RADIATION PROTECTION IN A NUCLEAR PHARMACY

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Abstract

Regional nuclear pharmacies are emerging throughout the world to meet the increased demands for radiopharmaceuticals. A radiation protection program for a nuclear pharmacy encompasses facility design, quality control, dispensing and documentation, and provides for increased utilization of radiopharmaceuticals. The resultant radiation protection program is synergistic between health physics and pharmacy principles.

Introduction

Regional nuclear pharmacies provide radiopharmaceutical services for multiple hospitals located over wide geographic areas. Such pharmacies provide the necessary pharmaceutical expertise for preparing radioactive chemicals into pharmaceuticals and also provide an increased assemblage of radiopharmaceuticals at reduced costs to many hospitals that cannot individually afford nuclear pharmacy services.

A regional nuclear pharmacy may have inventories of 5-10 Curies of radioactive materials, with greater than Curie quantities of Iodine-131, Xenon-133 and Molybdenum-99/Technetium-99m.

The University of Michigan Hospital Regional Nuclear Pharmacy, over the past two years, has evaluated radiation protection as applied to nuclear pharmacy practice. Facility Design, administered Doses, product Dispensing and quality control Documentation are considered to be the principle axioms for the development of a radiation protection program in nuclear pharmacy.

Nuclear Pharmacy Design

Nuclear pharmacies must always incorporate health physics principles associated with "wet" radiochemistry laboratories. In addition, special consideration must be given to pharmaceutical techniques, i.e. aseptic preparation of parenteral products, synthesis of radiolabeled organic compounds, dispensing of radioactive gases, repeated handling of syringes containing radioactive materials, maintainence of product quality and potential contamination of non-radioactive pharmaceuticals.

Traffic flow patterns within a nuclear pharmacy must be defined for efficient utilization, as well as radiation protection planning. A general consideration of functional separation of activities within the pharmacy aids in radiation protection and pharmaceutical quality. The package receiving and shipping area should be a separate room to minimize potential radioactive contamination and to reduce airborne dust and particulate matter from entering the compounding area. A dispensing area, separate from the compounding area, will minimize traffic where bulk quantities of radioactive material are used and parenteral products formulated. In addition, a dispensing window will reduce the access of unauthorized personnel. The quality control laboratory should be housed in a separate room, as it is predominately an instrumentation facility, and considered only to contain tracer quantities of radioactive materials. Finally, because adjunctive (non-radio-

active) pharmaceuticals are often stocked and dispensed with radiopharmaceuticals, a separate room for pharmaceuticals again provides radiological and pharmaceutical quality assurance.

An adequate floor plan for efficient nuclear pharmacy design is shown in Figure 1. The compounding and dispensing rooms form an integral, limited access area for the storage, preparation and dispensing of radiopharmaceuticals. Low traffic flow in the compounding area reduces potential spread of contamination. Dispensing of unidose radiopharmaceuticals to medical personnel is conducted through the dispensing window; a procedure which guarantees limited access only to authorized individuals and further reduces the potential spread of radioactive contamination. The non-radioactive pharmaceutical dispensing area and quality control laboratory are located across the hall from the compounding and dispensing rooms. Adjacent to the nuclear pharmacy is a separate radiochemical laboratory where packages are received and shipped. Included in the radiochemical laboratory is an absolute filtered radiochemical hood for the storage and dispensing of iodine-131 and xenon-133.

