Title

HEALTH PHYSICS ASPECTS OF IRRADIATION OF LARGE ANIMALS AND HUMAN BEINGS WITH CURIE QUANTITIES OF INTERNALLY ADMINISTERED ISOTOPES

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Publication Date

1963-04-03

UCRL-10215 Rev.

University of California

Ernest O. Lawrence Radiation Laboratory

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Submitted to Health Physics

UCRL-10215 Rev.

UNIVERSITY OF CALIFORNIA

Lawrence Radiation Laboratory
Berkeley, California

Contract No. W-7405-eng-48

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ABSTRACT

Total-body irradiation techniques using massive doses of chelated Y^{90} administered intravenously in dogs, monkeys, and man for the selective destruction of lymphatic tissue have been developed by biomedical research personnel at Lawrence Radiation Radiation Laboratory, Berkeley. Purchase cost and assurance of purity necessitate Y^{90} production at the site from a multicurie Sr^{90} source.

Health physics problems included design and construction of shielded and remotely operated Y^{90} extraction equipment, equipment for preliminary animal experimentation, multipurpose containers for efficient and safe utilization of curie quantities of beta emitters, enclosures for dogs and monkeys during isotope infusion in the hundreds of millicurie range, and enclosures for long-term maintenance of these animals. Provision was made for simple decontamination and waste processing. An enclosure was designed to comfortably house a human patient and the medical equipment for his treatment. This enclosure provides adequate shielding for the attending medical team, yet permits rapid access in case of a medical emergency. Methods were also developed to prevent spread of radioactive contamination following transfer of the patient to a pressurized reverse isolation hospital room.

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I. INTRODUCTION

For the past several years researchers at the Donner Laboratory of Medical Physics, Lawrence Radiation Laboratory, Berkeley, have been developing techniques for the selective destruction of lymphatic tissue by delivering high doses of radiation internally. The method and its results are described elsewhere.[1] This paper deals with the Health Physics aspects of this program.

II. RADIOISOTOPE PRODUCTION

A. Component Parts of the Sr^{90} - Y^{90} Separation Equipment

There are three interconnected enclosures. These are: (1) the enclosure containing the Sr^{90} - Y^{90} source and the equipment necessary for the chemical separation of these isotopes, (2) an enclosure free of Sr^{90} contamination for the manipulation of the Y^{90} following its separation from the Sr^{90} source, and (3) an air-scrubber system for clearing acid fumes containing radioactivity from air exhausted from the other two chambers.

1. Sr^{90} - Y^{90} Separation Enclosure

Y^{90} is separated from the Sr^{90} - Y^{90} equilibrium mixture by modifications of the method used by Oak Ridge National Laboratory,[1] which utilizes the different solubilities of the isotopes in di-2-ethyl-hexyl-phosphoric acid in toluene and strong and weak acids.

The "milking" process requires a radioisotope enclosure of about 12 cubic feet. Remote tong operation through a 2-in. lead shield (Jr. Cave) is necessary because of the intensity of bremsstrahlung from the 80-100 Ci of beta emitter.

The major design considerations in setting up this process were as follows: (a) Due to the strong acid fumes involved, nonmetallic materials were used, where practicable, and all metal surfaces were coated with epoxy resin or Bisonite. (b) Each piece of equipment was remotely replaceable to minimize residual Sr^{90} contamination and glassware damage. (c) All equipment was mounted from above to allow the use of disposable vinyl floor coverings, and to permit floor storage of the Sr^{90} - Y^{90} source anywhere within the enclosure. (d) To minimize manual tong manipulations, the pieces of extraction equipment were located in an arc around an electrically driven central cone holder moving both vertically and horizontally. (e) A "close capture" acid fume condenser was provided, with a removable condensate flask and a scrounge pipette.

Equipment that required significant amounts of floor space (an electric heating mantle, the acid fume condenser, and the condensate flask) were located in the left rear corner. A pass-through port, reached with one tong, was installed in the right rear corner for access to the adjoining Y^{90} enclosure.

Radioactive waste in ice cream cartons is passed out the left side of the enclosure (by tongs) into an enclosed polyethylene bag on a hydraulically operated carriage. After a heat seal is made and cut through, the plastic bag is lowered into a 1-1/2-in. lead waste-transfer container, and removed to a waste packaging area. The bagging and sealing unit is attached to the 2-in. lead cave and shielded with 2 inches of brass. Figure 1 is a view of the unshielded Sr^{90} - Y^{90} separation enclosure.

2. Y^{90} Enclosure

The Y^{90} enclosure is arranged end-to-back of the Sr^{90} - Y^{90} enclosure, and is connected to it by an "airlock" chamber which is accessible by tong from each enclosure. It is divided into a large and a small section by an internal 1/2-in. - thick lucite wall in which is a tong operated door. The large section, about two-thirds of the total floor area, is used for make-up of assay aliquots, addition of the DTPA chelating agent, and preparation of the Y^{90}-DTPA for final transfer. Figure 2 shows the unshielded Y^{90} enclosure.

The smaller section is used for filling the isotope transfer container. This container (Fig. 3) is placed in the small section within its lucite primary transport shielding, and Tube 1 is passed through an aperture in the lucite wall into the large compartment. There it is fitted to a 30-cc capacity hydraulic pipette into which the desired quantity of Y^{90} solution has been drawn. Lines 2 and 3 are clamped. Line 4 is fitted to a syringe; upon withdrawal of the plunger and simultaneous depression of the control on the 30-cc hydraulic pipette, the Y^{90} solution is drawn into the jar. Lines 1 and 4 are heat-sealed and the isotope in its container is passed out of the enclosure.

3. Air Scrubber

In addition to the close-capture condenser in the Sr^{90} - Y^{90} enclosure, a separate air-scrubber unit within a lead shield is provided for removal of residual acid fumes in the air exhausted from the entire train of enclosures. This feature was found necessary in the early days of the project because condensed acid from an aqua regia ashing process damaged the "absolute" filter in the exhaust system. The air scrubber used is a standard type developed by the LRL Health Chemistry Department some years ago for recirculating enclosure atmosphere in heavy-element separation procedures.[2] The unshielded air-scrubber unit is shown in Fig. 4.

All enclosures are connected via the scrubber and standard filters to a standard exhaust system pulling 3 inches of water at the inlet manifold.

B. Performance

One trained operator using this equipment can produce a 75% (plus) yield of high purity Y^{90} in less than six hours. The radiation field in the operator's area in front of the Sr^{90} cave ranges from about 1 to 3 mr per hour, and is low-energy bremsstrahlung. Figure 5 is a general view of the Sr^{90} - Y^{90} enclosure train.

III. ANIMAL STUDIES

The use of radioisotopes in biological and medical research has been rapidly increasing from "tracer"-level quantities to curie quantities, presenting complex Health Physics problems. Major problems which confront the Health Physicist as well as the Bio-Med researcher are the need for radiation protection and the absolute confinement of radioisotopes during long term studies on animals.

To achieve a controlled high total dose of radiation delivered internally, the researchers have developed a recirculation procedure in which fluids containing the isotope are pumped through a pressurized system. Figure 6 is a schematic representation of the system used in pumping urine and fluids containing hundreds of millicuries of isotope solution from the bladder to an intraveneous catheter for the 6-hour irradiation procedure.

