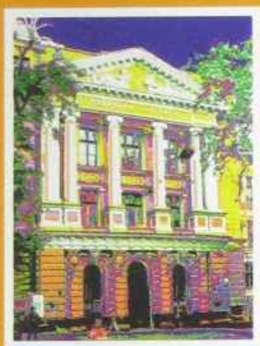

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FUNDAMENTALS of RADIONUCLIDE DIAGNOSTICS

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Навчальний посібник містить стислий нарис історії радіонуклідної діагностики і внеску українських вчених в її розвиток, основні принципи і методи радіонуклідних досліджень. Розглянуто найважливіші аспекти радіаційної безпеки, а також питання радіонуклідної діагностики.

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INTRODUCTION

Accurate and timely diagnostics is indispensable condition for effective treatment. The most widespread methods of imaging of pathological processes in an organism of the person are radiological and ultrasonic ones. Magnetic resonance imaging (MRI) and computer tomography (CT) became customary in the clinical practice. Radionuclide diagnostics occupies a prominent place in this series, which adds and sometimes successfully replaces the methods mentioned above. Radionuclide diagnostics is based on introduction into an organism of various compounds, tropic to one or another organ and tissue, labeled by radionuclides and named radiopharmaceuticals (RPh).

Methods of radionuclide diagnostics have great value in estimating functional conditions of separate organs and an organism as a whole.

It is known that both X-ray and ultrasonic study, as well as MRI and CT reflect structural features of organs without studying their function. Besides, radiation dose with RPh usage is considerably lower than with X-ray exam.

A bright example of unique opportunities of radionuclide study are results of their application in cardiology and oncology. So, they are a method of choice in early diagnostics of myocardial infarction with estimation of extent and localization of affection. The usage of tumor-tropic RPh in oncological practice gave an opportunity to conduct differential diagnostics of malignant and benign tumors and detect the extent of a pathological process spreading.

Methods of radionuclide diagnostics are applied in many countries of the world. The share of the USA makes 47% of the world market, the countries of Asia — 26.6%, Latin America — 2.5%, other world, including the CIS, — 4.6%.

Recently radionuclide diagnostics has been widely spread in a number of countries. For example, in 1988 in Portugal 31 gamma cameras were used, which corresponds to 4 units on 1 million of population. About 2000 researches per a year are conducted in 1 gamma camera. The research nuclear center in India supplies more than 150 hospitals with nuclear production for radionuclide diagnostics and more than 500 laboratories — with sets for nuclear analysis.

Part I
GENERAL PART

Chapter 1
HISTORY OF RADIONUCLIDE DIAGNOSTICS AND CONTRIBUTION OF THE UKRAINIAN SCIENTISTS TO ITS PROGRESS

The first application of radionuclide indicators is associated with Hevesy Gyorgy (1911). A young scientist while living in a cheap resort hotel noticed that the rests of his food, which had not been eaten before, were served again the next day. He added the radionuclide indicator to an uneaten portion, and by means of the detector of radiation has proved to his hostess that he was really right. The hostess turned him out from the hotel. As for him, he continued scientific work which resulted in the Nobel Prize for use of radionuclides as indicators in biology.

Radionuclide diagnostics studies transport, exchange, accumulation and excretion of radioactive isotopes and labeled compounds without making harm to biological functions of an organism. Now practically every medical specialty uses radioactive substances.

Herman Blumgart is called the father of clinical nuclear medicine, since he was the first who used radioactive labels for medical diagnostics (1924).

At the first stage of history radionuclide diagnostics (50-s years of the XX century) it was necessary to sum up the tasks of medical use of radioactive isotopes, spread of the tracers method among wide levels of the medical public and organize of RPh industrial production. The features of behavior of radionuclide compounds and their elementary inorganic compounds in an organism were studied that time.

The second stage of radionuclide diagnostics development took place at 60-s years of the XX century. Special attention was given to development of new RPh with application of organic and inorganic compounds.

The number of RPh increased and wide possibilities of various organs examination appeared due to it, which caused development of special medical equipment, such as multichannel radiographs with scintillation detectors and counters, scanners, etc.

Nowadays progress of nuclear researches in clinical medicine is to great extent connected with development and application of new radiopharmaceuticals on the basis of a label by short-life nuclides technetium and indium. Last years radionuclide diagnostics is provided by a new method — radioimmunoassay (RIA) *in vitro*, it gives a possibility to detect concentration of various biologically active substances in blood serum of a patient, in particular, hormones, enzymes, drugs, etc. This method is the most perspective methods of diagnostics by two reasons. Firstly, all studies *in vitro* are conducted noninvasive, secondly, sensitivity of these methods of study hundreds times as much than in chemical ones, and by accuracy of results they prevail over biochemical and chemical methods of the analysis.

On the basis of RIA data it is possible to carry out the control over the pregnancy course and effectively to plan the corresponding medical measures promoting birth of a healthy child.

For early diagnosis of cancer, tumor markers have been recently used.

There was established the technique of extracorporal labeling of autologic leukocytes which at reinfusion into a patient's bloodstream, actively migrate to various inflammation foci. ^{99m}Tc allows to reveal "hot" sites of these labeled leukocytes accumulation with planar scintigraphy. The subsequent scintigraphy studies allow rather reliably diagnose acute (including postoperative) abscesses of the abdominal cavity, brain abscesses, inflammatory diseases of the bowel and Crohn's disease, acute orthopedic infection, inflammation of vascular artificial prosthesis, can help with detection of source of unknown origin fever.

Rise of radionuclide diagnostics recently is connected with SPECT (single-photon emission computer tomography) method (which became routine), and also introduction in clinic of PET (positron emission tomography).

PET represents a unique opportunity of imaging of the biological processes course *in vivo* with the high spatial resolution. Using a set of labels, being radioactive isotopes of natural elements being constantly present in a human body ^{11}C, ^{13}N, ^{15}O, ^{18}F, it is possible to receive PET images. Application of PET in cardiology, oncology and neurology allows to diagnose Alzheimer's and Parkinson's diseases, to detect tumors of the brain and bones in the early stage.

The Contribution of the Ukrainian Scientists to Development of Radionuclide Diagnostics

In 70-s years of the XX century research workers of the Kharkov Institute of Medical Radiology (the chief — prof. V. I. Shantyr) extended the sphere of diagnostic application of radionuclides (^{32}P, ^{131}I, ^{24}Na, ^{133}Xe, ^{51}Cr, ^{59}F, etc.) and labeled compounds (^{131}I labeled rose bengal,

^{131}I labeled α-triiodothyronine, ^{131}I labeled vitamin B_{12}, ^{203}Hg labeled neohidrine) at studying the functional condition of some organs and systems of an organism at tumor and non-tumor diseases. So, V. V. Shishkina with research workers (Kharkov) used ^{32}P, ^{51}Cr and ^{59}F for examination of red blood in patients with polycythemia vera.

A. A. Dubinsky, A. A. Dundich, V. L. Shklyarevska (Kharkiv), studying changes of some parameters of radioisotope renogram in patients suffering from essential hypertention, improved the treatment scheme.

At the medical radiology faculty of the Kyiv Medical Institute of Advanced Medical Studies since 1964 there have been used a universal diagnostic device for diagnosis of diseases of the liver, the thyroid gland, the kidneys, the brain and the spleen. In particular, V. P. Slavnov has developed criteria for estimation of the functional condition of polygonal and reticuloendothelial cells of the liver.

V. P. Ishchenko (Kyiv) on the basis of radioisotope renography results has revealed great advantages of radioisotope study in detection of secretion and excretion disorders, as well as latent renal failure.

A. P. Lazar (Kyiv) has revealed greater sensitivity of radioisotope study of a single kidney function, especially at the early stage of disease.

F. P. Khripta, O. A. Lysyuk (Kyiv) have experimentally proved isotopes ^{67}Ga and ^{85}Sr usage value at diagnosing tumors of bones and metastases in the bones.

V. G. Pekur and Ye. D. Kalantarov (Kyiv) successfully used ^{133}Xe in preoperative examination with the purpose of estimation of zonal ventilation, evaluation of working ability, definition of efficiency of the conducted therapy in patients with different pulmonary pathology.

A. T. Tsygankov (Kyiv) has applied ^{133}Xe to study compensatory properties of lungs as diagnostic and prognostic test in thoracic surgery and revealed its properties for studying secreting, enzymatic, motive function of stomach in researches with ^{57}Co.

G. P. Sivachenko, Ye. V. Slobodyanik, M. A. Udovik (Kyiv) recommended radioisotope myelogrphy as a valuable additional method to obtain objective information on localization of pathological process, patency and extent of the subarachnoidal space block.

F. P. Khrypta, A. M. Zhvalkina (Kyiv) gave experimental substantiation to ^{99m}Tc clinical usage for diagnostics of diseases of some organs.

V. V. Demidas (Odessa) has introduced radiocardiography for detection of such important hemodynamic parameters as minute volume, volume of blood circulation, lung capacity, time of pulmonary blood flow, coronary blood flow.

A. K. Bondarchuk (Odessa) has informed about advantage of isotope renography and imaging combination in diagnostics of such renal diseases of kidneys as acute and chronic pyelonephritis, hydronephrosis, urolithic disease, nephrohypertension, tuberculosis, tumors, cystic disease, renal failure with infection arthritis.

