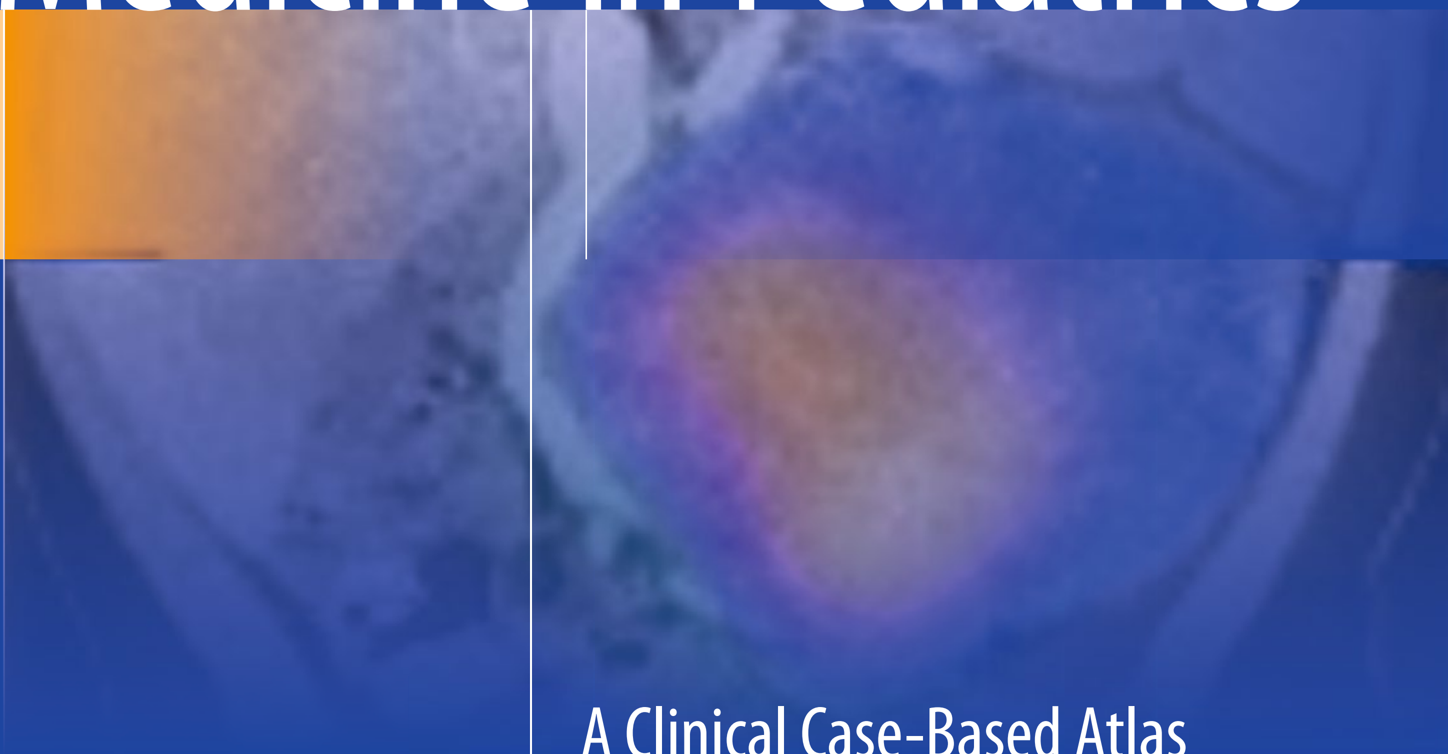
Maria Carmen Garganese
Giovanni Francesco Livio D'Errico
Editors

In collaboration with
Milena Pizzoferro · Maria Felicia Villani

Conventional Nuclear Medicine in Pediatrics



A Clinical Case-Based Atlas

Springer

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To Professor Gianclaudio Ciofetta
who dedicated his life to pediatric nuclear medicine and has contributed
to our vocational education with humanity and scientific strength
Our work is a way to remember him and thank him for what he has given us
and all the young patients.

Preface

> That is a good book which is opened with expectation, and closed with delight and profit. (Amos Bronson Alcott)

When Professor D'Errico and I decided to write this book, myriad of thoughts and feelings went through my mind.

The first feeling was the delight of being able to share with him the writing of a work started when I was "young," and he was the first tutor when I was a resident in nuclear medicine: he asked me what I was able to do and I said "nothing at all"!

The second one was the sadness for the passing of Professor Gianclaudio Ciofetta, to whom this work is dedicated, who would have been proud to see his greatest wish realized.

The last one was the enthusiasm felt in translating in word a daily experience – made of kindness, of fears, of commitment, and of devotion to the children who pass every day through our unit – in order to create something that can help those who approach pediatric nuclear medicine and those who wish to find a hint or a method and an answer I hope, a tangle of possibilities that open up in front of a child and in front of a test to which a child is submitted.

Furthermore, the thoughts about the best and the most educational possible way to set up and to perform the various topics and the study of the various body districts, my wish is to provide to those who open the book, searching a help or an answer, more and more than they search, to find a case similar to his one and an adequate answer to his question.

The work was long and it would not have started without the help of my colleagues, Dr. Milena Pizzoferro and Dr. Maria Felicia Villani, who, with utmost care and great detail, have researched the clinical cases, have made the scintigraphic images for publication, and supplemented them with radiological images. They have left out no detail, no possible explanation, no images, and no texts. And all the iconographic documentation would not have been so complete and so made without the cooperation of the technical staff, Gaetano Masi, Stefano Chiapparelli, and Elisa Villanucci, and nurses – Consilia Lella and Filomena Petrucci –that, with professionalism and affection, have followed and cuddled the children and their parents during the execution of scintigraphic studies.