The use of chelated Y^{90} up to 500 mc in a single irradiation episode posed challenging problems for the Health Chemistry Department. These included design and fabrication of enclosures in which to irradiate dogs and monkeys, and enclosures in which to maintain the animals immediately following the irradiation procedure, and for periods up to six weeks or more. These facilities had to ensure absolute confinement of the radioisotope and still allow for medical care such as bone marrow transplantation, blood transfusion, antibiotic injections, routine blood sampling, and normal feeding. Also needed were facilities for long-term animal maintenance, techniques for processing high level contaminated biological waste, and a unit in which the physician could perform surgery or autopsy on highly contaminated animals.

An enclosure constructed of 3/4-in. plywood lined with vinyl sheeting, and having a 3/4-in. lucite viewing front with glove ports, was provided to house the animal during the 6-hour irradiation procedure. The enclosure contains a centrifuge well lined with 1/2-in. lead which holds a container for contaminated urine. A 19-1/2 by 14-1/2-in. oval passout ring is located in one end of the

enclosure. The anesthetized animal is suspended in a vinyl hammock during the period of irradiation. Typical experiments have produced a radiation field within the enclosure as high as 20 R per hour. Radiation at the outer surface of the enclosure has been from 1 to 6 mr per hour.

After eight hours (6-hour irradiation and 2-hour isotope removal periods) the animal is transferred to a completely enclosed metal animal cage, the holding enclosure. Figure 7 is a schematic representation of the connection for transfer of the animal. When the enclosures are brought together end-to-end, a large polyethylene sleeve secured onto an oval passout ring on each enclosure forms a sealed pass-through tunnel. A polyethylene bag inside the tunnel, secured only to the irradiation enclosure, is pulled into the holding enclosure into which the animal is then transferred. Working through glove ports in the holding enclosure, the researchers cut open the polyethylene bag and remove the animal. The bag is then folded and pulled back into the irradiation enclosure. The enclosures are moved apart about 24 inches and the polyethylene tunnel is sealed and cut, thus separating the two enclosures while maintaining absolute confinement of any loose isotope in the irradiation enclosure.

The holding enclosure is a suitable facility for housing a radioactive dog or monkey for an indefinite time. Figures 8, 9, and 10 illustrate the enclosures now in use. The primary cage is a standard metal dog or monkey cage available from many laboratory supply vendors. The cage is altered to provide a 24- by 18-in. vertical sliding door in one end, as seen in Fig. 8. The opposite end (Fig. 9) shows alterations for food and water pans and a 6- by 8-in. vertical sliding door. On each side of the cage two apertures were cut to allow access with box gloves. The gloves, shown clearly in Fig. 10, are protected from the animal by 1/8-in. metal shields. These are pivoted to the outside of the metal cage to allow semicircular travel. The glove port shields are controlled by a rod that protrudes through the outer lucite enclosure. Hinged from the inside top of the cage is a

"false" ceiling of 1/4-in. lucite with outside control, which can be lowered to restrain a monkey by squeezing it against one wall. The cage is supported on a 1-1/2-in. shoulder of the drain pan that forms the bottom of the outer enclosure.

The outer enclosure, constructed of aluminum framing and 3/4-in. lucite, is essentially a 50×30×40-in. glove box for isotope confinement. It is equipped with eight 8-in.-diameter glove ports to give the researcher maximum freedom of manipulation. One end of the enclosure (Fig. 8) contains a 19-1/2-in. by 14-1/2-in. plastic bag passout ring used in the transfer described above. Following transfer of the animal, the end is closed by a double O-ring double-plastic-bag seal and the steel inner door is closed. A 1/4-in. plywood cover over the passout ring protects the plastic bags. The opposite end (Fig. 9) has a 7-in. by 9-in. vertical sliding lucite door allowing food and other supplies to be passed in.

The bottom of the enclosure is a sheet metal tray sloping 30 deg to a 3-in.-diam-aperture for waste collection. At one end the tray slopes very gradually for 12 inches to provide a small work area outside the metal cage. The aluminum frame and lucite rests on the tray shoulder inside of, and sealed to, a 1-in. lip. The tray in turn rests on an aluminum frame bolted to a heavy wheeled platform.

Lighting and ventilation is through the top, which is constructed of 3/8-in. plywood lined with vinyl sheeting. Adequate illumination is supplied by two 120-W fluorescent fixtures. Air is drawn in through PF-105 filters and down 2-in.-diam-aluminum tubes in the corners of one end, and out through a 2-in.-diam aperture in the top of the opposite end. All enclosures are connected via standard filters to an exhaust manifold pulling 3 in. of water at the inlet. In addition, the room containing these enclosures is exhausted by a separate high-capacity system.

Highly contaminated biological waste is collected in a wide-mouthed 5-gal jug beneath the enclosure. The jug caps are altered to provide a 5-in. -diam 3-in. -long neck. Approximately 1 pint of disinfectant and deodorizing solution is poured into a jug before it is connected to the drain pan by means of polyethylene sleeving. The process of removing and sealing such waste jugs is similar to that described for enclosure transfers. The liquid waste is moved to a waste processing area and solidified in the same container. It has been necessary to exchange the waste jugs about every five days. A quick-disconnect water fitting extends through the top to a short inside hose provided with a spray nozzle for cleaning the cage and watering the animal.

When no body radiation can be detected by direct survey, the animal is transferred to a long-term holding cage of approximately 45 cubic feet. This type of cage is extensively used by researchers at the University of California, Davis, California.[3] A push-in pull-out tray adapted to the front of the cage provides for feeding of the animals. A 30-gal drum in a secondary 55-gal drum is connected to the floor drains of each of four raised units to facilitate rapid waste processing if, after assay, the waste is too contaminated to dump.

On occasion it has been necessary to decontaminate the body fur of the animals. For this purpose a double-front liquid-proof glove box has been constructed, fitted with the same large passout ring used on the other units. For washing, the animal is anesthetized and the previously described technique for transferring a highly contaminated animal from one enclosure to another is employed. Decontamination is by mild detergent shower bath with water supplied inside the enclosure through quick-disconnect hose fittings. Contaminated water is collected beneath the enclosure in the same way as beneath holding cages. The same enclosure is used for surgery or autopsy.

To date, fifteen animals have been handled in these facilities, and approximately 7 Ci of Y^{90} have been utilized. No trace of contamination release to the experimental area has been detected.

IV. Y^{90}-DTPA IN HUMANS

In the fall of 1961 the Y^{90}-DTPA procedure in human therapy was begun, necessitating development of radiation-protection devices of a different nature than those used in the animal studies. The amount of activity used was to range from 6 to 14 mc of Y^{90}-DTPA per pound of body weight, thus in some cases approaching 1.5 Ci total dose.

A gloved enclosure suitable for housing a human patient was necessary. The Health Chemistry Department of the Laboratory was called on to provide an enclosure which would meet the following requirements.