Ye. D. Dubovyy and V. M. Sokolov (Odessa) have applied radioactive isotopes (^{32}P, ^{204}Tl, ^{146}Pm) for differentiation of malignant and benign tumors of the eye and the orbit and for diagnosis of non-tumor diseases of the eye.

Professors of the Odessa Medical Institute E. D. Dubovyy, S. I. Korkhov, S. G. Antypov (1973) proved the indications to radioisotope lymphography usage at malignant tumors and other processes of various localizations.

D. S. Mechev (Kyiv) and V. M. Tsvigovsky (Odessa) have demonstrated perspectivity of ^{67}Ga-citrate for the purpose of diagnostics of inflammatory process in joints and degenerative changes in patients suffering from rheumatoid arthritis and deforming osteoarthrosis. While carrying out comparative studies of patients suffering from pathology of joints with the usage of ^{67}Ga-citrate and ^{99m}Tc compound it was established that inflammatory changes were revealed with ^{67}Ga better than with ^{99m}Tc, and the scintigraphic picture does not change under the action of steroid and anti-inflammatory drugs.

V. M.Tsvigovsky (Odessa) has established that the radionuclide method is more sensitive in definition of the active phase of the rheumatoid arthritis process than X-ray exam data. Besides, the author has come to conclusion that the method of radioindication can serve as an objective criterion of estimation of both the basic treatment and intra-articular drugs.

T. K. Dorofeyeva (Odessa) by means of radiocirculography has revealed neurodynamic and neuromorphological changes of the brain both in acute and remote periods of a severe craniocerebral trauma.

A group of Odessa scientists has established high efficiency of radiological method in definition of lymphatic system defeat character (inflammation, tuberculosis, tumor), revealing of recurrent tumor, detection of clinically latent metastases in lymph nodes (V. M. Sokolov, V. V. Demidas, N. D. Kadyr-Zade, S. D. Denisyuk, I. G. Dondua, S. G. Antonov, 1976).

A possibility of the latent hepatic failure detection in patients who had suffered from Botkin disease before, by means of radioactive ^{131}I labeled bengal rose have been proved in Ternopol. (N. A. Kryzhanovsky, Ye. I. Barba, V. P. Syvolap).

The 70-s years have brought to Ukraine works of generalizing character: dissertations (Odessa): N. D. Kadyr-Zade, S. D. Denysyuk, I. G.

Dondua, V. M. Sokolov, V. V. Demidas, Ye. G. Brovarska, B. P. Malevich, S. K. Ternovyy; textbooks (Kyiv): V. I. Milko, A. T. Lazar, M. T. Nazimok, G. P. Sivachenko; monographies: Ye. D. Dubovyy, V. M. Sokolov, V. V. Reshetnyak.

In 1975 N. A. Puchkovska's, V. M. Sokolov's et al. monography was awarded by the State Prize of Ukraine.

So, S. V. Afanasyev, V. O. Matveyeva, O. V. Vladimirov (Dneperpetrovsk) have elaborated technology of quantitative estimation of results of use of radionuclide methods for diagnosis of absorptive function of the intestine and estimation of its condition in patients suffering from peritoneal adhesions.

O. A. Budrenko, S. Kh. Tcherevanova (Kharkov) have studied extent of strain of autoimmunity reactions of the insular apparatus of the pancreas.

Ya. S. Vikman (Kharkov) has shown that radionuclide splenoportography is an effective method of splenoportal bed imaging.

S. G. Kobyakov, Ye. V. Luchitsky, G. A. Zubkova, V. M. Slavnov (Kyiv) used the radionuclide angiography as a method of diagnostics of vascular forms of erectile dysfunction during diabetes.

S. S. Makeyev (Kyiv) has shown expediency of SPECT and scintigraphy of all the body for diagnosis of plural metastatic lesions.

D. S. Mechev, M. M. Firsova, M. I. Polyakova, M. V. Krushinsky (Kyiv) have studied possibilities of scintigraphy and one-photon emission computer tomography with modern tumor-tropic RPh in diagnosis of neoplasms of the head and neck, differential diagnosis of tumor processes and metastatic lesions of the lymphatic system.

O. A. Savich, V. M. Slavnov, V. V. Markov (Kyiv) by means of dynamic scintigraphy with ^{99m}Tc colloid introduction have shown possibilities of estimation of an arterial component in the liver blood supply, and in combination with radinuclide splenoportography — possible hemodynamic disturbances related to portal hypertension.

O. O. Khyzhnyak, S. Kh. Tcherevanova, S. I. Turchina (Kharkov) by means of radioimmune methods have revealed changes in the content of gonadotropic and sexual hormones depending on passport age of patients and rates of sexual developments.

The future of radionuclide diagnostics in Ukraine depends on realization of the program created by the Ukrainian Association of Experts on Nuclear Medicine. The program is directed at realization of the following questions: providing radionuclide diagnostics departments with domestic equipment; creation in Ukraine of 3–4 PET-centers; development of domestic radiopharmaceuticals; creation of the scientific-practical center of computer technologies.

Chapter 2
RADIONUCLIDE METHODS AND PRINCIPLES OF STUDY

2.1. Methods of Diagnostics

All the radionuclide diagnostic studies are divided into two great groups:

— studies when RPh are administered into an organism of the patient (*in vivo*);

— analysis of blood, slices of tissue and excrements of the patient (*in vitro*).

Study *in vitro* in its turn is of two types. The first type — registration of radio-activity of blood, excrements, urine or the slices of tissue taken from the patient in the organism RPh has been administered before. The second type — studying the reaction of blood of the patient who was not administered RPh, with standard radiopharmaceutical reactants.

Radionuclide diagnostics *in vivo* uses the methods allowing to detect the presence (radiometry), kinetics (radiography) and distribution (imaging) of the radioindicator in the investigated organ.

Radiometry is used for exam of ^{32}P accumulation in the skin, at investigation with ^{131}I, ^{99m}Tc — in the thyroid gland, all the body, for studying metabolism of proteins, iron, vitamins in a human organism.

The methods based on definition of peculiarities of distribution in organs and tissues of administered RPh, give the characteristic anatomic-topographic condition of organ or system and refer *to static radionuclide studies*.

The methods based on definition of RPh transport dynamics in patients, allow to estimate condition of functions of an investigated organ or a system and refer to *dynamic radionuclide studies*.

Radiography is a method of continuous or discrete registration of processes of RPh accumulation, redistribution and excretion from organism or separate organs.

If clinical radiometry is intended for unitary or several repeated measurements of radioactivity of an organism or its parts by means of radiography it is possible to observe dynamics of RPh accumulation and excretion from the lungs, kidneys, liver. Radiographic function in modern devices is combined in gamma-camera with visualization of the organ.

Choice of RPh depends on phrmacodynamics (conduct in an organism) and nuclear-physical properties. Pharmacodynamics of RPh is defined by the chemical compound on the basis of which it is synthesized. Opportunities of RPh registration depend on the type of decay of a radionuclide by which it is labeled.

Choosing RPh for investigation, the doctor should consider, first of all, its physiological orientation and parmacodynamics. We shall consider it on an example of RPh introduction in blood. After intravenous injection RPh at first distributes in blood and transports to all organs and tissues. If the doctor is interested in hemodynamics and blood supply of organs, he will choose the indicator which long time circulates in a vascular bed, without falling outside the limits of vascular walls in surrounding tissues (for example, human serum albumin). At investigation of the liver the doctor will prefer a chemical compound which is selectively taken by this organ. Some substances are taken from blood by kidneys and excrete with urine, therefore they serve for study of kidneys and urinary ducts. Some RPh are tropic to bone tissue in this connection they are irreplaceable at exam of the osteo-articulate apparatus. Studying terms of transportation and character of distribution and RPh excretion from an organism, the doctor judges the functional condition and structurally-topographical features of these organs.

However, it is not enough to consider only RPh pharmacodynamics. It is necessary to take into account nuclear-physical properties of radionuclide which is a part of its structure. First of all, it should have a certain spectrum of radiation. For visualization of organs there are used only radionuclides emitting γ-rays or characteristic X-ray radiation as these types of radiation are possible to register at external detection. The more of γ-quanta or X-ray quanta form at radioactive decay, the more effective the given RPh as a diagnostic device. At the same time radionuclide should emit corpuscular radiation as less as possible — electrons which are absorbed in the body of the patient and do not take part in visualization of organs. From this point of view the radionuclides with nuclear transformation by isomer transition type — ^{99m}Tc, ^{113m}In are preferable.

Radionuclides with half-life period of some tens of days are considered to be long-lived, some days — medium-lived , some hours — short-lived, some minutes — ultrashort-lived. It's quite natural that the short-lived radionuclides are preferably used. Use of medium-lived and the more so long-lived radionuclides is connected with the raised radiation dose, use of radionuclides is complicated for technical reasons. A method of creation of a picture of administered RPh spatial distribution (scanning) in organs and tissues, is called *radionuclide visualization*. Radionuclide visualization now includes the following kinds of investigation: scanning, scintigraphy, one-photon and two-photon emission tomography.

At scanning parameters in each point of the body by a moving detector transform into a corresponding speed of strokes. The sites of the body absorbing greater concentration of RPh look more shaded at the paper, and those with lesser RPh concentration are less shaded correspondingly.