Performing quality studies on children without using anesthesia is a daily challenge; it is a goal that we try to achieve every day, keeping high our guard and also the commitment toward the standards that the "Bambino Gesù" Children Hospital child struggles to respect and to keep.

Dutiful thanks go to Professor Tomà and to all our fellow radiologists and clinicians in our hospital who actively participated in the drafting of the various chapters of the book but also to all those of which the name does not appear but who work and take part in our activities, collaborating in the good success, each one for his role.

Special thanks also go to the colleagues of the Medical Physics Unit – Dr. Vittorio Cannatà and Dr. Elisabetta Genovese – who are alongside us every day, helping us to respect the continued efficiency of our instruments and handling all aspects of dosimetry.

Affectionate thanks to Professor Paolo Caione with whom we have shared countless patients and numerous scientific discussions.

This book is the result of collaboration, and it is based on a daily teamwork. Each chapter is derived not only from our consolidated experience by now but also from the exchange of information and from the contact with the specialists who formulate the questions which we strive to answer in a complete, clear, and standardized way, making the interpretative doubts clear to them. It shows that we can and we must work well with humility. It strongly shows that conventional nuclear medicine can still give much if the studies are conducted properly and integrated with the supporting diagnostics.

We hope that the readers, who occasionally perform studies on children, find in the book what we have proposed they will find, and we hope that it is also useful to all the colleagues who deal with pediatric nuclear medicine as a part of their activities not dedicated to children.

Rome, Italy Maria Carmen Garganese

Preface

It was in the early 1980s that I get interested in pediatric nuclear medicine and, in particular, of pediatric nephro-urology. In the 1990s, the young doctor Garganese meets me and "pediatric nuclear medicine," and, since then, this field has represented her "great love."

Nuclear medicine, revealing the physiological processes in vivo, has had, in recent years, incredible progress, but, since the child is not a "young adult," it is not enough to adapt procedures performed in adults to the age and size of the child. Considerable progress has been made in the field of pediatric nuclear medicine due to the high capacity of earlier diagnosis, easier management of young patients, and treatment that have benefited children. Just to this reason, pediatric diagnostic paths have been developed internationally (e.g., health.wa.gov.au). The pediatric nuclear medicine has become an increasingly important tool both to follow the success of therapy and to assess the progression. In other words, the development of pediatric nuclear medicine is because it provides information about the condition of the child physiologically, fast, safe, sensitive, and minimally invasive.

The novelty of this work consists in providing a systematic approach, as a textbook, with the simplicity of consultation of an atlas, on a niche topic in nuclear medicine, so important and widespread as the pediatrics.

This book, entitled *Conventional Nuclear Medicine in Pediatrics: A Clinical Case-Based Atlas*, fills a gap in the literature of a reference tool "clinical case based" in pediatric nuclear medicine imaging, by a collection of richly illustrated teaching cases and problem-solving, dealing with clinical history, technical informations, workflows, image descriptions, and pitfalls.

Each chapter describes the diagnostic nuclear medicine molecular imaging based on the availability of sensitive and relatively specific radiopharmaceuticals tailored for different targets that can be expressed in this complex pediatric scenario.

Authors with different tasks (M. Pizzoferro, M.F. Villani, and M.C. Garganese as nuclear medicine physicians; G. Masi, S. Chiapparelli, and E. Villanucci as nuclear medicine technologists; and C. Lella and F. Petrucci as pediatric nurses) contributed by writing Chap. 1 about the need for a dedicated "teamwork" and several informations on the management of children such as reception, administration, and interaction with parents.

In Chap. 2 ("radiation exposure"), V. Cannatà, M. Longo, and E. Genovese provide information about the activities to be administered, according to dosimetric considerations.

The role of the nuclear medicine physician, in the usual pediatric clinical scenarios, is carefully covered, in Part 2, "Clinical Pediatric Practices," with the important contribution of many coauthors, skilled clinicians in each field.

N. Capozza, S. Nappo, G. Torino, E. Mele, G. Di Zazzo, G. Mosiello, M.L. Capitanucci, M. De Gennaro, and D. Barbuti, expert co-workers, treat, in Chaps. 3, 4, 5, 6, 7, 8, 9, and 10, the different aspects of nephro-urology.

Oncology was treated by F. Locatelli, L. Vinti, A. Mastronuzzi, A. Castellano, R. Lombardi, and D. Barbuti in Chaps. 11, 12, and 13, while gastroenterology was dealt by L. Dall'Oglio, T. Caldaro, P. De Angelis, R. Tambucci, F. Torroni, G. Angelino, L. Del Prete, F. Rea, V. Balassone, A.C.I. Contini, E.F. Romeo, F. De Peppo, G. Torre, M. Candusso, M.S. Basso, A. Pietrobattista, A. Infante, and L. Monti in Chaps. 14, 15, 16, 17, 18, and 19.

F. De Benedetti, A. Insalaco, and A. Krzysztofiak have contributed, in Chaps. 20 and 21, interesting clinical cases about inflammation–infection and rheumatology disease; L. Menchini, clinical cases about bronchopneumology (Chap. 27); and A. Grossi and G. Ubertini, clinical cases in endocrinology field (Chaps. 22, 23, 24, 25) and G. Natali and D. Barbuti, benign bone disease (Chap. 26).

We are very fortunate to have had the contributions of coauthors, also our colleagues, skilled clinicians in each field, whose experiences enrich this atlas, and therefore, we are deeply indebted to all of them.