The enclosure had to provide a high-quality physical confinement for any radioactive fluids or dust, and provide reasonable shielding for operating personnel against the activity contained within. It would be operated at a negative pressure relative to the hospital room, and exhausted to the outdoors through high-efficiency filters to prevent release of airborne contamination. Every reasonable provision was to be made for the patient's comfort during a 24-hour period. In particular, the enclosure was to be cheerful and light to prevent panic or claustrophobia. In addition, the enclosure was to be fitted with enough glove ports to allow medical personnel to carry out all necessary procedures, including frequent blood and urine sampling within the enclosure, continuous electrocardiography, and monitoring of physiological parameters such as blood pressure and temperature.

Sufficient tube outlets, passin-passout apertures and auxilary enclosures were to be provided for all other procedures involved. The most complex procedures involved filtration and intraveneous recirculation of all the patient's urine during the first 6 to 10 hours in the enclosure. This involved pumping high levels of radioactive liquid throughout a complex pressurized system, and the subsequent continuous collection of radioactive urine following the irradiation

episode. Complete, rapid access to the patient was to be an absolute necessity in the event of a medical emergency. The apparatus was to be a self-substaining integral mobile unit to facilitate installation in, and removal from, a relatively crowded hospital environment.

With these requirements and limitations, the enclosure shown in Fig. 11 was constructed. This is a rectangular unit 7 ft long, 4 ft high, and 3 ft wide, constructed of 3/4-in. plywood with four side sections of 3/4-in. lucite. The side sections and the center support on one side are removable for emergency access to the patient by releasing outside clamps.

The patient rests on an ambulance cot modified to provide adjustable arm rests and head and knee sections. The latter are hydraulically adjustable from the outside. The hydraulic fluid lines have quick-disconnect fittings at the cylinders on the cot. Two hand bars are provided on the ceiling to enable the patient to shift himself. Conversation with the patient is by means of a battery-powered intercommunication unit. Illumination adequate for minor surgery inside the enclosure is provided by two banks of 120-W fluorescent lights mounted on its top.

A variable airflow of 0 to 12 CFM is maintained through the enclosure by an exhaust blower and damper mounted underneath. Air forced into the room through absolute filters is drawn into the enclosure through PF-105 filter material at each end. Air from the enclosure is drawn by the blower through suitable filters mounted underneath and then exhausted outdoors. The airflow rate is indicated by a ping pong ball in a plexiglass tube installed in the duct ahead of the blower. In the event of power outage, emergency battery power is provided to ensure continued operation of the isotope recycling system and the ventilation system. Additional emergency power is available from the hospital emergency generators.

Rotating 8-in.-diam-glove ports have been inset in revolving plexiglass discs in each of the four lucite panels. These versatile glove ports allow much freer access than do fixed ports.

A large passin-passout aperture is provided at one end of the enclosure. Located on the opposite end are two I. V. fluid infusion standards. The I. V. fluid lines are passed through small apertures in the top of the enclosure. Connections for physiological monitoring equipment are located in the fixed center support on one side.

During the 6 to 10-hour period of intravenous urine recycling, continuous radiological monitoring protects the attendent personnel and detects and controls any contamination that might be spread during a medical emergency. Periodic wet swipes around the enclosure are made, along with intermittent checks of the filter device that continuously sampling the room air at a rate of 4 CFM. The radiation field within the enclosure has been as high as 20 R per hour. Radiation fields at the outer surfaces of the enclosure have ranged from 0.2 to 5.0 mr/h. The overall radiation field in the hospital room has been 0.2 mr/h or less. Figure 12 shows the human irradiation enclosure in use.

Upon completion of the 6 to 10-hour irradiation procedure, the patient remains in the enclosure for an additional 15 to 20 hours, during which the body eliminates some 90-95% of the injected activity through the urine. During this period, urine is collected beneath the enclosure in polyethylene bottles that are shielded by a mixture of sawdust and plaster of paris. Radiation from the first six urine collections, spanning a 12 to 15-hour period, has ranged from 2 to 5 R/h to 150 mr/h at 1 foot unshielded.

Following this 15 to 20-hour period, the patient is transferred from the enclosure to a conventional hospital bed. Due to the increased susceptibility of the patient to infection after irradiation, a "reverse isolation" approach is mandatory. To maintain such an environment the room is hermetically sealed, except for the door, and is pressurized through an absolute filter. Constant

room temperature is maintained by an industrial type air conditioner.

Typical measurements at the time of transfer have shown from 40 to 100 mr/h over the patient's head and chest; radiation levels less than those seen in patients who have received the well-known therapeutic doses of I^{131} for metastatic disease of the thyroid. Because of the pressurized environment, it is necessary to control contamination release from excreta such as urine, feces, perspiration and saliva. All eating utensils are disposable. All laundry is monitored and the contaminated items are segregated for decay. For the first few days, the researchers require 100% body-waste collection in order to account for all of the injected isotope.

Experience to date has shown that after two to six weeks no radioactivity can be detected in the patient. During this time, because the patient is vulnerable to infection, the number of people entering the room has been held to an absolute minimum.

It also happens that untrained personnel must often perform such traditional health-physics tasks as changing filters on air-sampling devices, bagging waste, taking swipes for contamination assessment, and making direct body surveys of the patient. This has proved entirely feasible after only nominal training.

The results have shown that curie levels of radioisotopes can be administered to human patients by means of these techniques and procedures, with reasonably low radiation exposure to the medical team and no detectable contamination being spread to the hospital environment.

REFERENCES

1. H. S. Winchell, Selective Irradiation of the Lymphatic System Using Internally Administered Y^{90}-DTPA: Kinetics, Dosimetry, and Biological Evaluation. Lawrence Radiation Laboratory Report UCRL-9755, June 14, 1961 (unpublished).

2. J. S. Peck, Air Scrubber Report, Health Chemistry Memorandum JSP-621-59 Lawrence Radiation Laboratory, University of California (1959).

3. A. C. Anderson, Third Annual Report; AEC Project No. 6, Technical Information Service, AEC Report TID 11364, September 1960 (unpublished), pp. 10-15.

FIGURE LEGENDS

Fig. 1. Sr^{90} - Y^{90} separation enclosure.

Fig. 2. Y^{90} enclosure.

Fig. 3. Isotope transfer container.

Fig. 4. Air scrubber.

Fig. 5. Sr^{90} - Y^{90} shielded enclosure train.

Fig. 6. Schematic representation of intraveneous recycling system.

Fig. 7. Schematic representation of the enclosures' connection for animal transfer.

