A REPORT ON THE SYMPOSIUM TO REDUCE RADIATION EXPOSURE IN NUCLEAR MEDICINE

To evaluate ways of reducing radiation exposure from nuclear-medical procedures, a symposium* was held August 7–9, 1967, in East Lansing, Michigan. Co-sponsored by the National Center for Radiological Health (NCRH) and Michigan State University, the meeting was attended by 72 invited representatives from government agencies, medical disciplines, industry, and university centers who are actively concerned with nuclear medicine. We outline the highlights of the symposium here.

In his keynote address, Eugene L. Saenger of the Cincinnati General Hospital challenged the participants to debate the problem areas he feels are most germane to the future of nuclear medicine. These include radiopharmaceuticals, equipment and facilities, manpower development and the degree of regulation needed in nuclear medicine. Although this field has had a type of regulation unique in medical practice, he feels that it has prospered under these restrictions, and safe, effective radiopharmaceuticals have become available. He asked the group to discuss how nuclear medicine should be regulated in the future and reminded them not to lose sight of another important consideration: reducing radiation exposure by means that are compatible with medical necessity.

Richard Cunningham, Div. of Materials Licensing, U.S. Atomic Energy Commission, outlined the complex role of the AEC in regulating byproduct material used in nuclear medicine. At present, 36 diagnostic or therapeutic procedures using 17 different radionuclides are safe and effective for routine medical use in the opinion of the Commission. All others are considered investigational and require submission of a research protocol. In the future, the AEC considers that radiopharmaceuticals should be regulated on much the same basis as nonradioactive drugs, that qualifications for practicing nuclear medicine should be established and controlled by the medical community itself or by state and local examination boards and that the AEC's regulatory role should be limited to governing the radiation safety of employees and the public during the manufacture and use of radiopharmaceuticals.

Outlining the role of the AEC Advisory Committee on Medical Uses of Isotopes, E. Richard King, Medical College of Virginia, said the Committee advises the AEC in developing criteria for regulating and licensing the use of radionuclides in humans, defines the extent to which a proposed investigation will establish the safety and efficacy of a drug for routine use and recommends when the clinical use of a radiopharmaceutical can be routinely licensed. He stressed that the committee continues to scrutinize dosimetry calculations on applications for investigational use.

Raymond T. Moore, Deputy Director, NCRH, said the mission of NCRH is to identify exposure problems and develop ways of reducing unnecessary exposure. He said the National Center is interested in nuclear medicine because it involves the exposure of humans to radiation which should be as minimal as possibly commensurate with the benefits to be derived. Although the National Center has no authority to establish regulatory standards, it can provide recommendations through research and development which may be used by states or other public and private organizations.

Edward M. Smith, University of Miami School of Medicine, discussed the current status of internal radiation dosimetry and the activities of the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine as serving "to provide the best possible estimate of the absorbed dose to patients resulting from the diagnostic or therapeutic use of metabolically administered radiopharmaceuticals with the restriction that the committee make no judgment as to the medical significance of the estimated dose."

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After three years of collecting and evaluating data, the committee will soon publish five pamphlets which will include the history of the committee, a description of the unified absorbed-dose concept, tables of absorbed fractions and specific absorbed fractions, tables of energy buildup factors and absorbed dose calculations for neohydrin and selenomethionine. Future publications will include absorbed-dose calculations for macroaggregated albumin and other radioiodinated compounds, xenon gas, pertechnetates, iridium, iron, strontium and calcium.

Paul V. Harper, University of Chicago, discussed the production and use of short-lived isotopes, theorizing that the ideal isotope has an average life comparable to the time needed to investigate a physiologic process. However, he feels there are great deviations from this concept in practice. Parameters other than physical half-life which must be considered include dosimetry, photons per disintegration, radiation energy and absorption, and efficiency and collimation of detectors. In thyroid scanning, for example, ^{125}I will produce less than half the radiation dose of that from ^{131}I, even though ^{125}I has a longer half-life. This is significant because a thyroid scan with ^{131}I may often deliver 100 rads to the thyroid.

He described a recent preliminary study on figures of merit for ^{99m}Tc, ^{68}Ga and ^{113m}In in which a number of criteria were used to determine which isotope is most effective for a given procedure. These figures of merit relate inversely to the time needed to detect the difference in activity between the target and nontarget regions for 1-in. lesions. In most cases ^{99m}Tc had the highest figure of merit.

He found that the radiation doses to the liver from ^{11}C and ^{99m}Tc were about equal, even though the half-lives differ by a factor of 18. Thus, he concludes that the ultrashort-lived radionuclides may not replace those now being used but will allow for further examination of physiological processes. Even though short-lived isotopes do not seem to reduce the dose to the patient appreciably, he feels they are being used to obtain more information from an examination or to obtain the information more rapidly.