Our close collaborators, Dr. M. Pizzoferro and Dr. M.F. Villani, deserve special acknowledgments for the care given to provide images and clinical cases.

Rome, Italy — Giovanni Francesco Livio D'Errico

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Part I

General Considerations

Paolo Tomà

1.1 Introduction to Pediatric Imaging in Multimodality Diagnostic Era

As a pediatric radiologist, I have seen the impact of SPECT and PET on the clinical care of children. Our imaging practice has had to change to accommodate the powerful nature of these new images.

Image fusion overlays two or more three-dimensional (3D) image sets of the same or different imaging modality that are in the same orientation in the same space. Anatomic and functional imaging is complementary; this is the metaphor of the relationships between radiologists and nuclear medicine physicians.

In my opinion, nuclear medicine is a crucial part of pediatric radiology.

Pediatric radiology has peculiar characteristics depending on anatomical development and specific clinical conditions related to the different stages of growth. Other peculiarities specifically related to pediatric radiology include radiation safety and the need of dedicated environments and approaches.

In both pediatric and adult patient care situations, there are family members with whom the imager must interact. However, in the pediatric setting, there are several unique features in the relationship among imager, patient, and family. Most of the complaints by parents and families are not related to technical errors; they are more commonly related to issues of professionalism and communication.

Providing child-friendly surroundings may help to ease a young child's anxiety and cause him or her to be more cooperative. Paintings on the walls and equipment and cartoonish figures in the examination rooms can be helpful. Eliminating or minimizing painful portions of the examination can also be very helpful in keeping a young child cooperative.

In general, the physicians who choose to go into pediatric subspecialties, as well as health care workers who choose to work at pediatric institutions in general, have to be nice, gentle people. Aggressive, power-hungry people cannot work with children.

This edition of the book comes at a very propitious time. Revolutions in medical imaging are modeling and quantification. Imaging of physiologic and cellular processes displays them in four dimensions (three-dimensional images over time).

The goal of the book is to provide a comprehensive text on the clinical applications of nuclear medicine in a pediatric population.

As some techniques have faded (e.g., scrotal scintigraphy), others have been added to the nuclear medicine arsenal. The most significant development has been the dissemination of positron emission tomography (PET) into pediatric practice.

Writing a book is a task that requires time and commitment from many people.

I express appreciation to MG, who has transformed their lives in a text. Her dedication is reflected in the high quality of the final product.

It is my sincere hope that readers will find this work to be a cornerstone of pediatric imaging and one that they will use frequently in their daily practices.

Management of the Pediatric Patient: A Teamwork

1

Milena Pizzoferro, Maria Felicia Villani, Maria Carmen Garganese, Gaetano Masi, Stefano Chiapparelli, Elisa Villanucci, Consilia Lella, and Filomena Petrucci

1.1 Introduction

Pediatric nuclear medicine refers to imaging examinations performed in babies, young children, and teenagers. Carrying out nuclear medicine procedure on children requires a completely different approach than on adults. The complexity of the examination varies depending on the age of the patient, the degree of cooperation, clinical conditions, and duration of scintigraphic acquisition. Depending on the increasing complexity of pediatric nuclear medicine studies, a higher level of department expertise is necessary for the delivery of good quality examination and safe patient care.

In a pediatric nuclear medicine department, all members must be proficient in performing their competencies according to their role, and a trained teamwork is the winning strategy to achieve the main goal, getting a diagnostic imaging that allows to accurately respond to specific clinical question.

Within a framework of a well-coordinated staff (including specialized training pediatric nurse, technician, and nuclear medicine physician), it is easier to create a positive atmosphere that serves to take the child cooperation, limiting the sedation in few selected children.

Pediatric patient management requires considering the special status of these patients in relation to age and medical condition depending on the underlying disease.

Working with pediatric population requires adequate awareness: in order to obtain appropriate acquisition standards, the team approach must be shaped to the child's mind-set, rather than fitting the child into the paradigm of adult examinations.

In fact, children are not miniature adults and, as well as the normal values of the vital parameters of infants and children are different than adults, even methods of communication should be adequate for their developmental age.

Besides, pediatric patients are children with special health care needs who could have any type of condition that may affect normal growth and development; this may include physical disability, acute or chronic illness, peculiar clinical condition (pain, technological dependency, etc.). During the diagnostic procedure, even when the staff use distraction techniques to hold child still and calm, health care professionals must be ready to manage a possible worsening of the patient's clinical status (Fig. 1.1).

Taking care of a pediatric patient includes parental management, and the attitude of all staff members must be positive toward the child and parent (or other family components). In "family-centered approach," the family's input is the major driving force to achieve a good cooperation of the child and a high degree of satisfaction of parents.

A department structured with colored paintings on the walls, playful environments (equipped with toys, books, video games, or DVDs) and child-friendly spaces could help foster a welcoming accommodation, but it does not replace the right atmosphere that the nuclear medicine staff must be able to create from the first patient approach.