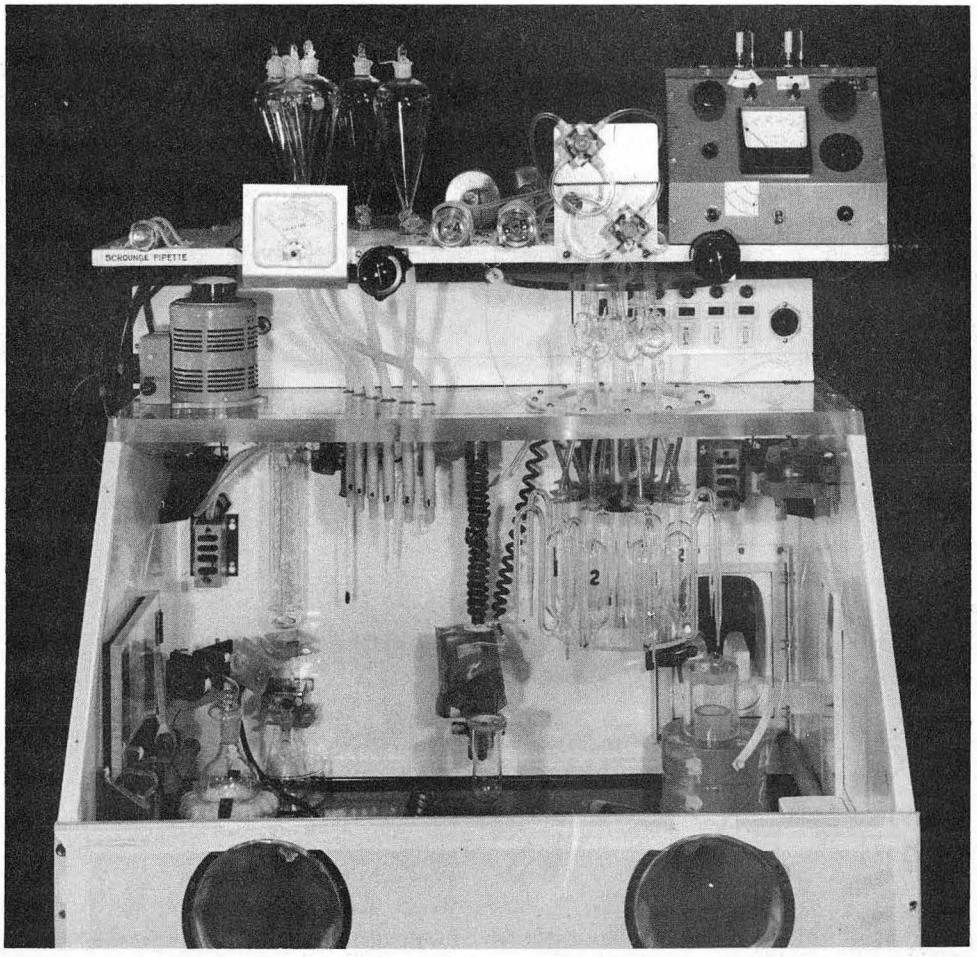
Fig. 8. Radioactive-animal holding enclosure, showing the passin port.

Fig. 9. Radioactive-animal holding enclosure, showing accessibility ports and sliding door.

Fig. 10. Animal holding enclosure in use.

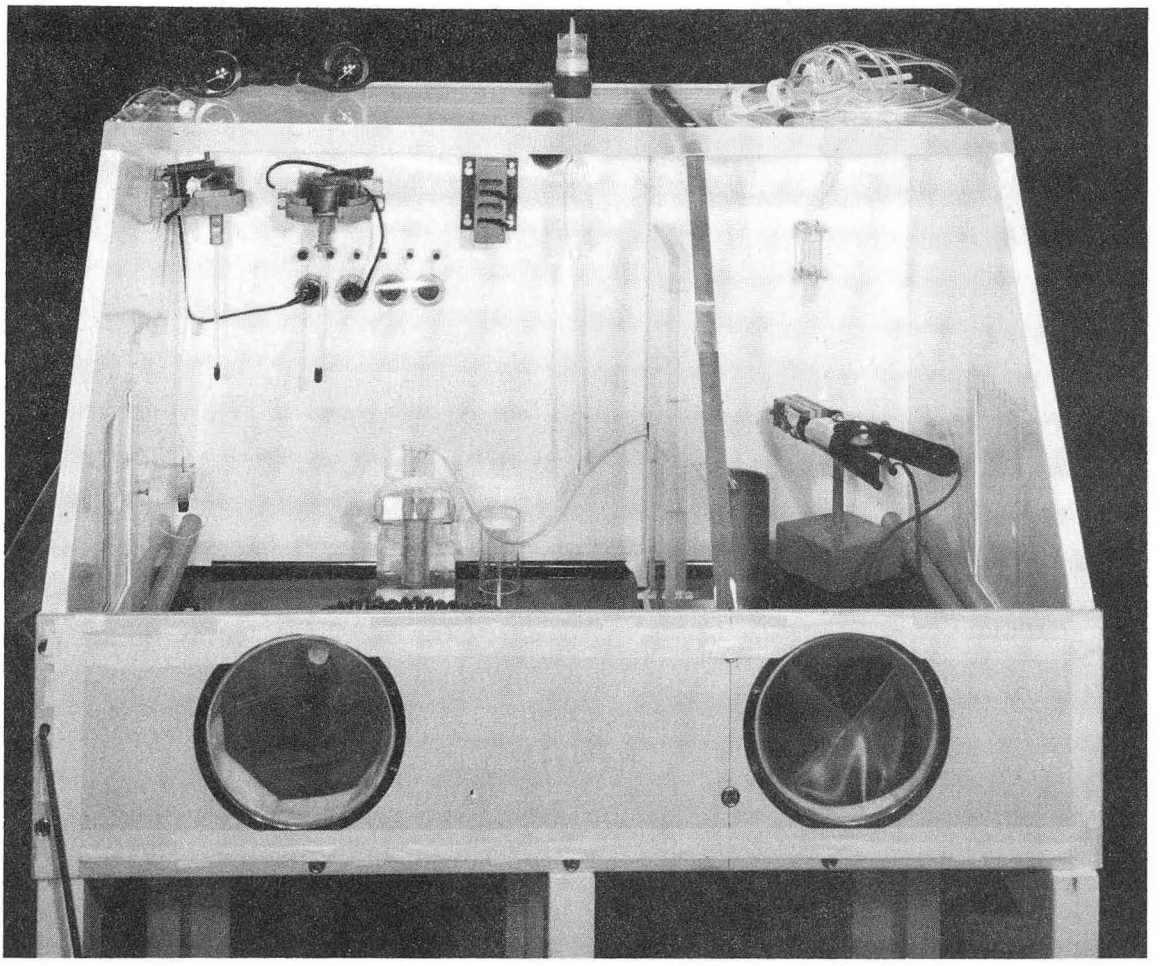
Fig. 11. Human irradiation enclosure.

Fig. 12. Human irradiation enclosure with patient.