Scintigraphy is obtaining image of organs and tissues by means of radionuclides registration in a gamma-camera, which are distributed in organs, tissues and in an organism as a whole.

Scanning and scintiraphy have almost equal technical opportunities in estimating anatomic-topographical condition of the inner organs. However, scintigraphy has certain advantages.

In the first place, scintigraphy is carried out more quickly at exposition up to 10 sec (scanning lasts not less than 10 min), which allows to exclude not only mobility of the patient and even the child during examination, but also biological mobility of organs, for example, during breathing.

In the second place, scintigraphy gives a possibility to combine static and dynamic investigations, which allows to obtain fuller diagnostic information without additional radiation dose on a patient.

Scintigraphy is the basic radionuclide visualization method in clinic now. It allows to study quickly proceeding processes of injected into an organism radioactive compounds distribution.

Positive scintigraphy is carried out with the aim to reveal primary malignant tumors, metastases and relapses after surgical or radiation treatment.

The idea of positive scintigraphy seems to be very interesting — introduction in an organism of the patient of chemical compounds, labeled by monoclonic antibodies. This technique was called *radioimmunoscintigraphy*. The first publications, concerning its application at pararectal cancer and tumors of the mammary glands, encourage. Development of positive scintigraphy of tumors is promoted also by new ways of visualization of organs — SPECT and PET tomography.

Single-photon emission computer tomography. The same RPh are used with SPECT and scintigraphy. In this apparatus the detectors are located in a rotational tomocamera which rotates around the patient giving a passability after computer processing to obtain image of positron radionuclides distribution in different layers of the body in space and time.

Positron (two-photon) emission tomography (PET). Positron-emitting radionuclides ^{11}C, ^{13}N, ^{15}O, ^{18}F are injected for PET. The positrons emitted by these nuclides annihilate near atom nuclei with electrons. During annihilation a pair electron-positron disappears creating two γ-quanta with energy of 0.51 MeV. These two quanta flow to strictly opposite direction and are registered by two detectors, which are also opposite located. Computer processing of signals allows to receive the volumetric and color image of the investigated object. Spatial resolution of PET is worse than on X-ray computer and MRI tomographs, but sensitivity of the method is really high. PET allows to fix changes of C labeled glucose demand, "the eye center" of the brain, at opening eyes. It is possible to reveal changes at the thinking process.

PET is based on use of metabolically active substances (for example, simple sugars, more often glucose) which are managed to reliably label by positron emitters (usually it is ^{18}F), the result of which is compound ^{18}FDG (fluorodexyglucose). Being parenterally administered with a diagnostic purpose and having reached the target organs or tissues in which metabolic processes are intensified, these compounds accumulate in them with an essential difference organ/background. The ^{18}F emitted positrons, have a very short run in tissues and "meeting" with electrons annihilate emitting quanta of energy which are taken up by PET-tomographs detectors. Having received the ^{18}FDG "card of distribution" in an organism, the researcher can draw a conclusion about metabolic, functional activity of one or another organ or tissue. PET is a powerful diagnostic tool in cardiological diagnostics (provides reliable diagnostics of myocardial viability), in oncology (inserting into tumor tissues, which are characterized by hypermetabolism, allows to diagnose malignant tumors and to distinguish them from benign ones, guarantees detection of metastases irrespective of their localization, helps with dynamic supervision over patients) and neurology.

On the way to wide PET introduction into daily clinical practice there is a number of obstacles, which can be overcome and which have already been — in the USA and the majority of the Western Europe countries. First of all, it is necessary to tell that ^{18}F is a short-lived nuclide and that is why PET can be conducted only in the medical centers located close enough to cyclotrons making positron emitters.

The majority of the developed countries have a net of small cyclotrons providing access to ^{18}FDG practically to any large medical institution. Moreover, it is developed and introduced in practice a mobile PET-camera, mounted in a trailer, constantly moving alongside a certain region and provides a relatively inexpensive access to PET practically of any medical institution.

Radionuclide study *in vitro* is used for definition in blood serum of the person the concentration of different biologically active compounds, the number of which now reaches more than 400 (different hormones, enzymes, vitamins, medicinal substances). They are used for diagnosis and estimation of pathology of reproductive, endocrine, hemopoietic and immune system of an organism.

The most part of modern sets of reagents is based on RIA which for the first time has been offered by Ialow and Berson (1959). In 1977 the authors were awarded by the Nobel Prize for this innovation. The essence of the method is that non-radioactive antibodies displace radioactive ones.

Nowadays side by side with RIA a new radioreceptor analysis (RRA) method develops. RRA is also based on the principle of concurrent balance of labeled lygand (labeled antigen) and investigated serum substance, but not with antibodies, and with receptor bonds of the cellular membrane. The RRA method differs from RIA by shorter time of execution and still greater specificity.

The method of RIA allows to find out and measure presence in biological liquids (blood, urine) of different substances of exogen and introgen origin, containing there in very small concentration: hormones, viruses, drugs, etc., and so-called "markers" which appear in an organism at cancer, myocardial infarction. All these unique studies are based on use of imunologic reactions antigen-antibody.

The principle of radioimunologic method consists in concurrent binding of required stable and similar to them labeled substances with a specific percepting system.

For performance of such analysis there are produced standard sets of reagents, each of which is intended for detection of a concrete substance concentration.

Radionuclide analysis *in vitro* is called radioimmunologic as it is based on use of immunologic reactions antigen-antibody. However, later the other methods of study *in vitro* have been created, they were close by purposes and technique, but differed by details.

So, if antibody is used as a labeled substance, instead of antigen, the analysis is called immunoradiometric; if the tissues receptors serve as connecting system, they speak about radioceptor analysis.

Radionuclide study in a test tube consists of 4 stages:

The first stage — mixing of analyzed biological test with reagents from a set containing antiserum (antibodies) and a binding system.

The second stage — incubation of the mixture which proceeds till it reaches dynamic balance (from several minutes till several hours and even days).

The third stage — division of the free and bound radioactive substance. With this purpose available sorbents (ion-exchange resins, activated carbon, etc.) which sediment heavier complexes antigen-antibody are used.

The fourth stage — radiometry of tests, calibrating curves construction, definition of required substance concentration. All these works are carried out automatically by means of the radiometer equipped by the microprocessor and the printer.

Thus, the radioimmune analysis is based on use of a radioactive label of antigens. However, other substances, in particular, enzymes, luminophores or high fluorascenting molecules can be used as a label of antigen or antibody. New methods of microanalysis are based on it: immuno-enzymatic, immunoluminescent, immunofluoroscent. Some of them are rather perspective and can compete with RIA.

Radioimmune methods in oncology are used for solution of the following problems:

— differential diagnosis of tumors (as an additional sign);
— disease prognosis;
— estimation of efficiency of conducted treatment;
— early detection of relapses and metastases of a tumor.

The following markers are revealed in practice now:

Alpha-fetoprotein (AFP) — glycoprotein with the content in blood plasma of healthy people of 2–10 mcg/L. Stable increase in AFP concentration is characteristic for hepatocellular cancer of the liver and metastases in the liver. Temporary increase of AFP level can occur at virus hepatitis, cirrhosis.

Carcinoembryonal antigen (CEA) — glycoprotein with concentration in blood plasma of healthy people 0–12 mcg/L. CEA raised content is typical for tumors of the gastrointestinal tract, the liver, sometimes at malignant tumors of other localizations and even at diseases of non-tumor origin.

Choriogonadotropic hormone (CGH) — glycoprotein synthesized by placental cells since the early terms of pregnancy. At absence of pregnancy CGH increase is characteristic for uterine chorioepithelioma.

Thyroglobulin (TG) and **antibodies to thyroglobulin (ATG)** is defined for diagnosis of thyroid cancer.

Monoclonal antibodies (the antibodies produced by one clone of cells) possess molecular identity and specificity, interact only with one antigen

Commercial sets for definition monoclonal antibodies to tumors of ovaries (CA-125), pancreas (CA-199m), mammary gland (CA-153) are obtained and produced.

As the increase in the content of the above-mentioned markers in the serum or in blood plasma can be observed during non-tumor diseases, not only normal parameters, but also a threshold (critical) level, the excess of which is a marker of a tumor process, are established for each marker. With increase in marker concentration above the threshold the disease prognosis is getting worse. Efficiency of the conducted treatment is evaluated by the level of decrease in markers concentration in blood. At radical treatment their level falls below critical, often up to norm. Repeated rise of markers in blood after a successfully conducted treatment is a sign of disease relapse or metastases.

2.2. Equipment

The basic scheme of construction of all types of nucleus-medical devices is identical and can be divided into 3 parts:

1) the detector;
2) the electronic block;
3) the display.

Detector is a perception part of the device which is directly turned to the radiation source.

Electronic block of management allows to provide a necessary voltage level and radiation registration regime.

Display — the block of data presentation. Displays vary, however, as usual they are represented in the form of oscilloscope with memory or TV.

As a detector they usually use scintillators or, less often, gas meters. Scintillator is a substance in which light flashes — scintillations arise under photons action. These scintillations are located by photoelectronic multipliers (PhEM) which transform light flashes into electric signals. Scintillation crystal and PhEM are placed at a protective metal casing — collimator, limiting crystals "visual field" with the sizes of organ or investigated part of the patient's body.