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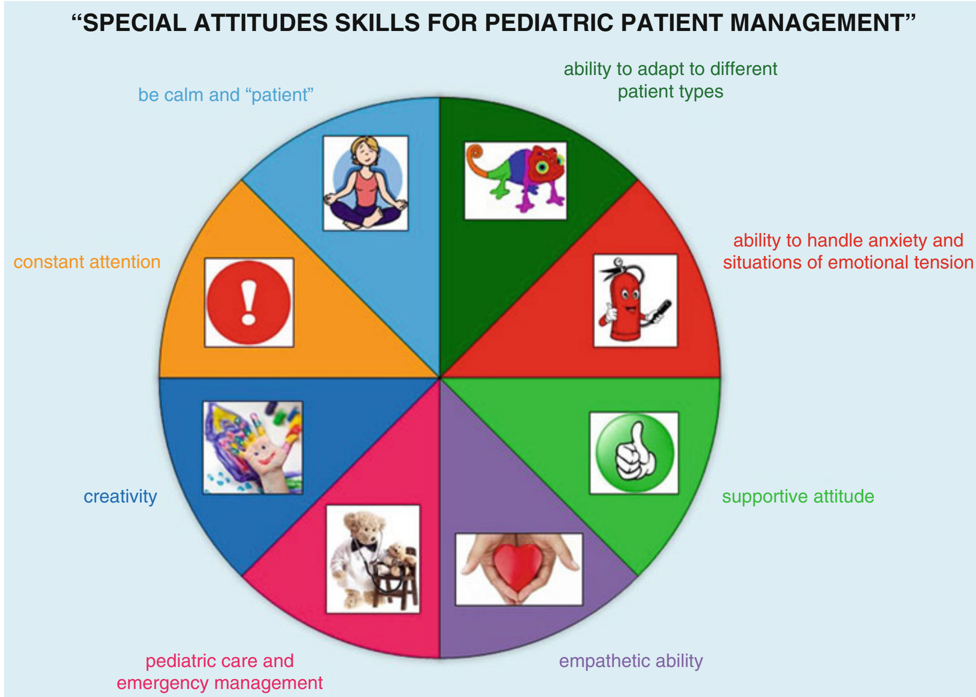

Fig. 1.1 Special attitudes and skills for pediatric patient management

1.2 Accommodate the Child and the Parents

Nurses usually handle the reception of the child and the parent. Based on a first quick observation, it is crucial to define an individual approach evaluating a child's personal features and familiar or sociocultural influences. In all cases, the first child approach must be slowly and calm in order to set the basis of a good relationship with all the nuclear medicine staff. The reception of pediatric patients must include an initial evaluation of clinical condition to set up an appropriate assistance and monitoring level in case of special health care needs.

From the first moment the child and parent enter the department, all members must be honest with both of them, in order to create a trusting relationship. In the case of both children and adolescents, the staff members must be able to adapt to different patient types, involving them in every moment and explaining the whole procedure in simple terms.

Starting from the first contacts, parents and children must be introduced into the department's environment by a specific education about correct paths within the department (with particular regard to the use of bathrooms and disposal of radioactive diapers) and explanation of the use of dedicated tools available in the waiting room (bottle warmer, electronic devices, etc.). To avoid the risk of accidental falls, it is necessary to enforce the standards of child safety, inviting the parents to buckle up the stroller and constantly monitoring the baby should not run or climb in the waiting room.

Parents are encouraged to stay with their children throughout every part of the examination (with the exception if the child's mother is pregnant), emphasizing the importance of their role in supporting the child for a good outcome of the examination. Generally, the idea to perform a scintigraphic examination generates fear in the child and the parent. Professionals in charge of the pediatric patient management have to be adequately trained handling anxiety and situations of emotional tension of child and the parents. This peculiar ability is closely related to a personal attitude (prone to a supportive and empathetic approach) as well as the capability to provide clear information.

To gain the trust of the child, put him at ease and reduce anxiety; one of the most used tricks in pediatrics is entertaining the patient speaking about his everyday life or family members before starting with the diagnostic procedure. Explaining same symptoms by metaphors could be useful to create a direct line of communication (i.e., we usually describe the puncture syringe similar to a mosquito bite or a little pinch).

Providing clear information is also the best form to reduce anxiety for parents. During the interview for the anamnesis and the acquisition of the written informed consent, nuclear medicine physician must explain the entire scintigraphic procedure, stressing the clinical utility within the global diagnostic–therapeutic iter. Providing instructions on how parents can collaborate together with staff is a helpful way to motivate them to be part of the team in order to improve the impact of diagnostic examination on their child.

One of the most difficult steps is minimizing and communicating radiation risk in pediatric nuclear medicine. Generally, parents can understand that their child will undergo an appropriate medical imaging test, but the explanation about radiation risk associated with nuclear medicine examination is always a critical point.

Nuclear medicine practitioners must be able to effectively communicate that the dose range associated with most nuclear medicine procedure results in a low radiation exposure and a very low risk of detrimental health effects. In case of scintigraphy, with a medium or high radiation exposure level, it is necessary to clarify that the potential risk associated to ionizing radiation remains still low compared with the benefits derived by the diagnostic information, unattainable using other imaging procedures.

Depending on the type of nuclear medicine exam, nuclear medicine physicians have to provide adequate radioprotection instructions to avoid undue radiation exposure of other children or pregnant women; in order to reduce global patient radiation exposure, proper indications should be suggested (good hydration with water or whatever is pleasing to the child and frequent urination).

1.3 Administration of Radiopharmaceutical

Depending on the type of nuclear medicine exam, the radiotracer is either injected into the body, swallowed, or inhaled as a gas in order to evaluate the functional information of the organ system being examined. Except for intravenous injections, most nuclear medicine procedures are painless and rarely associated with significant discomfort or side effects.

1.3.1 Endovenous Administration

If the tracer is given intravenously, a small needle is used to inject the radiotracer and removed immediately after. At times, an indwelling intravenous catheter may be used if it is already present, in case of multiple phases of administration or provocative examination (i.e., stress myocardial scintigraphy), when the patient is in poor clinical conditions. In oncological patients, the use of central venous catheter is limited only to certain types of scintigraphic examinations with proper antiseptic precautions.