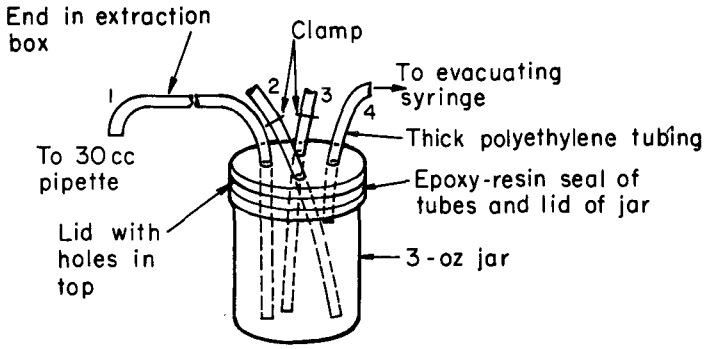
ZN-3140

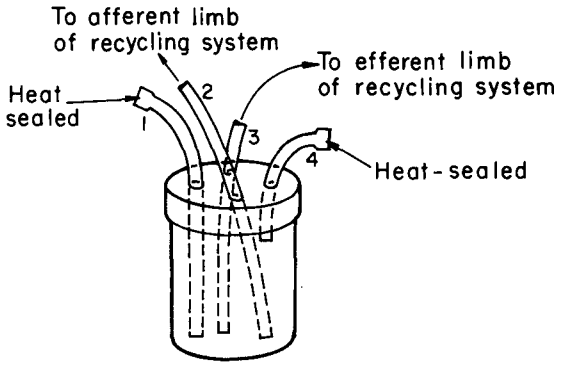
Fig. 1



ZN-3139

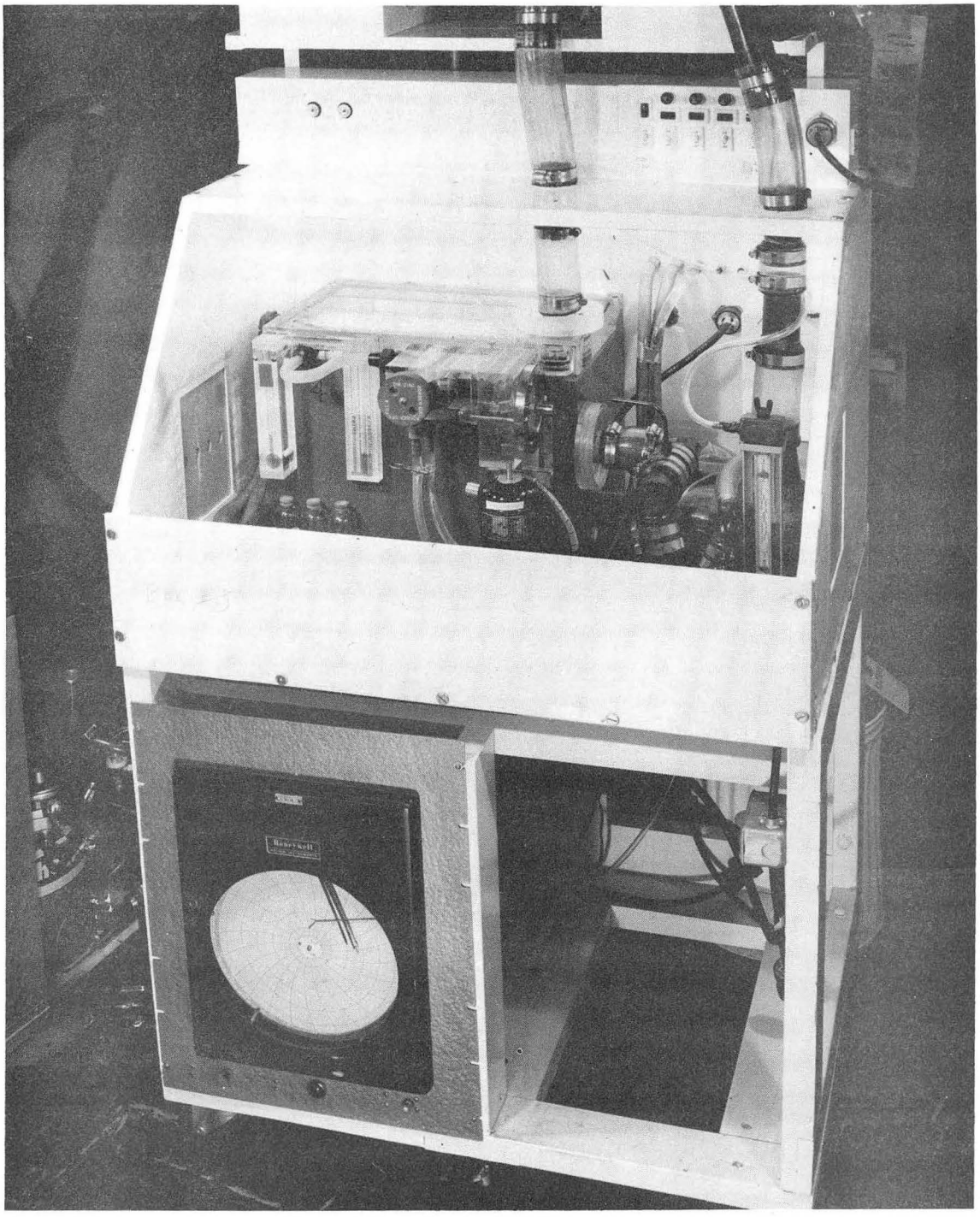
Fig. 2





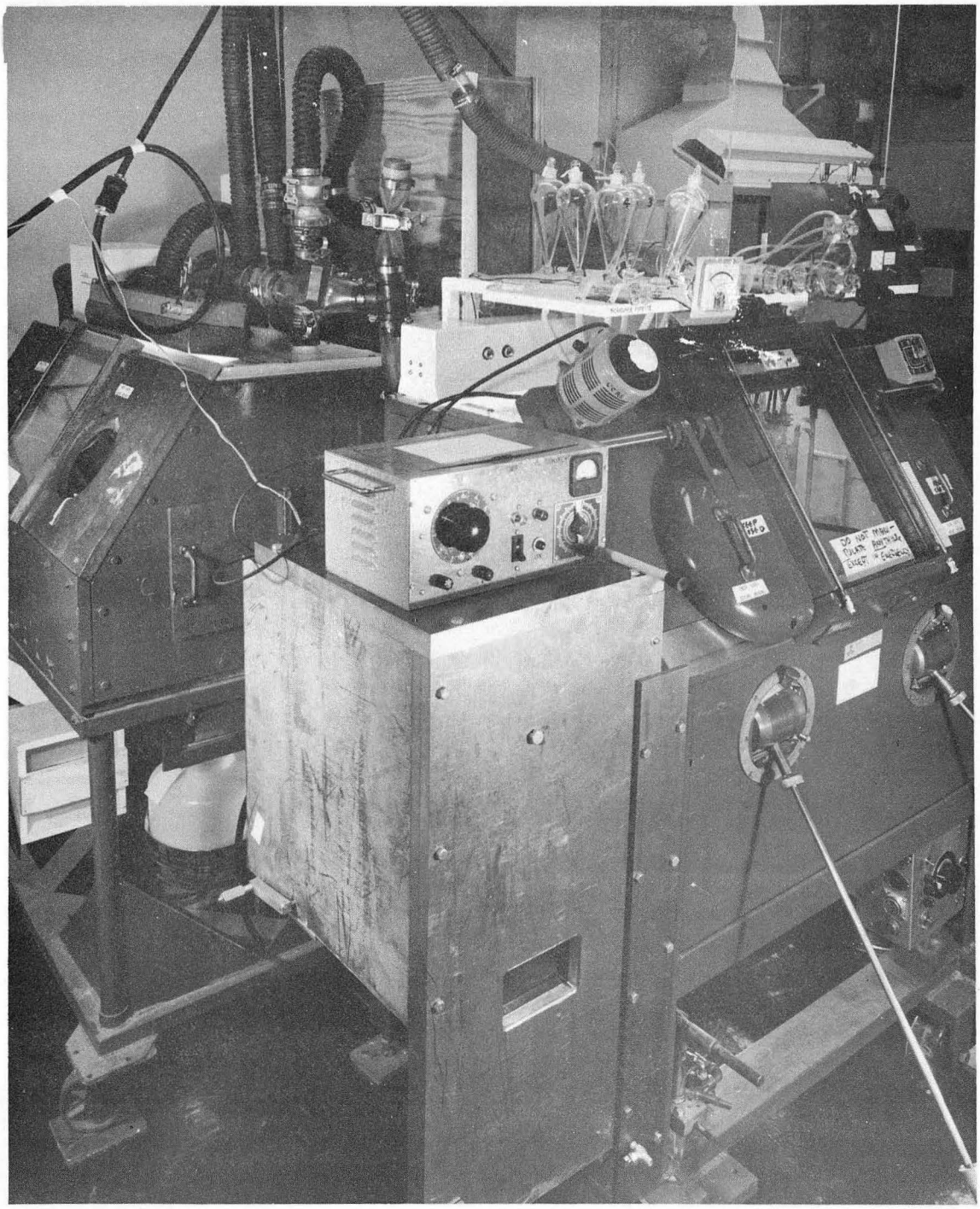
MU-26833

Fig. 3



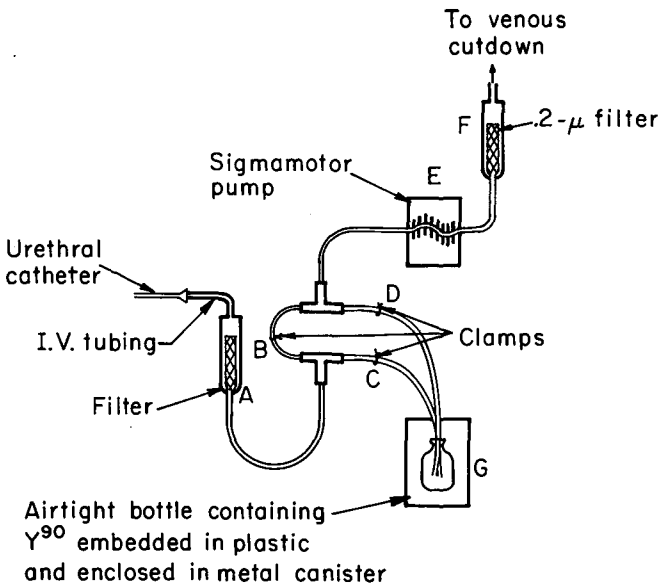