Usually a radiodiagnostic device has some replaceable collimators which are selected by the doctor depending on the investigation aims.

In modern collimators there are some tens of fine apertures which position is chosen with taking into account the best imaging of the examined object.

In the devices intended for definition of biological tests radio-activity, they apply scintillation detectors in the form of so-called well counters. Inside of the crystal there is a cylindrical channel in which a test tube with an investigated material placed. Such a device of the detector considerably raises its ability to locate weak radiations of biological tests. For measurement of radioactivity of the biological liquids containing radionuclides with soft β-radiation, liquid scintillators are used.

For definition of radionuclide amount one uses the devices with the general name — radiometers. Counters of radiation of different type among which Geiger-Muller's or gas and scintillation meters are most used in clinical practice as detectors. Unlike of detector-dosimeter, the aim of the detector-radiometer (radiation meter), is creation of a signal on its output by getting photon or a particle into a volume. Such a signal on the output from scintillation and Geiger-Muller counter is the electric impulse.

Practically all the diagnostic problems of nuclear medicine are solved by means of measuring relative activity of radionuclide which means the ratio of radionuclide quantity in various parts of space or during different moments of time.

For radiography one uses radiographs in which the account speed detector is connected with a curve recorder. In structure of the radiograph there can be one or several detectors, each of them conducts measurement of radiation independently on the other.

The scanner is a device in which the detector consistently and with a constant definite speed moves above the body of the patient, registering intensity of radiation in each point of the body. Instead of frequency of shading modern scanners use different color of shading depending on radiation count speed considered by the detector, that allows to define the RPh concentration levels distribution figure in the body of a patient or an investigated organ. Red color designates maximum levels of the count.

The profile scanner unlike a usual one gives the information on RPh distribution in the body of the patient not in the form of figure, but in the form of a curve constructed according to measurement of radiation intensity in different sites of the body.

Scintigraphy is carried out by means of scintillation cameras (gamma-camera) (Fig. 1). Modern scintillation cameras are the computer-scintigraphyc complexes allowing to obtain, store and process images of separate organs and all the body in a wide range of scintigraphic modes: static and dynamic, planar and tomographic. Irrespective of obtained image type, it always reflecting specific function of the investigated organ.

Essentially new equipment combines opportunities of CT and PET/SPECT. Result of combination in one device of opportunities of various ray technologies was absolutely new image in which there were presented both anatomic (CT), and functional (PET/SPECT) features of organs and tissues being in the topographical environment.

Analysing scintigram, basically static ones, side by side with topography of organs, its sizes and the form they define the extent of uniformity of its image. Sites with raised RPh accumulation are called "hot centers", or "hot nodes". They usually reflect the functioning sites of organ with excessive activity — the tissues changed by inflammation, some kinds of tumors, hyperplasia zones. If the area of RPh lowered accumulation is revealed, it means a space-occupying lesion which has replaced the normal functioning parenchyma of organs, so-called cold nodes. They are observed at cysts, metastases, focal sclerosis, some tumors.

There is a special type of gamma-camera intended for visualization of all the body of the patient. Thus, the camera detector moves above the observed patient (or, on the contrary, the patient moves around the detector). The scintigram obtained in this way will contain the information on RPh distribution in the whole patient's body. The method like this is used to obtain the image of all the skeleton, detecting the latent metastases.

For study of the systolic functions of the heart they use the gamma-cameras provided by a special device — trigger which under control of electrocardiograph turn on scintillation detector of the camera at strictly determined phases of the cardiac cycle — systole and diastole. As a result of it after the computer analysis of the received information on the display screen two images of heart appear — systolic and diastolic. Having combined them on the display, it is possible to study contractile function of the heart.

2.3. Radiopharmaceuticals

Radiopharmaceuticals (radiotracers) are chemical compounds permitted for introduction to the person with a diagnostic purpose and the molecule of which contains radionuclide. Radionuclide should possess irradiation spectrum of a certain energy, cause the minimal radiation dose and reflect condition of an investigated organ.

By their conduct in an organism the used RPh are conditionally divided into 3 groups:

— organotropic;

— tropic to a pathological organ,

— without pronounced selectivity (tropism).

RPh tropism is of 2 types: 1) direct, when the agent joins a specific exchange of cells of a certain organ in which its selective accumulation takes place; 2) indirect, when in organ temporary RPh concentration occurs on the way of its passage or washing out from an organism.

Besides, a secondary selectivity can take place, when RPh, able to accumulate, causes in an organism chemical transformations which provoke appearance of new compounds that have already been accumulated in certain organs and tissues.

RPh is chosen with taking into account its behaviour in an organism (pharmadynamics) and nuclear-physical properties.

All intravenously injected radionuclides circulate in blood at first, and then are deposited in various organs. While studying hemodynamics of a patient, it is necessary to choose the radiopharmaceutical drug able to circulate in the blood for a long time (for example, human serum albumin). At investigation of organs of the patient they choose the RPh tropic to a corresponding organ (hepatotropic, osteotropic, etc.).

Among nuclear-physical properties of RPh it is necessary to consider the spectrum of radiation (better γ-radiation) and half-life period, giving preference to short-lived radionuclides since application of long-lived radionuclides is associated with the raised radiation dose.

The most widespread radionuclide now is ^{99m}Tc, a daughter radionuclide of radioactive molybdenum — ^{99m}Mo, which forms a short-lived ^{99m}Tc by the way of β-decay.

The generator for ^{99m}Tc obtaining is insoluble in water salt of ^{99}Mo placed in a glass bottle which as a result of electronic uptake turns to soluble salt of technetium. From time to time, as far as necessary, technetium is washed out by sodium chloride isotonic solution.

There are synthesized RPh which selectively accumulate in the tumor tissue, — the tumorotropic RPh which penetrate exclusively the cells which have high mitotic and metabolic activity. Owing to raised RPh concentration the tumor will appear on scintigramy in the form of the "hot spot". Such technique of investigation is called *positive scintigraphy*. A number of RPh is created for this purpose.

Scintigraphy with labeled monoclonal antibodies is called *immunoscintigraphy*.

A variant of scintigraphy is binuclide study, when two scintiographic images are obtained with the use of simultaneously injected RPh. Such investigation is carried out, for example, for more distinct detection of fine parathyroid glands against a background of more massive tissue of the thyroid gland. With this purpose simultaneously two RPh are injected, one of which — $^{201}T1$-chloride — accumulates in both organs, another — ^{99m}Tc-pertechnetate — only in the thyroid gland. Then by means of the discriminator and computer from the first (total) image they subtract the second one, i.e. subtraction procedure takes place, as the result the final isolated image of parathyroid glands is obtained.

2.4. Principles of Radionuclide Diagnostics

2.4.1. Main Principles of the Measurements Optimum Organization

These principles may be formulated as follows:

— the field of sensitivity of each detector should include a minimally possible number of organs, mediums and structures participating in transport of the indicator introduced into an organism;

— if an investigated organs or structure is not functionally homogeneous, it is necessary to provide registration for all functional non-homogeneities;
— the organs and structures participating in the indicator transport and capable to distort the interpretation of results should be outside of the field of sensitivity of each used detectors.

2.4.2. Principles and Methods of Measurement Results Interpretation

The minimal distortion of the useful diagnostic information is possible taking into consideration two main principles:
— a principle of physiological essence means that parameters defined during interpretation should have concrete and single clinical-physiological meaning. For example, the coefficients of indicator transition rate through various physiological barriers, hemodynamic data may consider to be such parameters.
— a principle of physical correctness means that findings interpretation shouldn't depend on measurement conditions and, first of all on the detectors location and orientation geometry.

2.4.3. Principles of Decision-Making

In order to make a diagnostic supposition based on radionuclide study, it is necessary methodically and consistently:
— to get a complete investigation of clinical findings of a patient;
— to interprete data of radiodiagnostic investigation from the point of view of clinical syndrome observed in a patient;
— to conduct differential diagnosis.
In some cases a radiologist may just descript the radionuclide symptom group without any analysis of disease diagnosis.

2.5. Key Rules of Carrying Out Radionuclide Studies

Indications to radionuclide study are defined by a physician after consultation with a radiologist. As a rule, it is conducted after other clinical laboratory and noninvasive radiation procedures and there is proved a necessity in obtaining radionuclide data about function and morphology of one or another organ.
Information about the patient should be the following:
1. The examination date of the patient, its name, age, gender.
2. Clinical information, the diagnosis.

3. The official part of the conclusion consists of:
— number and type of used radioactive substances;
— use of additional (not radioactive) drugs;
— result of examination;
— results interpretation;
— recommendations.

Before the beginning of investigation a doctor-radiologist should have the following concrete information:
— identification of the person;
— height, weight of the body;
— menses analysis if the patient is a reproductive age woman (as a majority of investigations with radiopharmaceuticals usage are contraindicated at pregnancy). Majority of radioactive substances are contraindicated for breast-feeding mothers too. Some medical centers use "a rule of 10 days", i.e. radionuclide procedures are carried out only within first 10 days after the menses beginning.
— presence of allergy;
— when a radiation procedure has been recently conducted with the usage of the other radioactive agents;
— presence of artificial prostheses, inlayers or any other materials which are able to absorb radioactive elements.