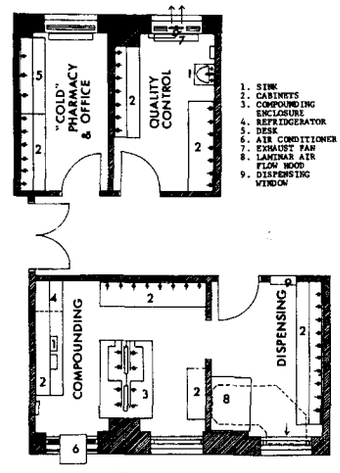

Figure 1
Floor Plan

Too often, one segment of a laboratory bench is chosen for all radiopharmaceutical preparation. Such a design can offer satisfactory health physics considerations, but poses a serious potential risk of product cross contamination and erroneous product selection and dispensing. Nuclear pharmacy design should provide separate work areas for the compounding and dispensing of radiopharmaceuticals. To facilitate both health physics and pharmacy requirements, the University of Michigan Nuclear Pharmacy has designed a lead laminated plywood (¼ inch lead) compounding enclosure shown in Figure 2. This installation is specific for technetium-99m compounding and contains sliding lead glass (1.7 mm lead equivalent) doors across the top. The primary design consideration of this enclosure was consolidated shielding with separation of compounding involved with technetium radiopharmaceuticals: a union of radiation protection with pharmaceutical quality assurance.

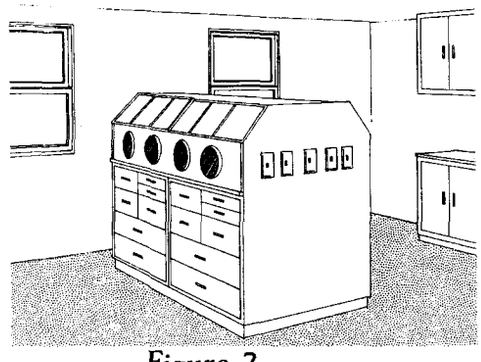
Figure 2
Compounding Enclosure

Within a nuclear pharmacy, laminar air flow hoods are used to provide a sterile work area for aseptic subdivision of parenteral products and not to vent volatile radioactivity. Laminar flow hoods are manufactured to provide either horizontal or vertical air flow. Since horizontal air flow is directed towards the operator and could lead to a severe personnel contamination hazard, it must be stressed that only vertical laminar air flow hoods should be chosen for use in nuclear pharmacy. Sterile air is provided in a laminar air flow hood by a series of HEPA filters which are designed to remove all

dust and bacteria from the air before entering the working space. To insure the sterility of the working compartment, articles should be autoclaved or suitably disinfected before entering the hood.

Several problems associated with shielding are evident with a nuclear pharmacy. Too often personnel without health physics training fail to consider the energy of associated radiation and assume that shielding designed for technetium-99m is suitable for fluorine-18, iodine-131 or phosphorous-32. The designation of separate work areas for different radionuclides allows for optimal shielding design associated with each product. Such considerations, however, should be flexible to allow for adaptation of new procedures and new radionuclides. Nuclear pharmacies should be cautioned against stacking heavy, free-standing, lead blocks, since they may present serious hazards, i.e. traumatic injury to legs and feet from accidental falling blocks, radiation exposure through non-interlocking joints, and excessive weight induced structural damage to cabinetry. Inexpensive and highly effective shielding for low energy radionuclides can be obtained with lead perchlorate shields suggested by Barnett and Harris.[1]

Radiopharmaceutical Dispensing

The proper dispensing of radiopharmaceuticals will affect the absorbed radiation dose to the patient and the pharmacist. Maximal patient protection is achieved by the utilization of unidose radiopharmaceuticals. All radiopharmaceuticals are dispensed from the nuclear pharmacy on prescription. The prescription indicates the requested study, the preliminary diagnosis, patient name, height, weight, age and the time that the patient is to receive the dose. With this information, the pharmacist can correlate the radiopharmaceuticals with the proposed study and patient information in such a manner that the patient will receive the optimum dose. Each product is dispensed precalibrated to the time of administration, and receives duplicate assays of the radioactive contents. The radiopharmaceutical is dispensed with a label indicating the patient's name, time and route of administration, date, prescription number, physician's name and pharmacist's initials. Unit dose dispensing has reduced the potential for dispensing and administration errors associated with major drug delivery systems.[2] It is believed that the concept of unidose dispensing of radiopharmaceuticals is an efficient and effective method of reducing errors associated with the administration of radioactive pharmaceuticals.