For a successful intravenous injection, a team approach is necessary to distract the child, to properly immobilize the limb of the child, and to explain to the parent, as he may cooperate reassuring the child. During administration, a bed pad must be positioned under the injection site to limit potential contamination. Different immobilization techniques are used depending on the age of the child and administration site (Fig. 1.2).

1.3.2 Aerosol Administration

The radioaerosol can be inhaled through deep breaths, using a mask of appropriate size for age. In case of uncooperative patient, the radioaerosol can be adequately administered during the whole inspiration phase, even if the child cries. Immediately following the radioaerosol inhalation, the patients must rinse their mouth by gargling, when the child is able. Then, the patient is placed in the supine position, and a gamma camera detector is posteriorly positioned for acquiring lung radioactivity. After an initial qualitative evaluation, if a satisfactory distribution is not obtained, a number of extra inspirations must be performed. Measurement of the administered radioactivity dose can be performed calculating the ratio of first frame counts and a conversion ratio, specific for each gamma camera.

Fig. 1.2 The newborn is made to lie on the stretcher, the parent remains close to the head of the child, the nurse immobilizes the upper limb (arm or hand), while the doctor administers (**a**); in the case of administration to the foot, the use of sandbags is useful to facilitate the blocking of the contralateral leg (**b**). The child is seated on the parent's legs that blocks the baby's legs between his, the nurse immobilizes the child's arm or hand, while the doctor injects the radiopharmaceutical (**c**)

1.3.3 Meal Administration

1.3.3.1 Gastric Emptying Scintigraphy (GES) Protocol

For gastric emptying scintigraphy, radionuclide-labeled test meals are used. The test meal can be liquid, semiliquid, or semisolid, according to the normal meal that the patient under study would generally consume. When swallowed, the radiotracer has no taste. Labeled meals, milk scan as well as homogenized, yogurt or chocolate drinks, are used for gastric emptying studies in newborn, infants and children. The meal should have a pleasant taste to encourage a quick and complete recruitment of the meal, ensuring a good nutritional intake to obtain reliable functional information about gastric emptying parameters. A good amount of meal taken is also closely linked to the sensitivity of scintigraphy in detecting the presence of gastroesophageal reflux. Meals must be consumed within a 10-min period, after which the scintigraphy study must be started to avoid the beginning of intestinal progression of the meal from the stomach.

In case of oral feeding, one of the parents can administer the meal, so that the child does not notice the difference from the usual. The nurse provides instructions to parents to avoid contamination, supervises the administration, and supports the parent in case of difficulty. The necessary precautions to limit contamination in case of vomiting must be taken always.

In such a condition, the technique is completely noninvasive, whereas in evaluating children with feeding difficulties, the nurse can place a nasogastric tube which can be removed after meal administration. If a child is unable to feed orally, the nurse manages meal administration using nasogastric tube or percutaneous endoscopic gastrostomy when already positioned. Meal administration is with the patient lying on the bed of gamma camera and, by monitor persistence, nuclear medicine physician evaluates gastric filling according to the patient's capability. Habits of the patient and presence of indirect signs (as high grade of gastroesophageal reflux or the beginning of intestinal progression of the meal from the stomach) allow to determinate the right amount of meal (Fig. 1.3).

