds have been part of the practice of nuclear medicine since its beginnings (*1, 2*). Recently, the increasing consciousness of radiation safety hazards has prompted us to begin surveillance of radionuclide shipments. Such surveillance has often detected contamination of shipments of therapeutic radioiodine, and in one instance this contamination was of serious magnitude. In many institutions handling practices in the laboratory are inadequate for the proper containment of radiation from radioiodine, and necessitate an examination of the properties of this especially hazardous agent. A set of rules for handling radioiodinated materials has been developed in our laboratory to prevent future incidents and as a guide to others.

Experience With Iodine-Containing Solutions

The manufacturers of radiopharmaceuticals deal with large quantities of iodine in solution, and several incidents of radiation exposure have been reported. One manufacturer was cited for two separate incidents in which an employee contaminated himself while filling vials under nonstandard conditions (*3*). Estimated amounts in his thyroid after the exposures were 0.4 μCi and 0.3 μCi.

Stricter control over the acceptance of radioactive materials has been mandated at our institution since our Radiation Safety Committee began discussions with the Nuclear Regulatory Commission (NRC) regarding the renewal of the Broad License. As a result, all shipments are wipe tested by personnel at a central receiving office at our reactor facility. Several shipments of ^{131}I have been found to have radioactivity on the outside of the lead container for the iodine bottle. This contamination has been noted on containers from both manufacturers from whom our therapeutic iodine is procured. One manufacturer's excuse is that it is very difficult to maintain a clean preparation because of the volatility of iodine (*4*).

We noted one instance of the effects of poor handling practice of radioiodine shipments. An order had been placed for 150 mCi of ^{131}I-sodium iodide, which arrived in two lots at the same time. The manufacturer shipped the material sealed in tin cans; the receiving personnel had wipe tested the outside of the tin cans and left them for assay by the nuclear medicine personnel. The cans were opened and the 100-mCi lot assayed for immediate use. It seemed in good order. The 50-mCi lot assayed at 27 mCi. A technologist checked the packing material from the tin can and found it to be radioactive. His hands were subsequently found to be contaminated. More important, when his thyroid was checked by the bioassay method discussed below, it contained 0.5 μCi of radioiodine. He was treated with Lugol's solution, and the packing material was encapsulated and held for decay. The difference between the manufacturer's stated amount of 50 mCi and our laboratory's first assayed amount of 27 mCi should have warned us of a potential problem.

Biochemists (*5*) at the Medical College of Virginia report finding that ^{131}I tagged to hormones contained in a water solution appeared in the airspace over the solution. They found that as much as 22% of the iodine was lost in two days. This escape of iodine can produce a distortion of experimental results as well as a hazard to personnel.

Chemistry of Iodine

In laboratory and clinical uses, the volatile iodine species is the elemental diatomic form I_2, which is responsible for contamination via airborne routes. Elemental iodine exists as an easily volatilized dark grey solid which sublimes as a diatomic violet gas, I_2. Iodine is slightly soluble in water, forming a brown solution. The solubility is 1.33×10^{-3} moles per liter under one atmosphere of iodine (*6*). In everyday work, solutions are under iodine pressure only when the vessel is sealed. When the cap is removed, the gas in the air over the solution is free to exchange with the surrounding air and to

For reprints contact: B. Y. Howard, Dept. of Radiology, University of Virginia, Charlottesville, VA 22901.

contaminate it. In addition, the iodine in the solution will begin to be exhausted into the air. Agitation of the container and heating the solution speed up this process.

The special hazard connected with the several chemical forms in which radioiodine is used in nuclear medicine is the ease with which the iodine can be oxidized to elemental iodine. Therapeutic iodine solutions consist of sodium iodide (NaI). The iodide ion is the anion of a strong acid and is fully ionized in water solution. It can be oxidized to iodine by atmospheric oxygen in acid solution:

$$4I^- + O_2 + 4H^+ \rightleftharpoons 2I_2 + 2H_2O.$$

The reaction is catalyzed by light, and iodide solutions are therefore usually kept in dark bottles. Atmospheric carbon dioxide dissolves in water to form a mildly acidic solution, creating the condition for air oxidation. The glass of therapeutic iodine bottles is coated to prevent any reaction of the iodide with the glass and to prevent shattering.

Losses of iodide from solution are important enough to be mentioned in analytical chemistry texts (*7*). There are several ways to prevent this escape of iodide and iodine, though their application in nuclear medicine is limited. For example, the solution of sodium iodide can be made basic to prevent the oxidation reaction, but this is not done to therapeutic solutions. The presence of a great amount of iodide ion causes the equilibrium in the reaction

$$I_2 + I^- \rightleftharpoons I_3^-, K = 725,$$

to be shifted to the right. The formulation of Lugol's solution is based on this reaction, but note that one can smell the odor of I_2 over Lugol's solution. Since the presence of carrier iodine would interfere with the desired effects of therapeutic solutions, this reaction cannot be used to any advantage. However, the presence of a reducing agent in iodide solution helps to prevent the oxidation reaction. The *National Formulary* allows 500 mg/liter of sodium thiosulfate in potassium iodide solutions as a reducing agent (*8*), but only some therapeutic radioiodine solutions contain it.