2.6. Dosimetry. Units

Dosimetry is a part of physics which deals with problems of definition of quantity, intensity and distribution of ionizing radiation in space and (or) time.

The concept of dose is essence of dosimetry. The dose is energy which is transferred to the substance mass unit by a stream of radiation. The dose characterizes the value of the factor which causes certain effects in irradiated substance and quantity of which determines the level of these effects. Such factor is energy which is absorbed by substance from radiation flow.

Not all the energy absorbed by substance, but its quantity in the given mass unit at the given site is considered to be a dose.

The radiation dose obtained from the photon radiation, calculated in the air of the ionized camera is called exposure radiation dose.

The units of the exposure radiation dose is roentgen (R) — a non-system unit and coulomb per a kg (C/kg) — a system unit (SI).

The exposure radiation dose received for a unit of time is called dose rate (DR) and is calculated in roentgens in a second (R/sec), roentgen in a minute (R/min) or roentgens in an hour (R/hr).

Absorbed dose is a quantity of photon radiation energy in environment (any) mass unit:

$$D = E/M,$$

where D — absorbed dose;

E — absorbed total quantity of energy;

M — mass of the irradiated environment.

The volume of the absorbed dose not always can be a measure of expected biological effect. The fact is that different types of radiation have unequal character of distribution of tissues atoms ionization in their micro volume, or different linear energy transfer (LET). Heavy particles with a greater charge, for example, alpha particles, on the way to tissue ionize atoms densely, and it leads to their greater biological activity (greater affection) at identically transferred energy on unit of tissues volume, i.e. at the identically absorbed energy. With the purpose to account such a phenomenon the notion of an equivalent dose is accepted:

$$H = D \cdot QF,$$

where D — absorbed dose;

QF — coefficient of quality.

The equivalent dose is intended for a quantitative estimation of affection of various types of radiation.

Factors of quality, or quality of radiation QF is the factor of dependence of biological effects of radiation on linear transfer of radiation energy to the environment.

The effective dose is a unique universal measure of the risk of radiation exposure under various conditions.

The effective dose is a sum of equivalent doses (H_T) in separate organs and tissues multiplying on corresponding tissues essential factors (W_T).

$$E = \Sigma W_T \cdot H_T$$

Organ (or tissue) essential factor (W_T) determines the ratio of risk of stochastic effect from radiation exposure of the given organ or tissue to the general risk with uneven radiation exposure of the body. Value of W_T for tissues and organs is experimentally and theoretically established (Table. 1).

The effective dose determines a possible total risk from an radiation exposure of various sites of the body in different absorbed doses during the periods of time being, probably, at a great distance from one another. The effective doses are summed up during the course of life and serve as a parameter of the accumulated risk of exposure.

The following units are used to determine the above-mentioned doses:

— coulomb per kilogram [C/kg];
— roentgen [R];
— joule per kilogram [J/kg];
— rem;
— rad;

— Gray [Gy];
— Sievert [Sv].

There are the following ratios between doses and units:
— radiation dose — C/kg, R;
— absorbed dose — Gy, rad;
— equivalent dose — Sv, rem;
— effective dose — Sv, rem.

The name of unit "rad" is an acronym from **R**adiating **A**bsorbed **D**ose. Its size equals 100 erg of energy in 1 g of substance.

Units values parity:
1 Sv = 100 rem;
1 rem = 10 mSv = 1sSv;
1 Gy = 100 rad;
1 rad = 10 mGy = 1 sGy.

The measure of radionuclide quantity is considered a special value, named "activity". Activity of radionuclide is an absolute number of decays of its nucleus for a second in the given sample.

Table 1

Value of the Factor W_T for Different Organs and Tissues

Tissue or organ	W_T
Gonads	0.2
Bone marrow (red)	0.12
Colon	0.12
Lungs	0.12
Stomach	0.12
Urinary bladder	0.05
Mammary gland	0.05
Liver	0.05
Esophagus	0.05
Thyroid gland	0.05
Skin	0.01
Skin surface	0.01
Other organs	0.05

Units of activity is (Becquerel) — (Bq) and (Curie) — (Ci).

1 Bq — quantity of radionuclide in which 1 nucleus decays for 1 second (1 decay/sec).

1 Ci — quantity of radionuclide in which $3.7 \cdot 10^{10}$ nuclei decay for 1 second ($3.7 \cdot 10^{10}$ decays/sec)

Derivative units are used in the medical practice:
kBq — 10^3 mBq = 10^6 Bq; mCi = 10^{-3} Ci: mcCi = 10^{-6} Ki.

Chapter 3
EQUIPMENT FOR RADIOLOGICAL LABORATORY

The laboratories for radionuclide diagnostics should be provided by the following premises:

1. A room for storing radioactive isotopes.
2. Packing room.
3. Treatment room.

4. Washing room.
5. A sanitary-shower block.
6. Cabinets for radionuclide investigations *in vivo* and *in vitro*.
7. Cabinets for serving staff.

In the radiological laboratory, radioactive isotopes are taken, accounted, stored, given out or injected to patients. Localization or distribution of radioactive substances in all organism or separate organs and tissues is determined, as well as their content in biological materials (tissues, blood, urine, etc.); dosimetric and radiometric control over observance of safety conditions of works with radioactive isotopes is carried out.

A radiological laboratory should be provided by central heating. The furniture should have simple design, painted by oil paint, with working surfaces made of non-porous material. Floors and walls are covered by special little-absorbing materials stable to washing means, the edges of floor coverings should be lifted and closed up flush with walls. The premises' corners are rounded off, and doors and windows have the elementary structure. The room for storing has an area of 8–10 m^2, its floor is covered by special plastic, and walls — with oil paint. Radioactive substances are stored in special single- or multisectional thick-wall metal safes.

The package room with the area of 18–20 m^2 is equipped with filtered hoods. The hoods have remote control devices for manipulations with radioactive isotopes. Water, gas, washing solutions are placed to the hoods, there is a device for collecting radioactive wastes or they are connected with a special sewer system.

In the packing room they open ampoules with radioactive substances, prepare working solutions, fill up dosers and distribute isotopes into separate portions. Distant pipettes, syringes, microburettes can be used as dosers.

A procedural room should have the area not less than 10–12 m^2. The patients are administered radioactive substances with the diagnostic and medical purpose there. The positive pressure ventilation should provide six fold air volume per an hour.

Radioactive wastes are neutralized in three ways:

1. 5–10 half-decay periods are kept.
2. They are diluted with water or air up to admissible concentration.
3. They are buried at special burial grounds.

All the people working with open radioactive substances, should be supplied by individual protection means depending on the kind and class of their work.

The means for an individual protection are used.

The overalls are made of the material with adding different substances and other materials for body protection or its separate parts from pollution during the work with radionuclide substances.

In case of a slightest pollution danger, all the work should be carried out in the overall and caps made of unpainted material (rough calico, atlas). Thin rubber gloves are also used. When putting on gloves it is necessary to take the internal part of the cuff with a naked hand, and its external part to take only in the glove. Before putting on gloves, it is necessary to sprinkle hands with talc. After gloves are put on, the cuffs are turned on and the gloves are set straight on the fingers. It is necessary to see to it that their external part never join the internal one and the naked fingers never contact the external surface of the gloves. The gloves are taken off thoroughly the same way as with putting on, following all the rules mentioned above. The gloves are kept in special boxes intended for storage. From time to time the gloves should be checked against damage.

During the work in the radiological laboratory, it is recommended to put on a second pair of shoes made of natural or artificial leather.

The respiratory system is protected by respirators, gas masks, pneumatic suits. The greatest advantage is brought with respirators of disposable use in which fabric is a material of 99% protective function. At higher danger a mask-shaped respirators are used. Isolation is used at presence of radon and xenon.

The overall and underwear should be deactivated in special laundries.

In connection with danger at work with radioactive isotopes, it is categorically forbidden:

— to be in the laboratory without proper equipment;

— to store food products, personal things, cosmetics, cigarettes and other subjects which do not concern the work;

— to smoke, eat, use cosmetics.

There is a special room in laboratory for smoking and rest. It is supplied by the equipment with detergents for washing hands with hot water and a radiometric device for self-checking. This room should be separated from premises where manipulations with radioactive isotopes are carried out.

Chapter 4
RADIATION SAFETY OF THE PERSONNEL AND PATIENTS

4.1. Risk of radionuclide diagnostics

Risk is a possible danger of harmful affection of environment, including ionizing radiation, on an organism of a person.

More than one third of inspections are people older than 64 years and more than two thirds — the people over 45 years old. The effective equivalent dose per a person from these inspections is 140 mSv at the dose of the natural radiation background 2 mSv. The last data testify to a possible hormesis (favorable effect of exposure) at the doses comparable with those used during radionuclide diagnostics.

During diagnostic exams with radionuclides, the used absorbed dose is considerably lower than with X-ray diagnostic exams. So, at functional investigation of the thyroid gland by radioactive iodine the dose influencing the skeleton during one inspection is 2.5 mrad, at functional investigation of the kidneys — 0.14 mrad. In some investigations (for imaging kidneys, bones, pancreas) these doses can reach 1000–2000 mrad, but even in this case the doses are considerably lower than those applied at X-ray exams.