ZN-3138

Fig. 4



ZN-3137

Fig. 5



Schematic representation of urine intravenous recycling system

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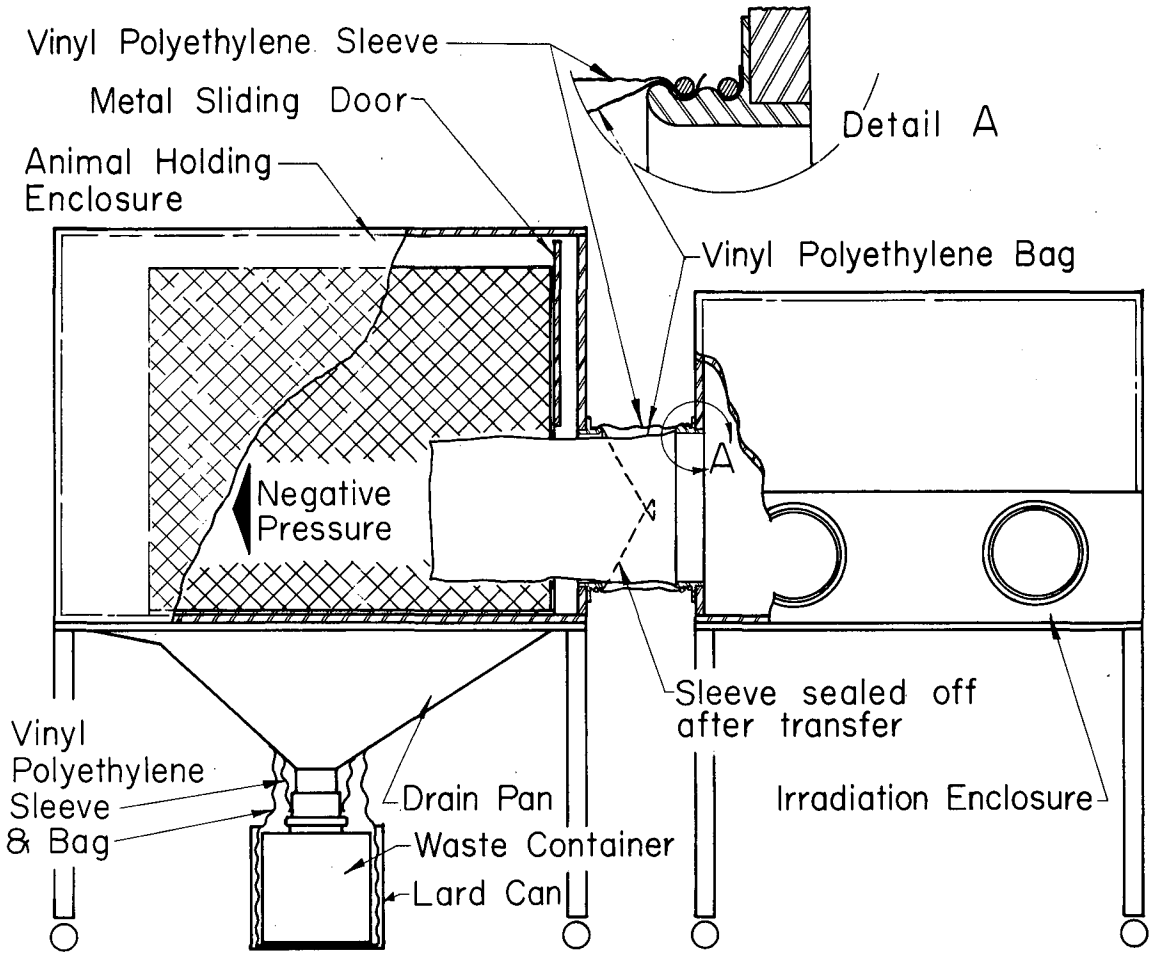
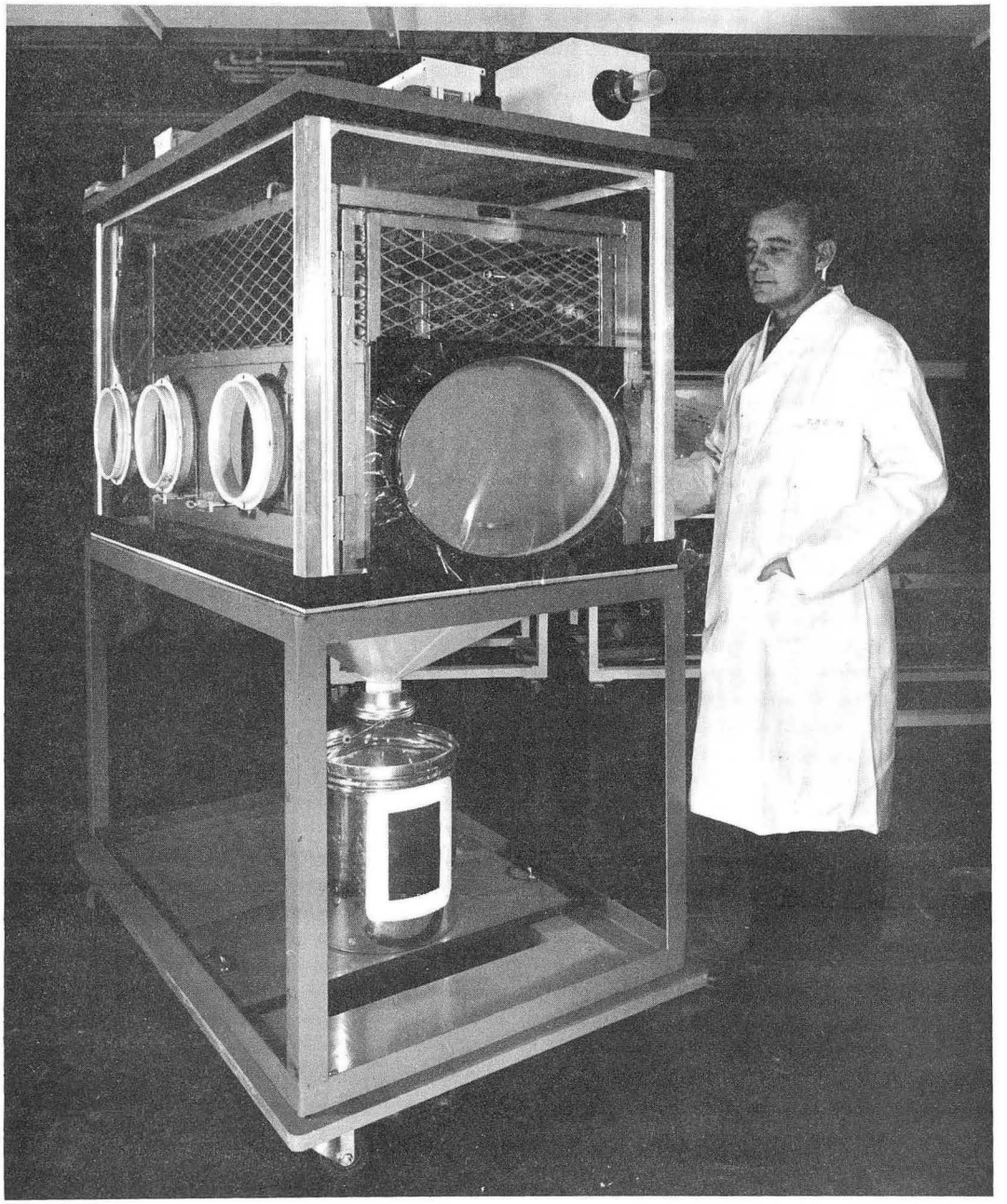
Fig. 6



