Preparation of Sterile Xenon-133 in Saline for Tissue Perfusion Studies

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A simple, inexpensive method of obtaining Xe-133 in sterile saline is presented. The method uses commercial xenon ampules supplied for pulmonary ventilation studies. As much as 10% of the gas activity can be recovered per aliquot by cooling the saline to 4°C. The specific activities obtained are adequate for most tissue perfusion studies.

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Tissue perfusion measurements derived from the clearance of radioxenon injected in saline are useful in the investigation of several clinical problems including: (a) presurgical assessment of limb amputation level (*1–3*); (b) the evaluation of peripheral vascular disease (*4*); (c) evaluation of cerebral blood flow (*5*); (d) diagnosis of strangulated small bowel (*6*); and (e) assessing placental perfusion (*7*).

Radioxenon has several advantages as a tracer for measuring regional blood perfusion: predictable tissue clearance proportional to perfusion over a broad range of flow rates; rapid clearance from the body through the lungs, resulting in minimal recirculation; a short biologic half-time and low radiation exposure; simple instrumentation required; and universal availability. Despite these advantages, at least one major obstacle prevents wider use: namely, high cost.

Commercially prepared xenon-133 in sterile saline is currently available at about nine times the cost of the gaseous form. High cost prompted us to seek a simple, inexpensive method of producing this solution with facilities available in most nuclear medicine laboratories. Previous methods of preparation have included the use of reservoirs with large amounts of activity, specially prepared xenon vials, and elaborate dispensing systems (*6,7*).

Xenon-133 gas is currently available at less than \$1.00 per mCi in small vials containing 10–30 mCi of activity. Parenteral, nonangiographic perfusion studies are easily performed with 50–500 μCi (*1,2,4*) and studies requiring intravascular injection can be performed with 2–5 mCi (*7,8*).

METHODS

Commercial xenon-133 used for ventilation lung imaging was supplied as 2-ml glass vials with black-rubber stoppers. At the time of study, they contained 0.16 to 19.8 mCi of activity. To these vials were added 1-ml aliquots of sterile saline. To test the conditions of maximum solubility, saline was added at room temperature, 27°C (N = 7) and at 4°C (N = 6), and degassed saline at room temperature (N = 6) was added to the vials. Saline was degassed before use by boiling sterile saline 10 min. After initial tests to determine optimum equilibration time, approximately 15 min were allowed for equilibrium between xenon and saline to occur.

After equilibrium was established, 0.3 ml of the xenon in saline was removed from each of the vials using a saline-primed 1-ml tuberculin syringe. Care was taken to remove all air from the syringe to prevent release of the xenon gas from solution. All samples were measured in a dose calibrator. Sterility was tested using thioglycolate broth and incubating for five days at 40°C. Pyrogens were tested using a *Limulus* kit.

RESULTS AND DISCUSSION

The percent activity dissolved in nondegassed room-temperature saline did not vary significantly from degassed room-temperature saline: 5.7% ± 1.4 and 5.5% ± 1.4, respectively. However, the samples using cold, refrigerated saline demonstrated markedly increased solubility: 10.5% ± 1.5 ($p < 0.02$). This result is not surprising since the solubility of a gas is proportional to pressure and inversely proportional to temperature (*9*). Serial 0.1-ml aliquots, withdrawn at 1, 5, 10, and 15 min following addition of saline to the ampules, demonstrated that the gas/saline equilibrium is reached between 10 and 15 min. All samples were found to be sterile and pyrogen free.

Many of the samples tested were vials that had decayed to activities too low for use in ventilation studies. Since the frequency of ventilation lung studies in any clinical laboratory is unpredictable, usable vials are generally on hand. When their contents decay, the vials can be saved and reserved for perfusion studies. Many tissue perfusion studies can be performed with 50–100 μCi. At 10% recovery, a vial containing 1–2 mCi is sufficient for this purpose.

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For larger quantities, xenon can be obtained by repeated harvesting from the same vial as the remaining gas activity equilibrates with new charges of cold saline. In studies that require intradermal and subcutaneous injections, small volumes are essential and vials containing higher activity must be used. The total time required for preparation of the xenon in saline by this method is about 20 min. Limulus testing can be performed concurrently. Results are available after an hour of incubation.

We did not test the dissolution time of xenon gas from saline except to measure syringe activity with time. In none of the syringes tested was there measurable loss of activity over 36 hr, other than by decay. In clinical applications we have let the syringes come to room temperature before injection. Residual activity remaining after injection was always less than 10%. We believe that during the procedure times encountered in clinical situations, dissolution of xenon from saline is negligible. Furthermore, in subcutaneous and intramuscular injections, a reference site in healthy, well-perfused tissue is usually chosen to compare perfusion to the test site. Thus the procedure provides a control whereby the injection of a bubble of xenon gas can be detected by a biexponential curve with the prolonged phase attributable to gaseous xenon. We have never experienced this mishap.

In summary, a simple, expedient and inexpensive method for producing xenon in cold saline exists for almost all nuclear medicine labortories. Specific activities adequate for most perfusion studies can be achieved without special apparatus. Because solution can be achieved so quickly (approximately 15 min) the need for specially ordered, expensive, commercial xenon in saline is obviated.

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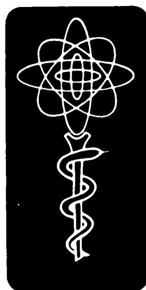

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