nm/CONCISE COMMUNICATION

SYSTEM FOR HANDLING AND DISPENSING ^{133}Xe

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A handling and dispensing system has been developed which is capable of simultaneously dividing the contents of an ORNL shipment of ^{133}Xe into both a gas and an aqueous form. The ratio of gas to aqueous xenon is adjustable. A high transfer efficiency is achieved and high specific activity solutions are routinely available. Transferring and dispensing of curie quantities of radioactivity is relatively uncomplicated and the radiation dose to the operator during these procedures is small.

Xenon-133, mixed with air or dissolved in sterile saline, is now widely used for a variety of clinical investigations. As a radiopharmaceutical, xenon is available from several commercial suppliers, but, while the convenience of having it delivered in this form is considerable, the cost is high. As a radiochemical, ^{133}Xe gas is readily and inexpensively obtained from Oak Ridge National Laboratory (ORNL). Techniques have therefore been developed by many laboratories for handling curie quantities of this radioisotope and for dispensing individual doses, as gas and in saline, for administration to the patient (*1–7*). But no single reported technique is considered entirely satisfactory since none can directly provide both xenon/saline solution of high specific activity and xenon/air mixture required for current clinical and experimental animal applications.

This paper describes a system for handling and dispensing ^{133}Xe gas which facilitates division of the contents of either a breakseal ampoule or of an ORNL cylinder into gas and aqueous solution fractions. The gas fraction is transferred into a 300-ml storage cylinder which is subsequently pressurized with air, shielded, and connected through a metering valve to a spirometer. The fraction of xenon required in solution is transferred to a specially constructed stainless steel syringe which is then filled with sterile, pyrogen-free water or saline. Dispensing of individual patient doses is simple, rapid, and involves no measurable radiation exposure to the staff.

By an appropriate choice of transfer fraction between gas and aqueous solution, and of aqueous solution volume, specific activities greater than 60 mCi/ml are readily obtained.

The cost of prepackaged or other radiopharmaceutical forms of ^{133}Xe varies. However, we estimate that an establishment which uses more than 100 mCi/week on a semiregular basis can offset the construction of the present system (exclusive of vacuum pump and gage) within 6 to 12 months through use of ORNL ^{133}Xe. Maintenance of the system is minimal.

MATERIALS AND METHODS

Apparatus. The transfer-dispenser system has three major components: (A) a transfer device, (B) a special storage syringe for the xenon solution, and (C) a gas storage cylinder for the xenon/air mixture.

The transfer device (Fig. 1) basically comprises a 4-in.-diam, 6-in.-long cylinder fitted with a movable piston, the cylinder and piston being O-ring coupled. The piston is actuated by a ½-in. shaft which exits the cylinder through a vacuum O-ring seal.

The storage syringe (Fig. 2) has a volume of approximately 60 ml. Since it must maintain a vacuum during transfer procedures, a sliding O-ring seal is employed between the piston and syringe body. In order that small quantities of solution may be dis-

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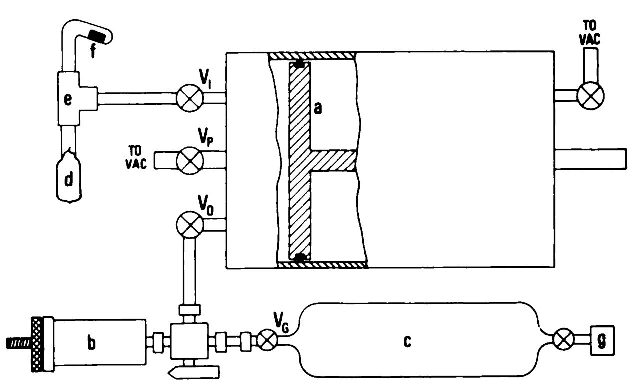

FIG. 1. Transfer device with syringe and cylinder attached: (a) piston, (b) storage syringe, (c) gas cylinder, (d) xenon ampoule, (e) O-ring Tee, (f) metal break-seal, (g) pressure O-ring connector, (V_I) inlet valve, (V_O) outlet valve, (V_P) pumping valve, (V_G) gas cylinder inlet valve.

pensed, the piston is driven by a fine lead screw. The syringe is permanently joined to one of the two side ports of a 0.125-in.-orifice three-way ball valve*; vacuum O-ring connectors are fitted into the remaining ports. As shown in Fig. 2, the valve may be set in three positions: (A) fill-dispense, in which the center port and syringe are connected, (B) off, in which all ports are blanked off, and (C) flush-dilute, in which the center and remaining side ports are connected.

The xenon/air storage system consists of a 300-ml stainless steel gas cylinder with shut-off valves in both ends. One valve is fitted with a vacuum O-ring connector through which the xenon is transferred into the cylinder. The remaining valve is attached to a pressure O-ring connector which serves two purposes: (A) by coupling to a mating piece the cylinder can be pressurized, with breathing air, to 100–150 psi, and (B) for attaching the gas cylinder to the spirometer.