NOTE: Gap shown between enclosures is for illustration only; during transfer the pass-out rings are butted together.

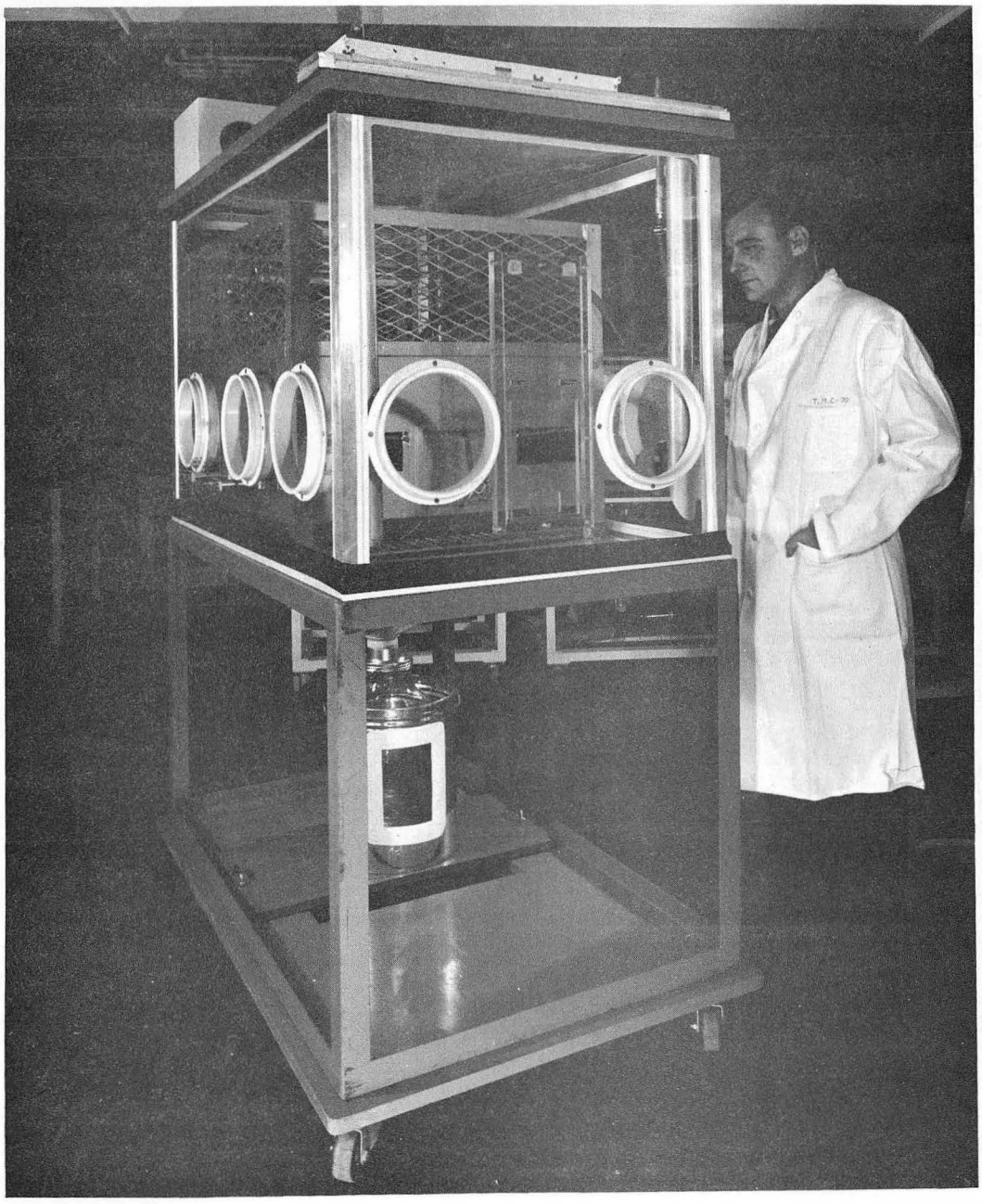
MUB-1655

Fig. 7