Edward Smith, Hal Anger, Thomas Mitchell and Craig Harris conducted a panel discussion on instrumentation dealing with instrument design. Specifically, they described the need for standardized instrument control panels, improved instruction manuals and wiring diagrams, easy access to test points and component parts, and coordination between medicine and industry to determine instrumentation needs before production. They said that the next decade may bring an expansion of *in vitro* tests which will eliminate the radiation exposure to patients and reduce the complexity of instrumentation. Under these conditions, existing instrumentation would be sufficient.

Wilfred Konneker, Mallinckrodt-Nuclear, spoke on quality control of radiopharmaceuticals, outlining 12 major points of the Good Manufacturing Practice section of the FDA regulations and presenting many facets involved in a total quality-assurance program.

He elaborated on radiopharmaceutical production problems associated with the increased use of short-lived radionuclides. Since some production steps now take place in the hospital, he stressed that the potential value of these radionuclides to the medical profession demands the close cooperation of suppliers, clinicians, medical researchers and governmental agencies to solve formulation and quality-control problems.

William Beierwaltes, University of Michigan Hospital, discussed training and manpower development. The results of his survey conducted in 1964 estimated that perhaps 90% of the small hospitals in the United States maintain nuclear-medical laboratories with no full-time physician trained in nuclear medicine. In many cases, technologists conduct tests with either inadequate or no supervision. He feels that the greatest contribution to decreasing radiation exposure would be to place full-time, well-trained physicians trained in nuclear medicine in every nuclear medical laboratory. There is a need, he says, for about 4,000 of these physicians.

The competition to recruit physicians is considerable because nuclear medicine is too new to attract men on a broad scale. Beierwaltes stressed that it is necessary to develop a residency program in nuclear medicine to compete in recruitment with other medical disciplines. Four levels for recruitment must be considered: the premedical student, the medical student, the intern and resident and the older practitioner who wants to change his specialty.

George F. Archambault, University of Florida College of Pharmacy, spoke as lawyer and pharmacist on the public's expectation relative to the safe and effective use of pharmaceuticals. He illustrated how the history of the food and drug laws evolved from the pressure of public opinion and reminded the participants that they were "opinion molders" on matters related to legal control of radiopharmaceuticals since the public would review their opinions and recommendations.

Archambault outlined practical points concerning sound legal and ethical bases for investigational procedures to protect both the public and the investigator. He confined his subject matter to the tort and criminal malpractice as they relate to clinical or investigational drug practices.

A day-long workshop followed the formal presentations. Four work groups were asked to propose ways of minimizing radiation exposure in nuclear medicine. The following is a summary of conclusions they reached.

1. Since there is no current threshold for genetic effects of radiation, radiation exposure should be kept to a minimum consistent with the risk-versus-benefit concept.

2. Total-body radiation exposure can be reduced by using new radionuclides or labeled compounds which result in a shorter effective half-life, by blocking nontarget organs with nonradioactive compounds and by facilitating elimination of radionuclides from the target organ.

For example, substituting isotopes with short half-lives (^{123}I for ^{131}I) or substituting compounds with shorter biological half-lives (^{131}I cholografin for ^{131}I albumin) will shorten the effective half-life. But in evaluating isotopes with short half-lives, the time-dose relationship must be considered. One must judge which poses the greater hazard—a smaller integrated absorbed dose from a short half-life radionuclide over a short period of time or a larger integrated absorbed dose of a longer-lived radionuclide delivered over a longer period of time. This depends on the differences in radiation effects on subcellular structures as a result of dose-rate deposition from similar cumulative doses. Additional research efforts should be encouraged to determine the radiation effects as a consequence of variations in dose rate.

Two groups reported that more emphasis should be placed on blocking nontarget organs so that a greater portion of the administered dose is collected in the target organ. This will let one reduce the quantity of administered radioactive material, reducing the total body dose.

One group encouraged the use of three current procedures for eliminating radionuclides from target organs: First, continued administration of nonradioactive iodide following thyroid procedures; second, administration of alginates to patients receiving radioactive strontium or calcium and third, administration of laxatives to patients receiving radiopharmaceuticals preferentially excreted by the GI tract. Additional research is needed to extend these approaches.

3. Absorbed dose calculations are used to evaluate the hazard to a patient receiving radiation from a nuclear-medical procedure. The physical aspects of these calculations are well known, but to be more meaningful, further research is needed to evaluate biological turnover data and to determine the significance of the absorbed dose.

4. All the work groups concluded that sensitivity of detection equipment is a primary determinant of the quantity of administered radionuclide and therefore the radiation dose to the patient. One group felt that a 2–10-fold reduction of radiation exposure could result from development of better instrumentation.