For the purpose of radiation safety of patients at conducting radioisotope diagnostics, the revealing of biological efficiency of radiation effects from radioactive substances has the great value. First of all, it concerns the thyroid diseases diagnostics as this very investigation is mostly conducted. At investigation of thyroid function when ^{131}I influence doses reached 15–20 mSv, chromosomal aberrations rate increased 1.5 folds. After scanning at the affection dose on the thyroid gland 110–220 mSv, chromosomal infringements rate exceeded the initial level 2.5 folds. Mitogenetic effect of irradiation was kept only within the next two weeks.

At radionuclide diagnostics with the usage of different radiopharmaceuticals: ^{131}I, ^{198}Au, ^{32}P and others, the paramedical personnel gets the basic radiation dose while packing RPh in a syringe and injecting it to the patient — 75–95% of the general dose depending on frequency of investigations by different techniques; the doctors — during carrying out examinations of patients — up to 90%.

At work with short-lived radionuclides generator ^{99m}Tc, the operations with eluate obtaining — 40–64% give the basic contribution to total radiation dose for doctors, carrying out investigations — 14–48% depending on the generator initial activity, at work with the ^{113m}In generator — operations with eluate obtaining up to 80% and carrying out investigations — up to 18%. For nurses of laboratories the basic source of irradiation, as it was before, is making working solutions and RPh pre-packing — 47–60%, as well as RPh injecting to the patient — 32–42% depending on a generator's type.

It is established that annual doses of the personnel of radiodiagnostic laboratories even at performance of all the methods with different RPh do not exceed TD max (15 mSv) on the body.

The modern condition of radiation-hygienic providing of medical and biologic application of open sources of ionizing radiation provides realization of radionuclide diagnostics which is entirely safe for patients, personnel and population.

The risk of remote genetic effects for descendants of medical radiologists makes 0.04–0.072 cases by 100 born children for all next generations.

The expected number of death from all the forms of malignant tumors for a group of medical radionuclide of Ukraine from 2500 person for 50 years of professional work makes 7.62 at a spontaneous level for this group 315 cases, and genetic effects in the next generations — 1.52 at a spontaneous level of 250 cases.

The accurate inspection of the persons who have received rather great doses of ^{131}I in the diagnostic purposes was carried out in Sweden (adults — about 1 Gy, under 20 years old — 1.59 Gy) and did not reveal increase in rate of the thyroid gland (TG) tumors.

Nevertheless, at appointment for radionuclide investigation, the factors increasing the risk of occurrence of thyroid gland cancer should be taken into consideration:

1. TG tumors induced by ionizing radiation arise in women more often. And, in women, unlike men, the papillary and sclerosing forms of cancer of TG are more often met.

2. The tendency to TG cancer development takes place in children more often.

3. Duration of the latent period before revealing a tumor is in linear dependence on the level of metabolism.

4. The raised level of thyreoglobulin at the moment of exposure increases risk of TG cancer.

5. The Jewish people have a raised risk of TG cancer.

Some limitations are also necessary if RPh are administered to a lactating woman. In this case a 24–36-hour interval in breast-feeding is recommended after introduction of radioactive iodine to a mother.

Radionuclide diagnostics during pregnancy is limited too, since the most radiosensitive mechanism is DNA transinduction. A developing organism or one or another tissue or organ enters the following phase of development due to changes of volume and quality of DNA information delivery (DNA transinduction).

It is recommended to accompany diagnostic inspection with RPh labeled by ^{131}I (except for hyppurate) with introduction of 20 mg of potassium iodide and to continue TG blockade within 3–10 days after exam.

The organizational-methodical actions directed to decrease radiation doses at diagnostic researches include: introduction of methods *in vitro*, application of short-lived radionuclides, washing out of radiopharmaceuticals from an organism after obtaning information, improvement of the equipment.

4.2. Radiation Protection Factors

There are three factors (methods) of protection against ionizing radiation: time, distance and shielding.

Buffer time — reduction of contact term, which proportionally reduces radiation dose. It is achieved by work intensification in the sphere of radiation action due to practical skills improvement. The radiation dose decreases with reduction of the working day and additional professional vocation.

Buffer distance — increase of a distance between a source of radiation and object of radiation (a person). According to the inverse square law the radiation dose of a point source (in vacuum) is inversely proportional to squared distance:

$$D = D_0 / R^2.$$

Buffer distance first of all is provided by a correct placing of radiation sources. At planning radiological laboratory, the room for storing radioactive isotopes should be placed a great distance away from other industrial premises. Remote devices (tweezers, nippers, captures, pipettes, mechanical hands, robots), remote control are widely used.

Shielding protection — placing on the radiation way of absorbing partitions made of dense materials, such as brick, concrete, baritoconcrete, steel, pig-iron, lead, uranium. Absorbing ability of materials increases as nuclear weight of chemical elements rises and some atoms location gets compact, i. e. directly depends on relative density.

A notion "half value layer" (HVL) is used for determination of both necessary thickness of a protected screen and penetrating ability of quantum radiation. It is such thickness of any material which reduces intensity of wave radiation (X-ray and γ-radiation) 2 times as much. Its size is directly proportional to energy of radiation and inversely proportional to density of a protective material. A necessary thickness of a blanket is calculated according to the equation:

$$K = 2^n,$$

where n — number of half value layers, necessary for achievement of the known K half value multiplicity.

4.3. Recommended Admissible Levels of Individual Effective Radiation Doses at Carrying Out Radionuclide Studies

The benefit of diagnostic procedures can be direct or possible depending on the purpose of research. Diagnostics of an urgent disease, differential diagnostics of severe somatic and especially ontological diseases, belong to the most important, vital indication for using radiomethods, which render direct advantage to the patient with the specified symptoms.

The possible benefit can be received by revealing the latent disease during preventive inspections of the risk groups population. In this case the value of specific activity of a single exposure can depend on the general number of inspections and revealing of latent diseases cases.

On the other hand, the risk of ray diagnostics is related to the age of examined population, a number of exposed persons, sensitivity of the investigation technique and radiation dose which it creates.

Therefore the division of patients into categories with estimation of maximum radiation levels for each of them is expedient. At classification of examined patients it is necessary to consider the purpose of study, a total number of persons which have been subjected to a certain X-ray or radionuclide inspection, sensitivity of the diagnostics method, its clinical or social importance, etc.

There are the following categories of patients which are indicated X-ray and radionuclide study:

1. Category AD. Patients with diagnosed or possible oncological diseases; the patients examined with the purpose of differential diagnosis of congenital cardiovascular pathology, including vascular peripheral malformations, patients which are carried out roentgendiapeutic interventions; the persons investigated urgently (including traumas) under vital indications.

Table 2

The Recommended Maximum Levels of Individual Effective Radiation Doses for Adult Patients Depending on Their Category

Categories of patients	Effective dose, mSv/year
AD	100*
BD	20*
CD	2
DD	1

Note. * — limitation of equivalent doses of irradiation of the most radiosensitive organs (tissues) is supplemented: eye lens — 150 mSv; female gonads — 200 mSv; male gonads — 400 mSv; red bone marrow — 400 mSv.

2. Category BD. The patients examined under clinical indications at somatic (non-oncologic) diseases with the purpose of specification of the diagnosis and (or) a choice of treatment mode.

3. Category CD. Persons from the group of risk, including working at the enterprises with harmful pathological factors, and who are taken on to specified enterprises who were being on professional selection; the patients struck off the register after radical treatment of oncological diseases during periodic inspections.

4. Category DD. The persons which are examined by all kinds of preventive inspection, except for those of CD category; the persons who are studied according to medical programs.

Such maximum level of effective dose which prevents occurrence of deterministic exposure effects is recommended for AD category. It is taken into consideration that it tops the threshold of the equivalent dose 500 mSv/year taken during several years for the majority of organs (tissues), exceeding of which may provoke deterministic effects of radiation.

For BD, CD, DD categories the limited levels of effective doses are lower than for the AD category in connection with a necessity to reduce the radiation exposure risk. The values of these levels are differentiated with taking into account the patients contingent number: limited for categories BD and CD and higher for DD (Table 2).

Taking into account greater radiosensitivity of children's organism in comparison with adults', the maximum doses for children of the AI and BI categories should be lower than ones given in the table 2.

4.4. Limits and Permissible Doses

Numerical values of limits of doses are established at levels which exclude a possibility of occurrence of deterministic effects of irradiation, and at the same time they guarantee so low probability of occurrence of stochastic effects of irradiation, that can be used for both individual persons, and a society as a whole.

Application of any sources of ionizing radiation in the medical practice should be carried out with obligatory keeping to the rules of individual protection and the control of radiation doses of patients and medical staff.

The radiation doses for patients and medical staff during medical practice should be as low as it is possible for diagnostic or medical purposes and never exceed the established norms.

The basic limit of individual radiation dose of the personnel of objects on which practical work is conducted, should not exceed 20 mSv of the radiation effective dose per a year, thus its increase up to 50 mSv is admissible provided that the mid-annual dose of exposure during five years running does not exceed 20 mSv.

The basic individual radiation dose of the population should not exceed 1 mSv of the radiation effective dose for a year, thus mid-annual real or expected radiation effective doses of the person from a risk group should not exceed the established basic dose limits irrespective of conditions and ways of formation of these doses.

4.5. Radiation-Hygienic Regulation of Medical Irradiation of Population

The medical irradiation is radiation of patients during medical examinations and treatment, and volunteers.

