Nuclear Medicine in Clinical Pediatrics

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Nuclear Medicine in Clinical Pediatrics

For Julius and Meyer Bloom, physicians,
for their inspiration, humanity,
and dedication to their patients.

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Preface

It is well accepted by the medical profession that pediatricians maintain a unique relationship with their patients and patients' families. This relationship begins at the dawn of life and frequently continues into adulthood, requiring the pediatrician to be neither first nor last to adopt new diagnostic and therapeutic methods. A realistic, cautious approach to the use of techniques involving complex technical information and equipment assures that the safety, reliability, and value of the studies is proven before they are made routine.

The rapid growth of pediatric radiology as a viable subspecialty is witness to this philosophy, and the use and contributions of the field are remarkable. In fact, there are pediatric "neuro"-radiologists and pediatric "cardio"-radiologists practicing in many centers. Caffey's desire for reduced pediatric patient exposure to ionizing radiation has been fulfilled by advances in technology and physician education (Caffey J, ed: *Pediatric X-Ray Diagnosis,* Chicago, Year Book Publishers, 1961, p vii). His concept of "minimal radiation dose" has a corollary later in this book (Chapter 16, p. 209). The similarities in the early beginnings of the field of pediatric radiology and pediatric nuclear medicine prompted us to solicit the comments of S. Scott Dunbar early in the preparation of this text because of his distinguished career in this field.

Equally dramatic to many of us in nuclear medicine has been the response of pediatricians to the applicability of nuclear medicine procedures to clinical pediatric problems. Again, because of technological advances (i.e., short-lived radiopharmaceuticals and improved detector systems) radiation exposures have become less of a deterrent to studying pediatric patients, and virtually all studies available can be performed in patients of all ages with "minimal irradiation dose".

The seeds for pediatric nuclear medicine were probably sown more than thirty years ago in Berkeley, as Myers points out in the Introduction to this book. Just ten years ago, a group of interested physicians met in Seattle under the auspices of Robert A. Aldrich, Professor of Pediatrics at the University of Washington, for the 45th Ross Conference on Pediatric Research, entitled "Clinical Use of Radioisotopes in Pediatrics". At that meeting a dozen topics were discussed, none of which involved the performance of an organ imaging technique. At the symposium held at Children's Hospital of San Francisco one decade later (upon which this

text is based), 90% of the discussions dealt with such imaging procedures. It is no surprise then, that in this short time, transfer of the data from the nuclear medicine specialist to the pediatrician has been delayed.

In many instances, procedures have been revised and improved by the time the original work finds its way into the appropriate clinical literature. This publication is an attempt to deliver the latest and most pertinent information on the useful procedures avaliable to practicing pediatricians, house officers, and nuclear medicine specialists who only occasionally see pediatric patients. It is understood that even those of us devoting most of our time to pediatric problems may not be providing all we might in service. To this end, we have tried to provide a current and inexpensive source book to make available and better understood the relatively new techniques of "pediatric nuclear medicine". Speakers for the symposium and their collaborators for this publication are all recognized for their expertise in the areas they have prepared. Tables and appendices are offered as a guide to the specialist unfamiliar with pediatric doses, normal values, etc., but are just that—a guide—and reflect only the experience and opinions of the authors and contributors. We urge that all who use them recall that, as A. Graeme Mitchell quoted, "the child is not a little man".

All studies involving the administration of radioactive substances to children should be individualized to answer the specific question asked by the referring pediatrician and the appropriate material and dose selected. "Cookbook" studies should never become the standard of practice. We further urge the rational use of sedation to assure high-quality studies and to prevent reinjections. Our small patients and their devoted physicians require that we do no less.

We wish to express our thanks and appreciation to all those who worked hard to see this publication to its completion. For their constant encouragement and support, a special thanks to the Women's Board of Children's Hospital of San Francisco, and their President, Mrs. Charles F. Lowrey. For assistance in technical matters, thanks to Marye Rose, Rose Ann Anderson, Judy Fletcher, the staff at Continuing Education in Health Sciences, University of California, San Francisco, and all those at the Society of Nuclear Medicine.