Most participants agreed that it is equally important to use the most sensitive and reliable instruments, but two groups indicated that instrumentation is not always used in accordance with sound physical principles. For this reason, standard procedures should be formulated for frequent calibration, and reliable standard radionuclide sources must be made available to insure accurate calibration.

5. Professional and technical personnel are receiving an increasing radiation exposure because of the increased use of high-activity radionuclide-generator systems. Although methods were suggested for reducing exposures, the basic need is to train laboratory personnel to handle the higher-activity short-lived radiopharmaceuticals with the same precautions used in handling therapeutic activities. Film badges alone are not adequate for personnel monitoring, and additional detecting systems are considered desirable for recognizing acute exposures. Periodic *in vivo* or bioassay monitoring was recommended to assess internal contamination levels and reduce the possibility of unsuspected high levels of contamination. Thyroid counts on personnel working with large amounts of ^{131}I and whole-body counting where appropriate is included in suggested monitoring procedures.

6. A majority of the participants agreed that one of the most important ways of reducing radiation exposure is to have a full-time physician responsible for the nuclear-medicine unit who can prevent useless exposures by educating and advising physicians. Because the shortage of trained physicians and technical personnel is an acute problem in nuclear medicine, training requirements and curricula should be formulated for nuclear physicians, nuclear technologists and radiopharmacists to combat the demands. This shortage would be partially solved by establishing a board certification of nuclear medicine as a specialty, which would define the qualifications desirable for physicians who practice nuclear medicine and assure certification of competence in the field. As a recognized specialty, nuclear medicine would have greater attraction for medical students and house staff. Residency programs could be established and support for the training programs provided by various federal agencies, as in other disciplines. A registry and a system of uniform accreditation of technologists would help define qualifications and assure certification of competence in the field.

7. With the advent of radionuclide generators and the demand for chemical modification of other radio-

nuclides, the burden of radiopharmaceutical formulation in hospitals is increasing rapidly. The potential for formulation errors was recognized but there was no agreement reached on how a laboratory can develop the capability for good manufacturing processes. To assure production of safe and effective radiopharmaceuticals in every nuclear-medical laboratory, the following alternatives were presented: A number of participants suggested that pharmaceutical manufacturers provide "preparation kits" with pretested components. Others thought that by decentralizing the pharmaceutical industry, short-lived isotopes could be supplied conveniently. However, an industry representative questioned these recommendations, pointing out that industry can solve the problem if it is given an adequate description of the formulation problem.

One work group proposed that the Society of Nuclear Medicine form a committee to establish uniform manufacturing standards and quality-control procedures for laboratories. The committee could provide basic principles or guidelines that could be easily understood by laboratory personnel. This endeavor would require intimate cooperation between industry and the Society.

Since hospital pharmacists are well trained in dose formulation of injectibles, they can perform effectively in a nuclear-medical laboratory if they have basic training in radiological sciences.

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DETECTION OF TUMORS BY SCANNING

When reporting results of phantom experiments on detection of brain tumors by scanning, authors frequently emphasize the importance of the ratio of tumor-to-brain concentration for detecting the tumor. In fact the absolute concentration is also very important as can be demonstrated easily by scanning phantoms with the same "tumor"-to-"brain" concentration ratios but different absolute concentrations. Furthermore the absolute concentration used is often unrealistically high so that smaller phantom tumors are detected than will be possible in practice.

Telander and Loken (*1*) state that their data from phantom experiments "indicate slightly poorer resolution for scintigraphic systems than predicted by the calculations of Beck (*2*) and Matthews (*3*)." In fact, for the same tumor-to-brain concentration ratio, their results indicate that smaller tumors can be detected than predicted by the calculations of Matthews. Thus Telander and Loken find that for a tumor-to-brain ratio of 10:1 a midline tumor of about 1.7 cm diameter can be detected with ^{99m}Tc (Fig. 3 of their paper in ref *1*), whereas Matthews calculates that only tumors greater than about 2 cm in diameter should be seen (*3*). This discrepancy is to be expected because Telander and Loken use absolute phantom concentrations about ten times greater than those considered appropriate by Matthews. These high concentrations were said to give the same counting rate as obtained *in vivo*, but with the camera the latter would be mainly due to muscle radioactivity and not brain radioactivity. Of course there are also a number of other factors involved, such as collimator efficiency, which are not specified by Telander and Loken.

Telander and Loken also quote both Long and colleagues (*4*) and Matthews (*3*) as evidence that ^{99m}Tc gives tumor-to-brain concentration ratios of 20:1. In fact, this value is that found by Long and colleagues (*4*); Matthews and Mallard find a lower ratio of 12:1. The difference is readily explained because Long *et al* perfused out the blood before measuring tumor and brain radioactivities so that their ratios are higher than for the whole organ *in vivo* due to the small blood volume per unit weight of the brain.

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