The medical irradiation is directed only on achievement of an obvious benefit for a definite person (a patient) or a society in order to receive a necessary diagnostic or scientific information or therapeutic effect.

Taking into account the peculiarities of this practical activity, antiradiation protection is based on the following principles:

— irradiation should be well-grounded and appointed by the doctor with the purpose to get useful diagnostic and therapeutic effects which cannot be received with other methods of diagnostics and treatment (a principle of proving value);

— collective doses of population irradiation during X-ray and radiological procedures should be as low as it is reasonably achievable (ALARA) with taking into account ecological and social factors (a principle of optimization);

— the size of radiation dose is established only by the doctor for each patient according to clinical needs and with taking into account a necessity to prevent occurrence of deterministic effects in healthy tissues and in an organism as a whole (a principle of non-exceedance).

Maximum doses for limitation of medical radiation are not established, and necessity of carrying out a certain X-ray or radiological procedure is proved by the doctor on the basis of medical indications.

Non-proved repeated X-ray and radiological diagnostic procedures of the same type are admissible only for clinical need and a possibility to obtain new or advanced information. Unreasonable duplication of the same diagnostic procedures is forbidden. For prevention (duplication) of the roentgen-radionuclide procedures and to receive valuable clinical information (control of quality of X-ray examinations) certification of the personnel and workplaces, certification X-ray and radionuclide diagnostic and radiotherapeutic equipment and RPh according to the order established by the Ministry of Health of Ukraine.

At carrying out prophylactic investigation of the population the effective annual dose should not exceed 1mSv.

Oversizing this level is permissible only under conditions of adverse epidemic situation in coordination with the State Sanitary-Epidemiological Service of MH of Ukraine.

Persons who assist patients at carrying out diagnostic and therapeutic procedures of their own free will should not be irradiated by doses over 5 mSv.

The women of reproductive age (till 45 years) with the diagnosed or possible pregnancy, and during lactating period should avoid X-ray and radiological procedures, except for urgent ones.

The medical radiation of volunteers who participated in the medical and biologic researches, should be conducted with the permission of the Ministry of Health of Ukraine under the following conditions:

— not to exceed the radiation levels recommended by the Ministry of Health of Ukraine;

— a written consent of the volunteer;

— to inform a volunteer about possible consequences and the risk related to exposure.

4.6. The Procedure of Calculation of Individual Effective Doses of the Medical Diagnostic Radiation of Patients

The individual effective dose received by the patient during radiodiagnostic procedure (H, mSv) is calculated according to the formula:

$$H = H(1) \cdot A,$$

where H (1) — an effective dose by a unit of administered activity (mSv/mBq), the value of this activity is determined by the table;

Table 3

Act of Radiation Dose During Radiological Diagnostics

Surname, name, patronymic ____________________

Sequence of total	Date	Type of study	Effective dose for 1 study, mSv

A — activity administered to the patient (mBq).

The radiologist should write down the received value of the dose in the act of administered radiation dose of the patient according to the form established by the Order of Ministry of Health of Ukraine N 118 of 19.06.90 (Table 3).

If during a year the patient have been conducted other X-ray or radionuclide diagnostic studies, the obtained doses are entered in the act of radiation dose as well. At the end of each year it is calculated the total dose received by the patient within a year at medical diagnostic radiation (mSv/year).

The act of radiation dose is kept in the medical card of the outpatient or in history of development of the child.

The information concerning the exposure dose remains in archives of medical institutions during 50 years, and at the end of the term should be given to the National Archival Fund.

The patient at his request may receive the full information about expected or received radiation dose or its possible consequences.

4.7. The Basic Ways of Radiation Safety Improvement in Medical Radiology

1. Improvement of systems of radiation protection in laboratories of radionuclide diagnostics — improvement of systems of remote dosing and RPh introduction to patients in order to decrease radiation exposure of wrists in paramedical personnel.

2. Optimization of system of radiation monitoring by introduction of the modern dosimetric and radiometric equipment for the control of levels of radiation, common techniques of the control and estimation of radiation safety condition.

3. Making of the National Registry of data about exposure doses of professional workers by results of dynamic supervision over health condition of the personnel and their descendants.

Chapter 5

INFORMATION AND PSYCHOLOGICAL PROBLEMS OF RADIOPHARMACEUTICALS USAGE. DEONTOLOGY

A rather small number of doctors want to get into radiology and nuclear medicine to great extent because of wrong ideas about real influence of ionizing radiation under professional conditions. The overwhelming number of the colleagues at the beginning of their work pass the stage of psychological adaptation to the work in hazardous conditions. At this period young doctors reveal a little raised anxiety and intensified attention to a possible radiation influence. The doubt and uncertainty, especially with little and insignificantly proved reason, can be a source of very serious anxiety concerning disturbances of reproductive function. Sometimes it can lead to undesirable consequences impeding a normal creative work, change the attitude to the specialty. The broad circle of doctors of different specialties should know that all the disturbances of the reproductive function are out of question today under conditions of strict keeping to working rules and norms of radiation safety.

With increase of a working period there arises inclination to anxiety, and asthenization takes place in some persons. At psychological inspection the tendency to anxiety states in the majority of working personnel (up to 56%) is detected.

As a whole, the attitude of population to a possibility of any contact with irradiation became more careful, including cases of health service. To overcome psychological alarm of patients it is necessary to fully inform them about examinations by methods of radionuclide diagnostics.

The doctors are responsible for patient being kept informed. In 1972 the American association of hospitals has published "The list of patients' rights". One of 12 rules of this document says: "The patient has the right to receive the necessary information from the doctor before giving his consent to any procedure or treatment". It is necessary to answer all the questions of the patient related to coming procedure, to explain what will happen to him during procedure.

Patients often associate the notion of nuclear medicine with hazardous radiation and even with cancer.

Patients are interested in the following as a rule: "How long do the radioactive substances persist inside my organism?", "Will radioactivity make me any harm?", "May I stay in the company of other people after the radionuclide injection?".

The patients are often informed about X-ray action and hence the doctor should be ready to answer the questions about difference between X-ray action and procedures of nuclear medicine.

While informing the patient it is necessary to take into account that people obtain information much better if they are physically healthy, have had a good rest and feel comfortable.

Special and complicated problems are those concerning estimation of possible influence of irradiation on reproductive function of the patients exposed to radiodiagnostic inspection.

When the doctor considers that the patient cares for these questions and is disturbed, it is not necessary to expect when the patient will ask, the doctor must touch the problem by himself. The slightest doubts should be removed.

There were cases when some women wanted to make abortion being scared that the future child will appear defective because of the prenatal irradiation.

It is necessary to notice that all preventive and sanitary-epidemical work should be not only highly-professional but also go on in atmosphere of pleasing psychological influence on persoñal working with ionizing radiation. Women should be firmly convinced in efficiency of provided preventive measures.

Despite of severe restrictions of radioisotope inspection carrying out in pregnant women, individual cases of examination take place because pregnancy is untimely detected, or a doctor doesn't get a necessary information.

There are summary radiation dose tables for the most widespread radionuclides and radiopharmaceuticals, including gonads.

Due to radiological studies various radioisotope inspections have been regulated and limited by strict indications.

Experimental studies revealed that radiation influence with several sentigray may cause different somatic mutations.

Some authors recommend to make abortion at doses of 0.1–0.2 Gy.

The doctor shouldn't go into professional details, such knowledge will bring the patient no good, but do harm. Nevertheless the doctor must give exhaustive information concerning possibility of timely or constant infertility. It's a moral aspect of the problem. The patient makes the final decision about his plans to have children.

Both doctors and patients should be convinced of safety and necessity of diagnostic application of radionuclides.

Efforts of doctors-radiologists in pediatric practice should involve both a patient and his parents. Encouragement of parents can promote success of radionuclide procedures. Beside of psychological support of pediatric patients it is necessary to take care of devices for keeping the patient in a proper position. But restriction methods can be inadequate if the child is very active or excited. In such cases it is necessary to use sedatives and hypnotics.

Chapter 6
RADIONUCLIDE DIAGNOSTICS IN CASE OF EMERGENCY

At diagnostics of urgent conditions it is necessary to apply express-methods and treatment modes, suitable for a lying position of the patient.

Perspective direction of radionuclide diagnostics application is detection of fractures which are hardly recognized by radiological methods.

The rapid test of the liver radionuclide studying consists in determination of constants (C_1, C_2, C_3) of relative rate of agent concentration change at the accumulative site of hepatogram. Constant C_1 allows to estimate liver blood supply, C_2 — its absorption function, C_3 — excretory function.

At craniocerebral trauma, scintigraphic investigation with the help of pertechnetate ^{99m}Tc reveals impairment of the cerebral blood flow, the least one — at cerebral concussion and cerebral contusion with compression.

Traumatic damages of heart and myocardial infarction can be revealed in cardiac resuscitation department during scintigraphic investigation of the thorax with pyrophosphate ^{99m}Tc. This method is recommended especially with insufficiently informative electrocardiogram, as well as enzymatic diagnostics. Other approach to myocardial necrosis diagnostics is ^{201}T1 using, which gives image of a healthy myocardium.

Radionuclide methods allow to execute the rapid tests of multiple damages. At combined trauma it is possible to reveal infringements of hemodynamics, breathing and metabolism.