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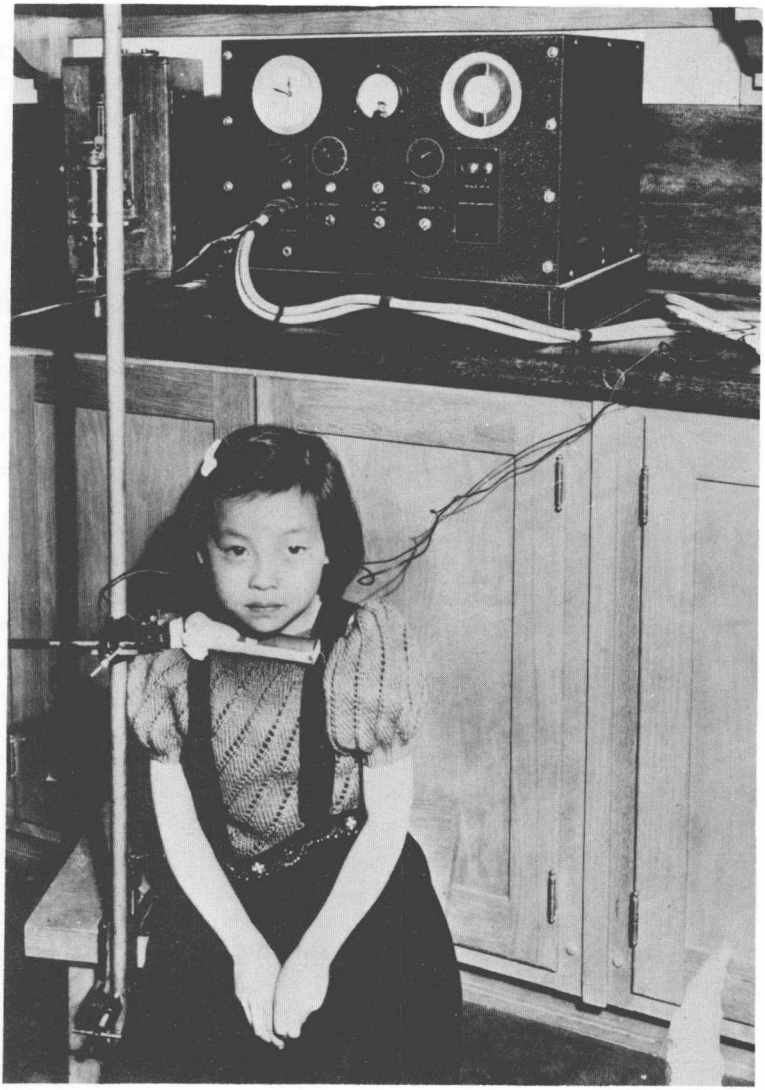

Fig. I-1. **Method published in 1941–1942 (*1, 2*) for measuring the radioiodine uptake by the thyroid in situ by means of the interactions of penetrating γ-rays with a Geiger-Mueller tube placed against the neck over the gland.**

Contents

Introduction:

HISTORICAL PERSPECTIVES

William G. Myers, Ph.D., M.D.*

Great institutions are but the lengthened shadows of great men

Figure I-1 (frontispiece) depicts the method devised by Doctor Joseph Gilbert Hamilton (Fig. I-2) to measure the uptake of radioiodine by the thyroid gland in situ. The Geiger-Mueller tube was placed against the anterior neck over the child's thyroid. It detected penetrating γ-rays emitted from "inside-out" by radioiodine accumulating in the gland, as a function of time.

Figure I-1 was published first in a physics journal in June 1941 (*1*). Similarly, many of the early biomedical applications of man-made radioisotopes first were described in physics journals. For example, much of the April 1941 issue of *The Journal of Applied Physics* contained brief disclosures of many varieties of such uses.

The picture in Fig. I-1 (frontispiece) was shown at a Symposium on the Cyclotron, held in San Francisco in December 1941. And it appears again in the November 1942 issue of *Radiology* (*2*). The seven papers presented at The Cyclotron Symposium fill this entire issue; and they constitute good sources of the early history of "nuclear" medicine during the first half dozen years after the announcement of the finding of artificial radioactivity in Paris early in 1934 (*3*).

It is appropriate, therefore, that the symposium on "Pediatric Nuclear Medicine" was held in San Francisco, just three decades after The Cyclotron Symposium there in 1941. For, the San Francisco Bay Area is the "cradle" of much of nuclear medicine. And many of the pioneers in this region are active still.

Here it was that Professor Ernest Lawrence and his coworkers (*4*) generated radioactive Nitrogen-13 in his cyclotron in Berkeley by bombarding carbon with deuterons, less than two weeks after this possibility had been projected by the discoverers of artificial radioactivity (*3*). Seven

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Fig. I-2. **Joseph Gilbert Hamilton, M.D. He was the originator of "inside-out" assays in situ by means of γ-rays emitted by man-made radionuclides. He was born 11 November 1907 in Waverly, Massachusetts. This picture was made 23 April 1956 by the author at The Crocker Medical Cyclotron Laboratory (*6*) of which Doctor Hamilton then was director. He died of leukemia on 20 February 1957, in Children's Hospital in San Francisco.**

months later, he became the father of nuclear biomedicine when he found that radioactive sodium could be produced with his cyclotron in multi-millicurie amounts and he prophesied (*5*) . . . "In the biological field radio-sodium has interesting possibilities that hardly need be emphasized here" . . . When his 37 inch cyclotron went into operation in 1936 (*7*), it became evident that it was the only practicable instrument with which to generate radionuclides of "physiological" elements in amounts adequate for the zestful biomedical colleagues who soon clustered nearby to embrace new opportunities provided by the man-made tracer (*9*) "radio-indicators."

And among these workers was Ernest's physician brother, John Lawrence. After successful results in treating leukemic mice, Doctor John became the father of "radiopharmaceuticals" when, on Christmas Eve in 1936, he administered ^{32}P-phosphate to a patient who had leukemia (*8*). He and his colleagues published (*10*) their early findings with radiophosphate for treatment in more than 100 patients among the papers of The Cyclotron Symposium.