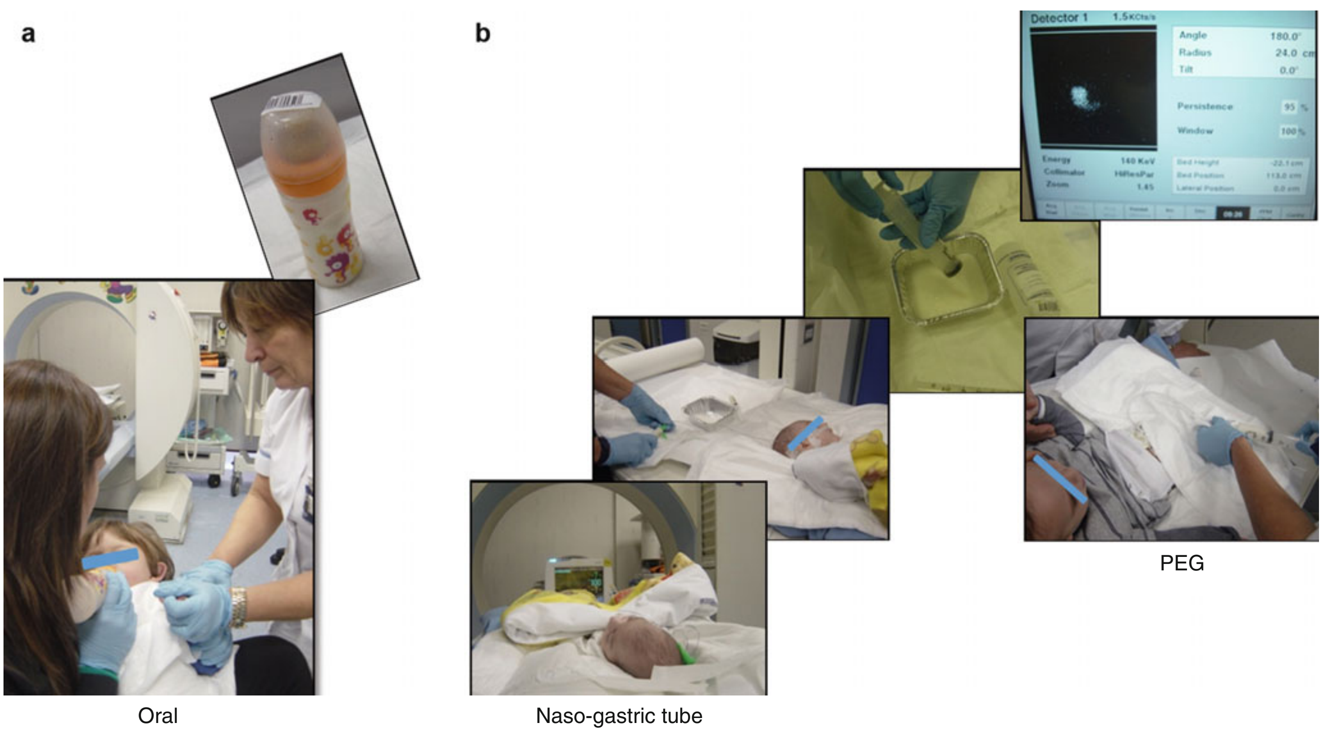

Fig. 1.3 In case of oral feeding, one of the parents can administer the meal so that the child does not notice the difference from the usual. The nurse provides instructions to parents to avoid contamination, supervises the administration, and supports the parent in case of difficulty (**a**). If a child is unable to feed orally, the nurse manages meal administration using nasogastric tube or percutaneous endoscopic gastrostomy when already positioned (**b**). Meal administration is with the patient lying on the bed of gamma camera and, by monitor persistence, the nuclear medicine physician evaluates gastric filling according to the patient's capability. The right amount of meal is determined by the habits of the patient and by the presence of indirect signs as high grade of gastroesophageal reflux or the beginning of intestinal progression of the meal from the stomach

1.4 Acquisition of Images: Take the Child's Cooperation

Though nuclear imaging itself causes no pain, children may experience some discomfort from having to remain still during imaging, in particular for procedures of prolonged duration.

Approaching as much as possible the gamma camera to the patient is crucial to achieve good quality images using the recommended pediatric amounts of radioactivity, but it could be technically difficult when the child is frightened and does not cooperate. In a pediatric nuclear medicine department, drug sedation can be used only exceptionally using an alternative way, consisting in an adequate approach of the patient. Specific education of technologists is required, including proper handling of the child during the procedure and adequate psychological attitudes toward child and parents. Parents are encouraged to stay with their children to help them remain calm and still during imaging.

From a technical point of view, the way to get better results with less stress for the baby is to match the time of the acquisition with the natural sleep of the child. The importance of this simple method must be clearly explained to the parent who, knowing the habits of the child, is the major driving force to achieve this goal. In such a way, it can be possible to perform procedures of prolonged duration (as SPECT acquisition) or whole-body acquisition protocol without sedation. In order to avoid having scintigraphic images affected by the presence of radiourine, it is necessary to remind the parent to change the diaper before letting the child fall asleep.

Good image quality can be achieved even when the baby is awake with particular technical tricks. A whole-body acquisition can be divided in several static scans to give way to the child to relax between an image and the other, allowing staff to better block that part of the body. Sandbags are the most used means of restraint (Fig. 1.4).

Whenever possible, the camera should be rotated in the posterior view to ensure that the child does not feel "sandwiched" between the camera bed and the detector. With this arrangement of the gamma camera, the child can see and feel near to parents, and the team members can more easily block the patient, when necessary. In this position, the mother can actively collaborate for a good outcome of examination, also in newborns, breast-feeding the baby; this represents the best natural sedative. This setting with the gamma camera rotated in posterior view is also helpful for anterior acquisition, turning the child in prone position.

A practical tip to remember is that the most distressing acquisition view should be performed last on infants and younger children. Moreover, for particular scan views (like anterior skull acquisition), the parent can collaborate lying on the gamma camera bed next to the child, but turned on the contrary to bring his head to that of the child. In this way, even young children can remain calm and still during imaging (Fig. 1.5).

The use of books, toys, video games, or DVDs can be helpful to distract the child. A good staff is also able to take the patient's cooperation, interacting with him and capturing his interest by age (Fig. 1.6).

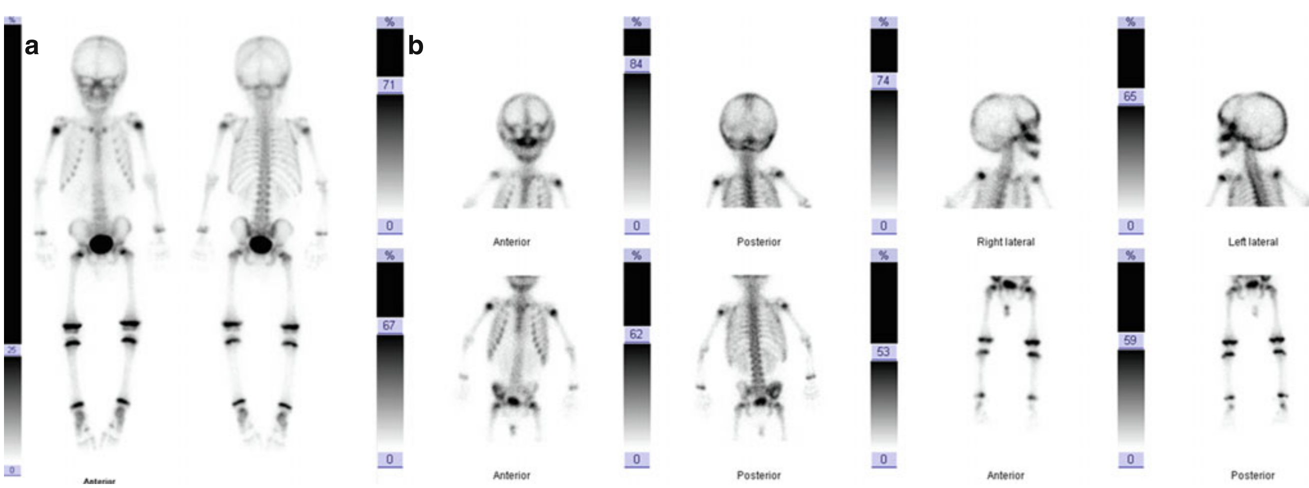

Fig. 1.4 If the child collaborates or sleeps, a whole-body acquisition protocol can be performed, using EANM procedural guidelines about speed scanning by age (**a**). In case of lack of cooperation of the child, the whole-body acquisition can be divided in several static scans to give way to the child to relax between an image and the other and allowing the staff to better block that part of the body (**b**)