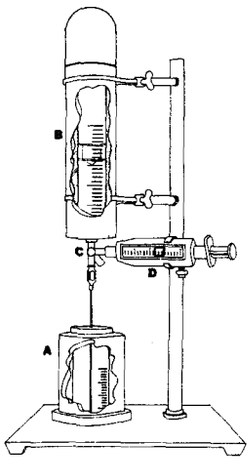

Figure 3
Dispensing System

As an additional radiation protection device for the pharmacist, as well as maintaining the pharmaceutical quality of the products, our pharmacy utilizes a shielded syringe-valve dispensing system as modified from Hoar.[3] A schematic diagram is given in Figure 3. The solution to be unidose dispensed is drawn from the shielded vial (A) into the shielded large volume syringe (B) via a 3-way valve (C). A unit dose is subsequently dispensed by attaching a small volume syringe (D) to the dispensing part of the 3-way valve, drawing off the desired volume, attaching a needle, assaying the contents and affix-

ing the label. This dispensing process is conducted within the laminar air flow hood to insure sterility of the product.

The use of the 3-way valve dispensing unit not only insures pharmaceutical quality of the product, but decreases the hand and finger doses to the pharmacist with an average dispensing time of 25 seconds. Several reports [4,5,6] indicate the potential problem hand and finger doses to medical personnel. Implementation of a 3-way valve dispensing system significantly reduces exposure problems since the pharmacist need not handle the barrel of the syringe.

Administered Radiation Dose

The reduction of medical exposures and patient protection have always been the goals of nuclear medicine personnel. Tremendous gains in reducing medical exposures have been accomplished by using shorter half-life radiopharmaceuticals, by increasing biological turnover times, and by selection of the best radionuclide for labeling purposes. However, little consideration has been given to the administered dose. The relative assessment of benefit versus risk can only be accomplished if the administered dose is tailored to the individual patient. Too high an administered dose results in increased absorbed dose. To low an administered dose may result in a missed diagnosis or a readministration of the drug. The Nuclear Pharmacy has evaluated the administered dose regarding the genetically significant population, the method of dose determination and the pharmacists role in product selection.

An evaluation of 200 randomly selected patients receiving a radiopharmaceutical indicated that 12.5% were less than 18 years old; 34.5% were between 18 and 45, and 53% were greater than 45 years old. The genetically significant population (less than 45) represents a 13% increase as compared to the national average of 1970. Leblanc and Johnson[7] have also indicated that exposures from nuclear medicine procedures increased from 5% gonadal exposure/admission in 1964 to 11% in 1968.

Administered radiopharmaceutical doses vary from clinician to clinician. The selection of an administered dose may be from a table of doses determined from past experience,[8] the application of body weight, e.g. mCi/Kg or from a series of rules, e.g. Young's rule, Clark's rule or surface area.[9,10,11]

While adult administered doses are fairly well established, large variations in pediatric doses are apparent. Administered doses based upon age show great limitation when one considers the variability of a given age. For example, the 3rd percentile of a 10 year old girl is 53.2 lbs., while the 97th percentile is 101.9 lbs.[12] Administered doses determined by weight, while better than doses determined by age, usually underestimate the requisite clinical dose. The underestimated dose is due to 1) weight changes as a function of the cube of linear dimensions while the necessary photon fluence for adequate lesion localization varies with the square of linear dimensions, and 2) ratios of organ/body weights in infants are greater than those observed in adults.

To provide a uniform and reliable method of computing administered radiopharmaceutical doses, for the broad spectrum of patients seen in our clinic, Nuclear Pharmacy employs body surface area as modified by height and weight. Administered doses, in mCi/m^2 are usable for all patients regardless of variations in weight, height, age or sex.