ZN-3716

Fig. 8

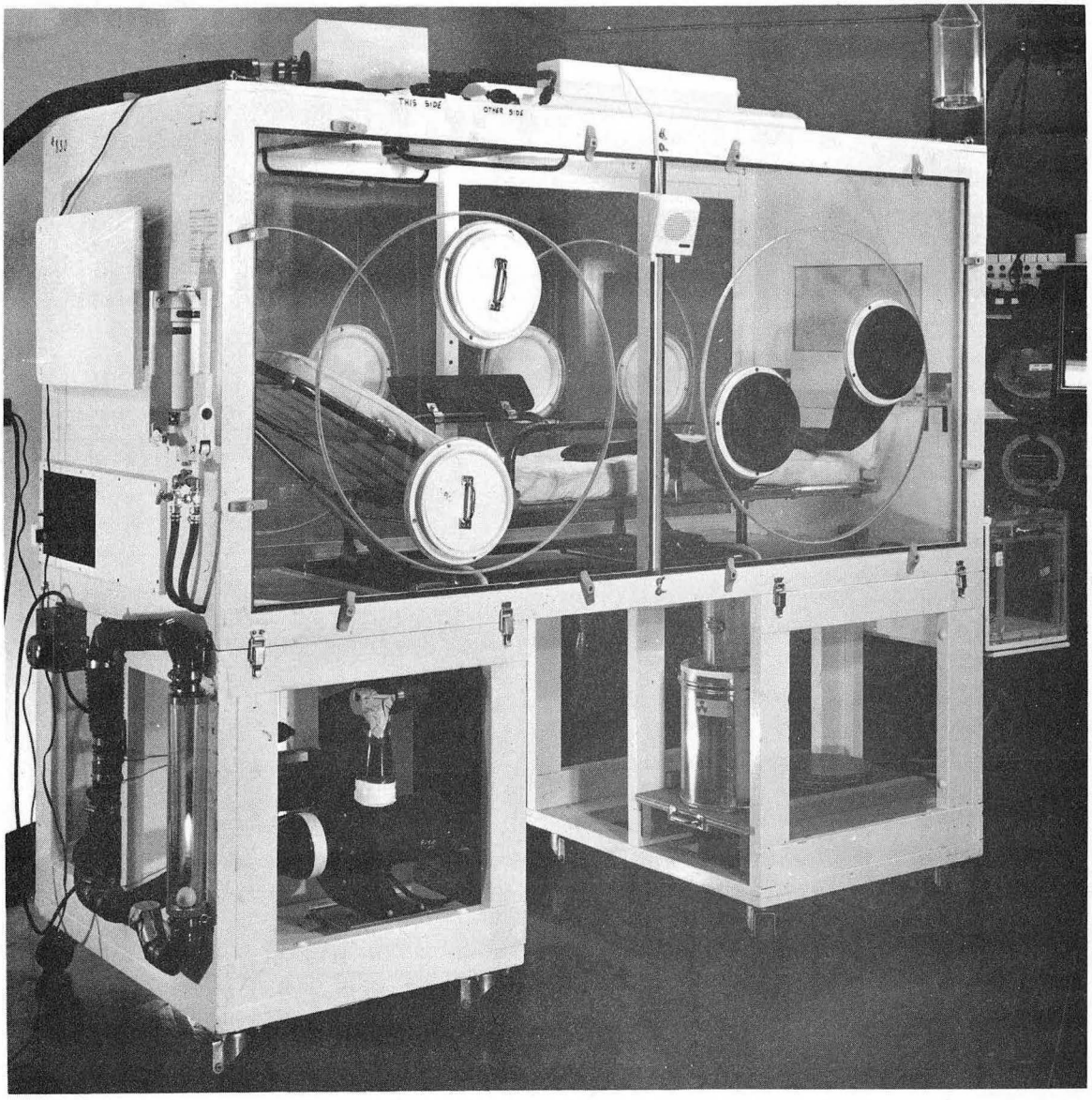


ZN-3717

Fig. 9

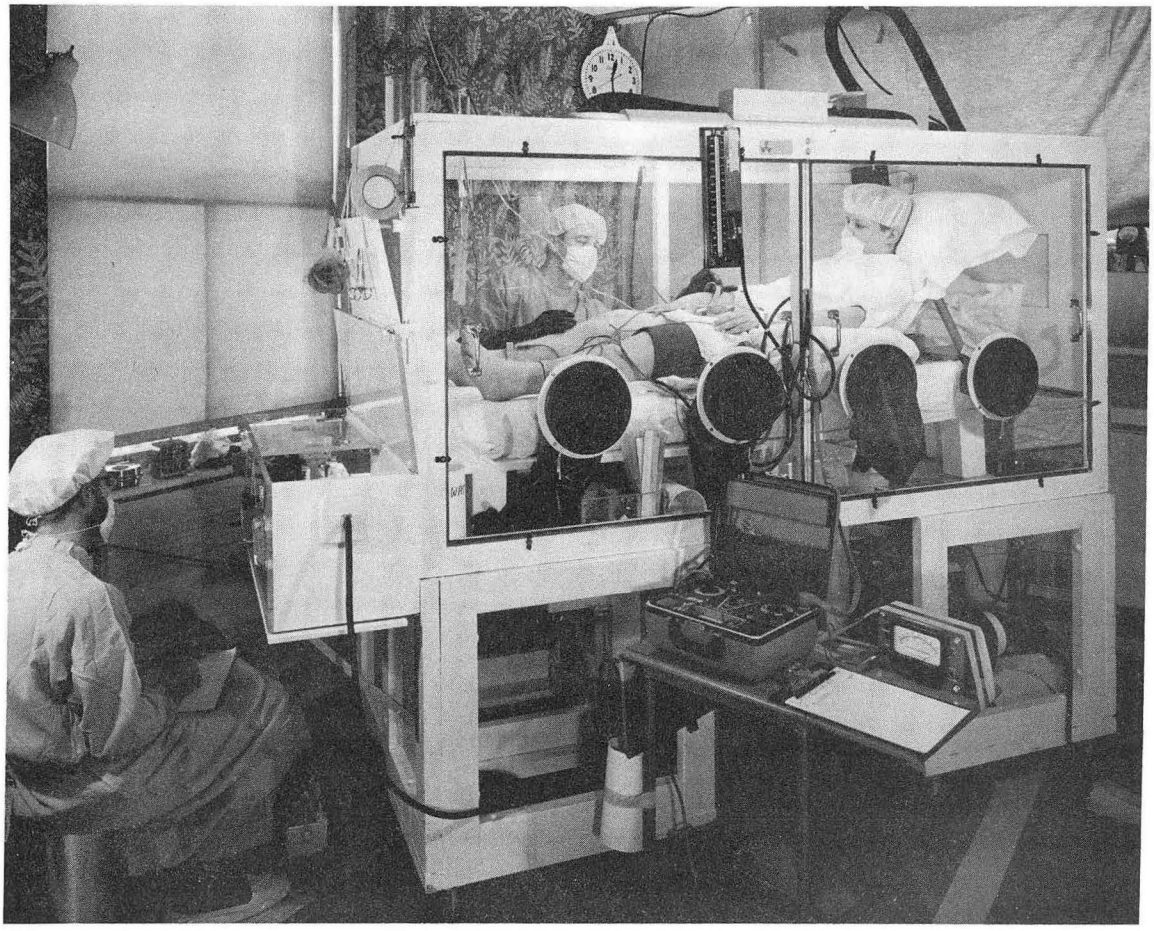
ZN-3718

Fig. 10



ZN-3719

Fig. 11



ZN-3136

Fig. 12