The 37-inch cyclotron was used in the discovery of two radionuclides that are used commonly in nuclear medicine today. Iodine-131 was announced by Livingood and Seaborg on 15 June 1938 (*11*). And, less than five months later, on 1 November 1938, Segrè and Seaborg reported on the discovery of what is now known as 6-hour Technetium-99m, together with the finding that it is the daughter of a 66-hour molybdenum radio-

nuclide (*12*). It is estimated that more than ten percent of patients hospitalized in the United States now receive injections of a form of Tc-99m in various diagnostic procedures (*13*), chiefly when used in conjunction with a scintillation camera.

The next year, in 1939, Ernest Lawrence announced . . . "The medical cyclotron of the William H. Crocker Radiation Laboratory" . . . and that . . . "the yield of radioactive iodine is 20 times greater at the higher voltage" . . . generated by the new 60-inch apparatus (*6*). Later in 1939 he was awarded The Nobel Prize in Physics, and became the first of a dozen Nobel Laureates to grace the campus of The University of California at Berkeley, including Professor Seaborg (1951) and Professor Segrè (1959).

The impact of the successively enlarged cyclotrons on biomedicine was described ably by Doctor Paul C. Aebersold in his first paper of the 1941 Cyclotron Symposium on (*7*) "The Cyclotron: A Nuclear Transformer" and later (*8*) in his succinctly comprehensive survey of "The Development of Nuclear Medicine."

Presumably it was Professor Robert Newell at Stanford University who coined the name "Nuclear" Medicine (*14*). Because he anticipated many of the ramifications of this emerging new lore, he staunchly supported The Society of Nuclear Medicine in its early formative years. Also he gave us the focused collimator.

Professor Robert Hofstadter, also at Stanford University, discovered the thallium-activated sodium iodide crystal used in virtually all of the present scintillation detectors that are central to much of nuclear medicine, and without which inside-out imaging would not have evolved to its present state.

Hal Anger invented the scintillation camera in 1957 (*15, 16*) at The Donner Laboratory of Medical Physics, The Lawrence Berkeley Laboratory, on the campus of The University of California at Berkeley. And he displayed the first working model of this camera at the meeting of The American Medical Association in San Francisco in June 1958. The NaI(T1) crystal, which was only four inches in diameter and one-fourth inch thick, was viewed by seven multiplier phototubes. He demonstrated good images of the distribution of Iodine-131 in normal and diseased thyroid glands made with the pinhole version of this first scintillation camera.

By 1961, Anger's scintillation camera at The Donner Laboratory was equipped with a NaI(T1) crystal eight inches in diameter and one-fourth inch thick, which was viewed by nineteen phototubes. The first industrially-fabricated version of the scintillation camera, at this stage of development, was installed in the author's laboratory at The Ohio State University in September 1962 (*17, 18*).

A year later, Anger had built a scintillation camera with the diameter of the crystal increased to 11½ inches and the thickness to one-half inch

(*16*). Since then, the thousands of scintillation cameras installed in laboratories throughout much of the world are used to make many millions of images annually; and . . . "The Anger scintillation camera has revolutionized the practice of clinical nuclear medicine" (*19*).

Anger has provided a scintillation camera at The Donner Laboratory for several years that is equipped with a NaI(T1) crystal sixteen inches in diameter and one-half inch thick which is viewed by 37 multiplier phototubes. Thus, it would be well suited for the making of "whole-body" images of distributions of γ-nuclides in small babies.

The I-131 (*11*) used by Hamilton and Soley in 1939–1940 (*20, 21*) was generated in Professor Ernest Lawrence's 60-inch medical cyclotron (*6*). The bombarded target contained natural tellurium, which is comprised of eight stable nuclides. Because indiscriminative Geiger-Mueller tubes were used for the inside-out assays depicted in Fig. I-1 (frontispiece), it seems probable that, when counting was done soon after bombardment, two radionuclides may have been involved (*24, 28*) which had not been discovered yet, viz. Iodine-123 and Iodine-125!

Professor I. Perlman used the same medical cyclotron (*6*) a decade later in the discovery of the 13-hour Iodine-123 (*22*), when antimony was bombarded with He-4 ions. Efforts designed to match the advantageous physical properties of Iodine-123 (13-hour half-life, 159-keV γ-ray, no beta particles) with the developing scintillation camera were reported briefly in 1962 (*23*). Especially significant for pediatric nuclear medicine is the greatly reduced radiation exposure, together with the much improved resolution of images, when cyclotron-generated I-123 replaces I-131 (*25–28*).

These spin-offs of Professor Ernest Lawrence's intuition now are recognized by the nuclear medicine practitioners and pediatricians who are embracing the commercial availability of I-123. This is because it is the "ideal" among the 29 radionuclides of iodine (*25*) for studies involving radiation exposures not exceeding a few percent of those from I-131, as well as for generating images having superior resolution by means of The Anger Scintillation Camera (*27–28*).

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