As a further consideration of the absorbed radiation dose, our pharmacists participate in the selection of the radiopharmaceutical for the patient. Qualified nuclear pharmacists have the

necessary training in radiopharmaceuticals, biopharmaceutics and metabolism to guide the physician in selecting the optimum drug to obtain the maximum diagnostic information. In addition, the nuclear pharmacist has played a vital role in identifying patients that may have drug interactions which prevent the meaningless use of a radiopharmaceutical. For example, a request for a red cell survival test one week after a gallium-67 scan.

Radiopharmaceutical Documentation

Good radiation protection principles require adequate record keeping to evaluate personnel methods and product control. Pharmacy requires substantial record keeping to validate a product's suitability for human use. To meet the requirements of both health physics and pharmacy, a product quality control system has been developed. A schematic diagram of the quality control program is shown in Figure 4.

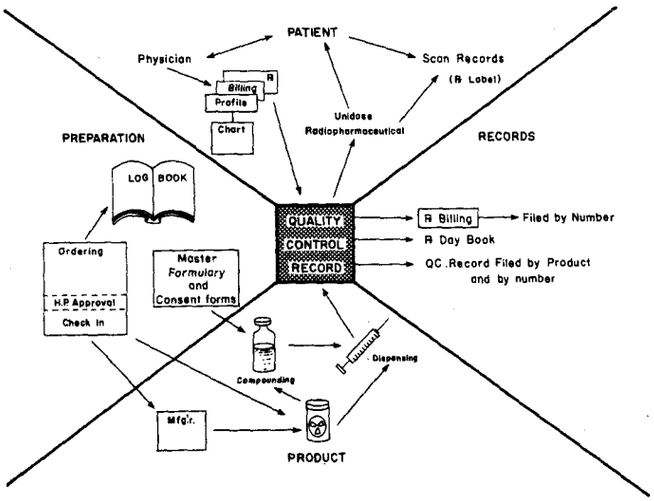

Figure 4
Quality Control Program

Each product received into or compounded by the nuclear pharmacy has an assigned quality control card (center). Each product is further designated by a number indicating the date received or compounded. All compounded radiopharmaceuticals are prepared in accordance with a master formulary. All records of tests, e.g. sterility, apyrogenicity, particle size, radiochemical purity, chemical purity, radionuclidic purity, pH, etc. are indicated on the quality control card. All unidoses dispensed from the product are also recorded with the quality control record. In this manner, a complete history of any radiopharmaceutical can be ascertained with a brief glance at the quality control record card.

As part of our quality control program, we require that used syringes be returned to the nuclear pharmacy. This alleviates the hazard of loose contaminated syringes and also allows the syringe to be reassayed. In this manner, complete assessment of the administered dose can be determined. LeBlanc and Johnson[13] and Abdel-Dayem[14] have reported on retained activity of Xenon-133 within syringes. Freedman[15] has described a similar deposition of technetium-99m sulfur colloid in the rubber plunger of disposable syringes. Our reassay procedure indicates that many radiopharmaceuticals have residual activity in syringes, especially radiolabeled proteins.

As part of the documentation concern for radiopharmaceuticals, our pharmacy has assumed the responsibility for the maintenance of all records necessary for clinical trials of new radiopharmaceuticals, as well as validating drug interactions or adverse reactions. Within our hospital, the patients chart is available to the pharmacist during the prescription preparation. A review of previous or existing drug therapy by the pharmacist can offer lead to the

explanation of modulation in drug distribution. When an adverse reaction occurs, our nuclear pharmacy coordinates the compilation of associated data and the reporting of the reaction to the professional societies and concerned authorities.

Conclusions

1. The objectives of pharmacy and health physics are synergistically compatible in reducing personnel and patient radiation exposure.
2. Methods for reducing radiation exposures within regional nuclear pharmacies while maintaining large inventories and increased utilization of radiopharmaceuticals requires adequate facility design, consideration of administered dose, unidose dispensing and quality control documentation.
3. Surface area measurements used in consideration of administered doses have aided in providing uniform and reliable scans between patients, especially in pediatric nuclear medicine.

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