In the production of radiopharmaceuticals and compounds for in vitro use, iodine may be attached to many substances either by an exchange reaction or by substitution across a bond. The chemistry of these reactions includes the oxidation of iodide ion to monatomic elemental iodine, often called "nascent" iodine, which reacts with the substance to be tagged. The iodine is attached by a covalent bond. If the iodine becomes dissociated from the tagged material, it appears in solution as iodide ion. Once this occurs, the iodide ion is subject to oxidation and may escape from the solution.

The above discussion of the chemistry of iodine provides evidence of the facility with which iodide ion is oxidized to iodine and the difficulty of keeping that iodine in solution. It is these two properties, together with the avidity of the thyroid for iodine, that make radioiodine-containing solutions especially hazardous.

Recommendations

Very careful handling of radioiodine-containing materials is necessary. There are some specific rules which may serve as a guide to other laboratories to obviate unnecessary exposure to radioactivity.

Open packages in hood. Therapeutic iodide solutions should be opened in a hood with a good flow of air and no direct path from the open bottle to the respiratory system. In a hood system, filtration will not remove I_2 from the air stream unless a cooled activated charcoal filter is used (*9*). When larger amounts of iodine, such as are emitted by nuclear reactors, are run through ducts, the iodine seems to precipitate on the walls of the duct and revaporize, moving along the duct. It is most important to have good flow of air to protect personnel. The protection of the public must also be assured in the design of the duct outlet and the fan housing.

Handling and wipe testing. Gloves should be worn when handling a radioiodine container, even if the bottle is not to be opened. Therapeutic iodine should be shipped in closed containers, such as tin cans, so that any material that leaks out of the bottle cannot escape beyond the can. The outside of the package should be monitored to detect a spill that has passed beyond the lead shield. Careful procedures should be followed when the container or tin can is opened so that any volatile material inside is not immediately inhaled by the opener. The package should be wipe tested and the results recorded.

Bioassay of personnel. The NRC now requires the bioassay of personnel for the presence of iodine. In this laboratory the thyroid glands of all persons handling more than 1 mCi of radioiodine are counted and compared to an iodine capsule in the standard uptake procedure. The estimated amount of radioiodine in the thyroid is calculated. The results of bioassay should be recorded.

All iodine handlers should be educated as to the hazards of the material in the form they are using and the potential for I_2 escape. Iodine-containing materials should be treated as if they contained a rather easily liberated poisonous gas.

References

1. Hertz S, Roberts A, Evans RD: Radioactive iodine as indicator in study of thyroid physiology. *Proc Soc Exp Biol Med* 38:510–513, 1938

2. Hamilton JG: Rates of absorption of radioactive isotopes of sodium, potassium, chlorine, bromine and iodine in normal human subjects. *Am J Physiol* 124:667–678, 1938

3. Cramer EN: Safety-related occurrences reported in April–May 1969. *Nucl Saf* 10:436–439, 1969

4. McDowell WB: Personal communication

5. Bogdanoff EM, Strash AM: Radioiodine escape is an unexpected source of radioimmunoassay error and chronic low level environmental contamination. *Nature* 257:426–427, 1975

6. Kleinberg J, Argersinger WJ, Jr, Griswold E: *Inorganic Chemistry*. Boston, Heath, 1960, pp 456–485

7. Kolthoff IM, Sandell EM: *Textbook of Qualitative Inorganic Analysis* 3rd ed. New York, Macmillan, 1952, pp 587–588

8. *National Formulary*, 13th ed. Washington, American Pharmaceutical Association, 1970, p 575

9. White PAF, Smith SE: *High-Efficiency Air Filtration*. London, Butterworths, 1964, pp 199–208

Answers to Survey Questionnaire

These are the answers to questions 11–35 of a questionnaire which appeared as an appendix to the paper "Effects of technician training levels on Quality of Diagnostic Services in the Nuclear Medicine Department," by Wanda M. Hibbard, in the Dec. 1975 (Vol. 3, No. 4) issue of the *JNMT*.

11-C	20-C	28-C
12-C	21-C	29-C
13-D	22-B	30-A
14-C	23-D	31-C
15-A	24-C	32-C
16-D	25-D	33-D
17-C	26-B	34-C
18-C	27-C	35-A
19-B		

—submitted by Wanda M. Hibbard