Operation. After autoclaving, the syringe is assembled, set to the required volume, and attached to the output valve of the transfer device through the ball valve center port (Fig. 1). The gas cylinder is attached to the remaining port. The xenon ampoule is connected to the inlet valve through an O-ring Tee-connector; the remaining arm of the Tee is attached to a glass side-arm containing a metal break-seal.

With the system assembled, the inlet and outlet valves are opened and the system pumped out, the ball valve being rotated such that the syringe and gas cylinder are both evacuated. When a good vacuum has been obtained (20 microns achieved in 30 min), the ball valve is set in its fill-dispense position, the transfer volume (volume on transfer side of piston) reduced to a minimum and the pumping valve closed. Xenon is now released into the system. Complete retraction of the piston allows more than 95% of the xenon to enter the transfer volume. The inlet valve is then closed, and by an appropriate reduction of the transfer volume the desired fraction of xenon is transferred into the syringe. By rotating the ball valve to the flush-dilute setting and reducing the transfer volume to a minimum, the remaining fraction enters the gas cylinder.

Most of the xenon remaining in the transfer system may be added to the contents of the gas cylinder by repeating the procedure outlined above. The gas cylinder valve is then closed, the ball valve set to its off position, and the syringe and cylinder removed. The cylinder is subsequently pressurized and attached to the spirometer.

The storage syringe is then filled with either saline or water. (We have found it preferable to dissolve the xenon in sterile, pyrogen-free water since higher aqueous-xenon concentrations may be achieved and the corrosive effects of saline avoided. The xenon/water solution can be diluted with saline at its time of use. If saline is used to fill the syringe, special attention should be given to cleaning the syringe components, and occasionally, the O-rings should be replaced.) Female Luer-lock adapters joined to ¼-in. stainless steel tubes are placed in the two available ports. A sterile syringe containing water or saline is attached to the center port and an empty sterile syringe to the remaining port. With the ball valve in the flush-dilute position, the air is removed from the valve orifice. Changing to the fill-dispense position allows water or saline to completely fill the metal

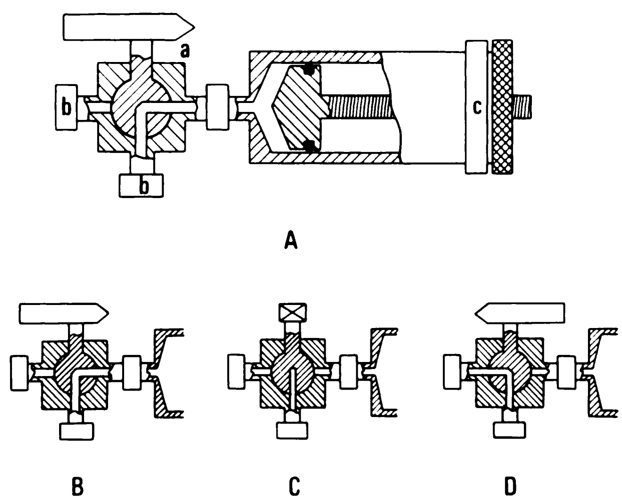

FIG. 2. (A) storage syringe: (a) three-way ball valve, (b) vacuum O-ring connectors, (c) lead screw retraction mechanism. (B) fill-dispense. (C) off position. (D) flush-dilute.

* Whitey Research Tool Co., Emeryville, Calif.

storage syringe. The center-port glass syringe is removed and the system is ready for dispensing.

With this device we find it possible to recover about 99% of the ampoule xenon. To date, xenon/water concentrations of 60 mCi/ml have been routinely obtained; however, higher concentrations could readily be achieved if required. The part of the operation beginning with assembly of the syringe and ending with filling of the syringe with water requires approximately 45 min excluding pumping time.

Dispensing. Following the fill procedure, we find that between 12 and 24 hr is required for the xenon concentration in the aqueous solution to reach its expected level. (The use of two storage syringes insures a continuous xenon supply.) To dispense, a glass syringe partially filled with sterile saline solution is placed in the center-port. In the flush-dilute position the saline solution together with the residual air is forced into the side syringe. On changing to the fill-dispense position, the required xenon is dispensed. If the xenon solution is to be diluted, the ball valve is returned to the flush-dilute position, and saline solution from the side syringe added. When not in use, the ball valve is placed in the off position and a sterile plug fitted in the center Luer-lock adapter. Generally, the side-port syringe is left in position.

Radiation safety. Both the storage syringe and cylinder are enclosed in lead shields (¼ in. offers adequate protection). During a transfer procedure the syringe is contained within its shield but the cylinder is unshielded. The maximum radiation level observed at a distance of 1 meter from the apparatus during a transfer procedure is 1 mR/hr when 1 Ci of ^{133}Xe is transferred. Radiation exposure to the operator extends typically for a period of 5–8 min. Dispensing of individual patient doses (1–2 mCi) typically requires about 1 min and involves no direct handling of any unshielded activity. Glass syringes are used routinely for dispensing and these are placed inside lead tubes for the handling required to inject the xenon solution.

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