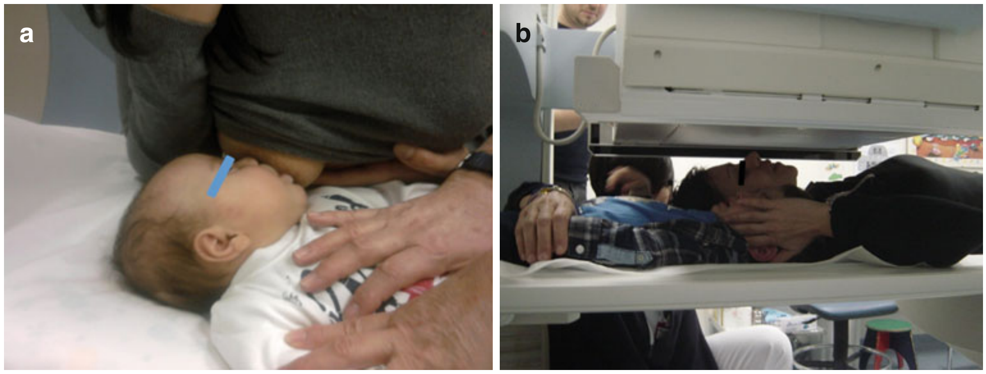

Fig. 1.5 In newborns, the mother can actively collaborate for a good outcome of examination, breast-feeding the baby; it is the best natural sedative for her child (**a**). The parent can also collaborate to perform distressing acquisition view, lying on the gamma camera bed next to the child but turned on the contrary to bring his head to that of the child (as represented in **b**)

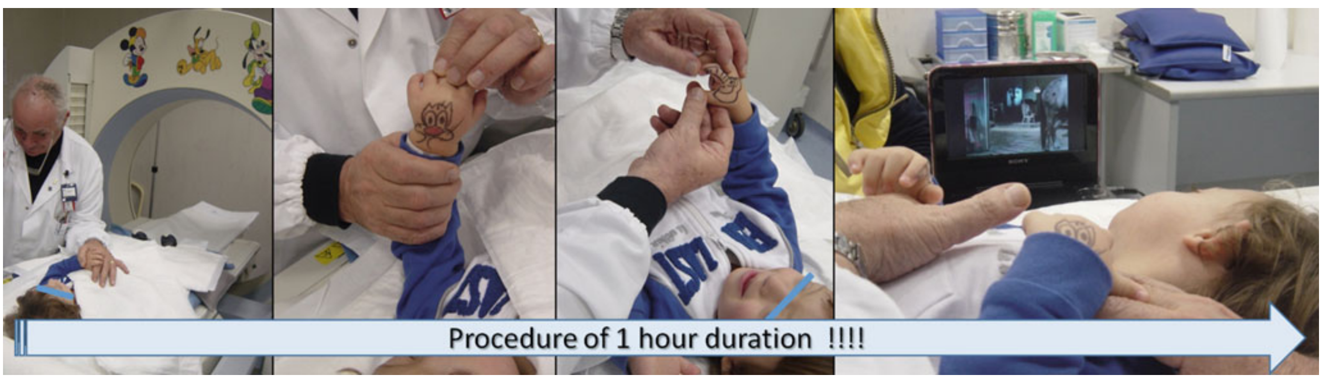

Fig. 1.6 For an adequate approach of the pediatric patient, it is necessary to create a positive atmosphere that serves to take the child's cooperation. Specific education of technologists is required, including proper handling of the child during the procedure and adequate psychological attitudes toward pediatric patient

Further Readings

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Radiation Risk

2

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2.1 Introduction

The practice of nuclear medicine leads to a potential risk of exposure for the patient. The activity of radiopharmaceutical should be administered in order to guarantee the correct balance between risks and benefits. In the last years, the introduction of technological advances, the increased availability of scanning equipment, and new radiopharmaceuticals lead to an intensified use of nuclear medicine examinations. On the one hand, these improvements involved in a remarkable progress in image quality; on the other hand, technological advances do not necessarily imply a decrease in patient exposure to ionizing radiation. The implementation of radiation protection practices aimed to limit radiation exposure in nuclear medicine exams is an utmost need. For pediatric patient, a more attention has to be paid as they have higher tissue radiosensitivity and longer life expectancy.

2.2 Effects of Ionizing Radiations

A type of radiation which has enough energy to eject electrons from atoms or molecules is defined as ionizing radiation. It is well known that the interaction between ionizing radiation and biological tissues or organs may cause changes in cells which may later cause them to become malignant or bring about other detrimental functional changes in irradiated tissues and organs. It is important to note that irrespective of the nature of the primary radiation (which may be composed of particles and/or electromagnetic waves), the energy transfer mechanism always occurs via the secondary electrons which are produced by interaction between the primary radiation beam and the biological targets. At the microscopic level, when incident rays or particles interact with orbital electrons within the atoms, two processes through which radiation interacts with matter can happen: one of these processes is the excitation, the other one is the ionization [14]. Excitation involves raising a bound electron to a higher energy state, leaving the atom in an excited state, while ionization happens when the electron receives sufficient energy to be ejected from its orbit and to leave the host atom. These physical interactions between radiation and specific structures within the cells can cause more or less serious biological damages. These latter are associated to the interaction of radiation with deoxyribonucleic acid (DNA) and can mainly occur through direct and indirect processes.

