

RADIOPHARMACEUTICAL TESTING

There has been in recent years and especially in the last few months considerable controversy concerning what constitutes adequate testing procedures for radiopharmaceuticals at both the pharmaceutical house and the investigator levels. Current concepts and procedures for testing nonradioactive pharmaceuticals do not appear to be appropriate for agents used in nuclear medicine. Most compounds used in therapeutic medicine must be given in much larger quantities as compared to the usual administrative dose of radiopharmaceuticals. Drugs such as antibiotics and innumerable other pharmaceuticals are usually given in gram quantities and are administered over periods of weeks to months. Smaller doses of very potent drugs such as digitalis are also given over prolonged periods of time. With regard to these agents, there can be no doubt that a very exhausting search for both acute and chronic toxicity must be made. Nuclear medicine procedures, however, are unique in that the actual mass of radiopharmaceutical administered is rarely more than a few milligrams and is generally administered only once. The rare exceptions are renal transplant patients. Multiple renal function studies are used to follow these individuals for evidence of incipient transplant rejection. Even then, a specific radiopharmaceutical is used no more than six or eight times during the patient's hospital course.

In the 15–20 years that nuclear medicine techniques have been used as diagnostic modalities, they have proved to be extraordinarily safe. The problems that have been of concern have been related almost exclusively to the potential effects of radiation on the various body organs rather than the pharmacological effect of the nonradioactive carrier involved. Thus it would seem to the undersigned that the degree of animal testing required for a radiopharmaceutical agent should not be as extensive as that required for nonradioactive drugs administered in large quantities for long periods of time. The question then arises: What constitutes proper or appropriate testing for a radiopharmaceutical? It would appear that a search for an LD₅₀ for such drugs would be absurd. Likewise, chronic toxicity experiments using enormous quantities of radiopharmaceuticals in large numbers of animals over a period of months would be both unreasonable and extraordinarily wasteful. On the other hand, it would

appear that acute toxicity experiments using very large quantities of the finished radiopharmaceutical in multiple animal systems would provide the greatest and most useful predictive information concerning the radioactive agent's effect on the human being. In such testing systems, one must be cognizant of the fact that the very solution in which the agent is dissolved may be the basis for toxicity and pathological changes [sodium chloride concentration in ^{99m}Tc-Fe-ascorbic acid complex—see method of Stapleton, et al (1)].

The public deserves to be properly protected from the potential dangers of radiopharmaceuticals; however, they also deserve to receive the benefits from newer and better radiopharmaceuticals. Under existing pharmaceutical testing programs, progress is excruciatingly slow. Currently, the radiopharmaceutical field is burgeoning with new compounds, some of which have important clinical value. However, until a better system of evaluating the safety of these agents is worked out, there will continue to be an enormous time lapse between the discovery of a new radiopharmaceutical and its eventual availability to the nuclear medicine community. Efforts must be made to alleviate this problem or the future growth of the field of nuclear medicine will be stultified.

We recommend that the Special Committee on Radiopharmaceuticals of the Society of Nuclear Medicine address itself to this important problem. It is our belief that this is an urgent problem deserving of the highest priority. It is our hope that appropriate recommendations will be forthcoming at an early date and that such recommendations will serve as guidelines to investigators, radiopharmaceutical suppliers, and the concerned agencies of the U.S. Government.

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REFERENCE

1. STAPLETON JE, ODELL RW, MCKARNEY MR: Technetium iron ascorbic acid complex; a good brain scanning agent. *Amer J Roentgen* 101: 152–156, 1957