The direct interaction implies a direct damage of DNA structures after ionization of atoms or molecules, through a sequence of chemical events which can provoke the final biological damage. This is the dominant process for highly ionizing particles, i.e., heavy charged particles, proton and neutrons. On the contrary, the indirect interaction involves secondary electrons which are ejected during the ionization process. These secondary particles, energetic and unbound, are capable of migrating away from the site of their production giving up their energy to the surrounding medium, through a series of interactions with other atoms and molecules. This energy absorption process results in the formation of free radicals and other chemical species, i.e., more reactive molecules which are the true causatives of damages of critical targets in the cells [2].

For example, when the radiation interaction happens with water molecules, the created highly unstable free radicals, such as water ions (H_2O^+) and hydroxyl ($OH^·$), can spread through the cell interacting even with distant cellular target. The indirect interaction and its consequently biological detriment are mainly caused by sparsely ionizing radiation, i.e., electrons or x-ray.

In the events timescale, the initial ionization event occurs instantaneously (~10^{-18} s) at the microscopic level, while the chemical changes may appear to operate over a timescale of about 10^{-5} s. Thus, the period during which the chemical damage is caused is relatively long on the microscopic scale.

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These events are the precursors to a chain of subsequent events which may eventually lead to the clinical (macroscopic) manifestation of radiation damage. The clinically observable radiation effects, whose timescale may extend to years, are expressed as the results of the functional impairment after lethal damage inflicted to large numbers of cells or critical substructures [3].

Dealing with these macroscopic effects, an important distinction has to be made between low and high dose effects, whose consequences on biological tissues are really different. This concept is highlighted by the NCRP Report No. 136 [15] and by the BEIR VII Report [10] where a fundamental distinction is made: low to moderate doses encompass the values between 0 and 100 mSv, while high doses include values greater than 100 mSv.

Moreover, a distinction of the effects of ionizing radiation on biological tissues is often made according the required time for the effects to manifest. If an effect occurs within several hours or days after the exposure of the individual to extremely high doses, it is considered as an acute effect. Conversely, delayed or latent effects manifest several weeks or years after the exposure.

In some cases, the damaged component of the genetic material is essential for cell survival, and the cell may die or not be able to undergo proper mitosis. The removal of these cells will not contribute to late radiation effects such as carcinogenesis. Instead, late effects occur when the cell survives the initial genetic damage. The consequences of this damage manifest later, perhaps decades after the initial exposure; such late effects may result from genomic instability due to the initial radiation damage. In particular, cells that are growing rapidly and undergoing mitosis at a higher rate may be more susceptible to late radiation effects than those that are growing more slowly [9].

On the basis of these considerations, the radiation effects can also result in a radiation detriment, which is defined as the harm that would eventually be experienced by an exposed group and its descendants as a result of the group's exposure to a radiation source [11].

The radiation damage may be classified as being either deterministic or stochastic.

Deterministic effects are characterized by a threshold dose level. These effects manifest themselves in the form of harmful tissue reactions, i.e., cataract induction, general radiation syndromes, bone marrow ablation, which could manifest after an exposure to high radiation doses. Above the threshold dose level, the severity of the effect is linearly dependent with dose: if the amount of radiation dose is increased, the lesion severity also grows depending on the number of damaged cells [11].

Stochastic effects, which include both carcinogenic and hereditary effects, are those for which the likelihood of occurring is dose related, but the severity of the resultant condition is not related to the dose received. They may occur without a threshold dose, and for them, an increase on radiation dose will result in a growth of the probability of occurring [11].

In the field of Nuclear Medicine (NM) diagnostic uses, stochastic effects have to be predominantly considered as potential side effects while, for radionuclide therapy applications, the concerns relate to both stochastic and deterministic effects [12].

In addition, there are other parameters that influence the radiation effects and that need to be discussed. In fact, it is well established that the risk of ionizing radiation varies with both age and sex. In particular, for pediatric patients, the risk of radiation effect is higher than in adults. This behavior can be attributed to a twofold cause: on one hand, the tissues of younger subjects are more radiosensitive as they are actively growing and, on the other hand, life expectancy in young people is higher than in adults allowing a longer time for the risk to be realized. Moreover, girls demonstrated a higher risk for cancer induction than boys, which is, in large part, attributable to the excess risk of breast cancer in this population [9].

2.2.1 Evaluation of Radiation Exposure in Nuclear Medicine

Nuclear medicine procedures involve the use of radiopharmaceuticals that emit radiations such as γ-rays, α-particles, β-particles, and positron. These emissions expose the patient to ionizing radiation that might lead to detrimental health effects [11]. Nuclear Medicine offers the possibility to detect early stages diseases, and its noninvasive nature allows to use it as a powerful diagnostic tool in examinations involving children. The administered activities in nuclear medicine procedures are well established in many specialties including oncology, urology, cardiology, gastroenterology, and orthopedics. For pediatric patients, it is highly recommended that practitioners of pediatric nuclear medicine have to develop a knowledge in understanding radiation risk and dosimetry and how this risk may vary in children relative to adults. Using nuclear medicine procedures, expected clinical results can be guaranteed using the lowest possible administered activities and, thus, the minimum necessary risk for patients. To this purpose, as recommended by the Society of Nuclear Medicine and Molecular Imaging, the key to