Presence of intraperitoneal bleeding can be detected during scintigraphy of the pelvic organs by means of short-lived isotopes after determination of the RPh concentration rate increase.

Dynamics of the clinical course and severity of cardiovascular failure is determined by the method of radiocardiography with the use of gamma-camera and ^{99m}Tc. This method in emergency surgery and traumatology is used for making indications to operative intervention at elderly people.

At acute poisonings and burn disease they use the quantitative analysis of reno- and hepatogram curves parameters. Dynamics of changes of curves depends on the kind and severity of poisoning.

The mechanical jaundice manifests itself by depression of absorbing liver function the extent of which depends on degree of biliary tracts obturation.

The edematous form of acute pancreatitis manifests itself by diffuse increase of the gland (of the whole gland or its part), misty outlines.

Part II
SPECIAL QUESTIONS OF RADIONUCLIDE DIAGNOSTICS

Chapter 1
RADIONUCLIDE DIAGNOSTICS OF HEART AND GREAT VESSELS DISEASES

Radionuclide diagnostics is used in cardiology side by side with X-ray method of heart and great vessels investigation. It allows obtaining important, and sometimes unique information on heart condition; it does not demand catheterization of the vessels and heart; it is performed both at rest and after physical activity.

The following radionuclides are used: human serum albumin (HSA), ^{99m}Tc-pertechnetate; thallium-201; ^{99m}Tc-pyrophosphate; tantalum-178; iridium-191m; gold-195m; C-butyrate-sodium; ^{99m}Tc-tetraphosmin; ^{99m}Tc-technetril.

Methods of diagnostics:

Radiocardiography. The purpose of this investigation is to determine key parameters of central hemodynamics, including minute and stroke volume of blood, time of blood circulation in lungs, the general peripheral resistance. ^{99m}Tc labeled human serum albumin is used as RPh.

Equilibrium radionuclide ventriculography — is one of widespread studies of the heart. The pump function of the heart and character of movement of walls are determined by means of this technique. The principle of the method is registration of a series of images on the gamma-camera's monitor. Gated ventriculography gives a possibility to calculate regurgitation fraction at heart diseases accompanied by valvular failure. This technique has an advantage that investigation can be conducted during a long time period, for some hours when studying, for example, medical drugs action on the heart. HSA with ^{99m}Tc is used as RPh.

Radionuclide ventriculography (bolus ventriculography). The purpose of investigation is to determine parameters of central hemodynamics, intracranial shunts from left to right, mobility of left ventricle walls, congenital heart diseases, exudative pericarditis, aneurisms, thromboembolism. Usually they apply ^{99m}Tc-pertechnetate with activity of 4–6 mBq by 1 kg of body weight with volume of 0.5–1.0 ml. It is injected quickly by a bolus according to the Oldendorf's technique, a so-called cuff method (intravenous RPh introduction, with rapid cuff release). At some congenital heart diseases the reversed (left-to-right) shunt takes place. Such shunts happen at cardiac valve septa defects. With acquired heart diseases this technique allows to establish the extent of regurgitation through mitral and aortal apertures.

Myocardial perfusion is carried out by studying thallium uptake by myocardial cells. This extraction depends on regional perfusion and vital activity of cells. Ions of thallium are similar to ions of potassium and extracted from the blood by heart. About 4% of thallium injected intravenously accumulates in the myocardium within first 5 min after the injection. Defects of distribution which take place in 2–4 hrs after the injection are used for diagnostics of ischemic foci of the myocardium. Defects which remain after 3 hrs relate to areas of myocardial scars after a heart attack.

Sensitivity of tallium-201 for detection of acute myocardial infarction is the most effective during the first 6–4 hrs after corresponding symptoms and falls up to 72% after 24 hrs. The image with tallium-201 is more sensitive at diagnostics of trasmural heart attacks (88%) than with non-transmural heart attacks (63%).

The image with tallium-201 is also applied for diagnostics of the coronary artery disease to determine physiological value of known coronary diseases or to estimate a degree of myocardial viability after myocardial infarction. Sensitivity at definition of ischemic disease considerably rises if the myocardial flow increases (with the help of exercises or drugs). Sensitivity to stress with tallium-201 for revealing coronary stenosis is 82% and specificity — 91%.

Tallium-201 helps to detect angiostenosis, in particular with collateral circulation of the regions supplied by stenotic vessels. It is especially important for patients prepared for coronary surgery, angioplastic, fibrinolytic therapy and differentiations of ischemic, but a viable tissue from a myocardial scar.

The patient should take orally nothing 4 hrs before diagnostics. ^{201}T1-chloride is injected rapidly through a permanent catheter or another one which was inserted beforehand. Because of possible arrhythmia or other cardiac complications, ^{201}T1-studies with loading should be supervised by the cardiologist or another qualified doctor. Defibrillator and all necessary medicines should be ready for immediate use.

The tension caused by physical activity before it is displayed in the studies with ^{201}Tl has two goals. For the first time when myocardial need in oxygen is raised due to tension, cardiac tissue perfusion rises and myocardial uptake of the radioactive indicator occurs faster and more complete. Due to strain caused by loading, in comparison with studies at rest, thallium concentration in the myocardium will rise and lesser activity in the liver, spleen, kidneys and gastrointestinal tract will be observed. For the second time, the areas of myocardial ischemia which may be unseen in the investigation with thallium in rest, can be revealed at tension procedure as stenotic blood vessels of the myocardium with normal perfusion are not able to dilate in response to faster blood stream at loading. Hence, distribution of thallium in the myocardium can be uneven (sign of ischemia) during loading but seem to be homogeneous or normal at rest. Both procedures are usually performed: scanning of thallium during loading is accompanied by approximately 4-hour subsequent investigation at rest.

Induction of coronary vasodilatation with pharmacological agents is an alternative to loading in myocardium studies with ^{201}Tc use.

Infarction imaging. Technetium-99 pyrophosphate which is widespread for bones imaging, is also used for definition of the age and extent of myocardial infarction manifestation. It is used in patients with known coronary heart disease which were admitted to hospital in 24 or 48 hrs after a heart attack, when the enzyme sample is still normal and in the patients which have not been established fresh infarction at electrocardiograms.

The method consists in administration of 555 mBq of ^{99m}Tc pyrophosphate intravenously 90 min before visualization. The anterior, left anterior oblique (40°), left anterior oblique (60°) projection and left lateral projection are recorded.

Ventricular function. Deranged wall movement is estimated on the basis of both subjective analysis of data transformed by a cinedisplay and computer investigation results, which record the output regional fraction. The other measurements of cardiac function containing primary-transitory data determine: cardiac output, average volumes of chambers and average time of passage through the chamber.

Ejection fraction for right ventricle can be most accurately obtained at the first transitory stage in a patient at 30° right anterior oblique projection. It is accounted by the fact that the right atrium is not below the right ventricle like in case with 40° left anterior oblique stage.

Determination of minute volume. Minute volume — volume of blood (L) which the heart puts out during a minute (in the norm — 6–8 L). The patient is laid on his back. The transducer is established above the heart area. The indicator — human serum albumin (HSA) labeled by ^{131}I, ^{99m}Tc-

pertechnetate. The drug with activity of 20 kBq/kg and volume of 0.2–0.3 ml is fast injected. The curve is recorded.

A steeply ascending curve reaching maximum within 3–4 sec corresponds to radioactive blood supply of the right ventricle. Curve descending is evidence of transition of the drug with blood to the pulmonary vessels. Return of the drug from lungs to the heart (but already to the left chambers) is accompanied by fast rise of blood. Subsequently concentration of the drug decreases to a standard level caused by its even dissolution in the blood. The minimal volume of blood stream is calculated by the formula

$$Mv = Av/At,$$

where Av — activity of the injected isotope, A — average concentration of indicator agent during the first passage through the cardiac cavity, t — time of the first isotope circulation in the heart.

Considering the value of MV, there are calculated the other hemodynamics parameters: stroke volume (Sv), minute index (Mi), stroke index (SI).

$$Si = Sv : \text{heart rate per a minute.}$$

Determination of cardioportal blood flow rate (studying of linear heart-liver blood flow rate). It is applied ^{131}I labeled HSA. The technique is the following: before intravenous introduction of albumin labeled ^{131}I, the detectors are installed — one in the heart area, the other — above the liver. Albumin ^{131}I is injected — 25–30 μCi per 0.3 ml of physiological solution. Time of cardioportal circulation is determined as time from peak of activity in the liver region, which makes out 24–26 sec in the norm. With presence of pathological processes in the liver the rate of cardioportal blood flow decreases considerably. So, with chronic hepatites, metastatic tumor masses and hepatites caused by diabetes mellitus, this time makes out 34–36 sec. At liver cirrhoses the time of cardioportal circulation increases up to 55–60 sec, which serves as an objective test in differential diagnostics between cirrhoses, chronic hepatites and metastatic defeats of the liver, as well as for definition of efficiency of surgical treatment of liver cirrhosis.

Analysis of myocardial condition. Myocardial condition in patients suffering from ischemic heart disease is studied with a new radiopharmaceutical ^{11}C-sodium-butirate by means of positron emission tomography (PET). In zones of cicatricial changes there are observed stable defects of the drug accumulation, and at the ischemic zones — slow radioactivity excretion associated with decrease in oxidizing metabolism rate.

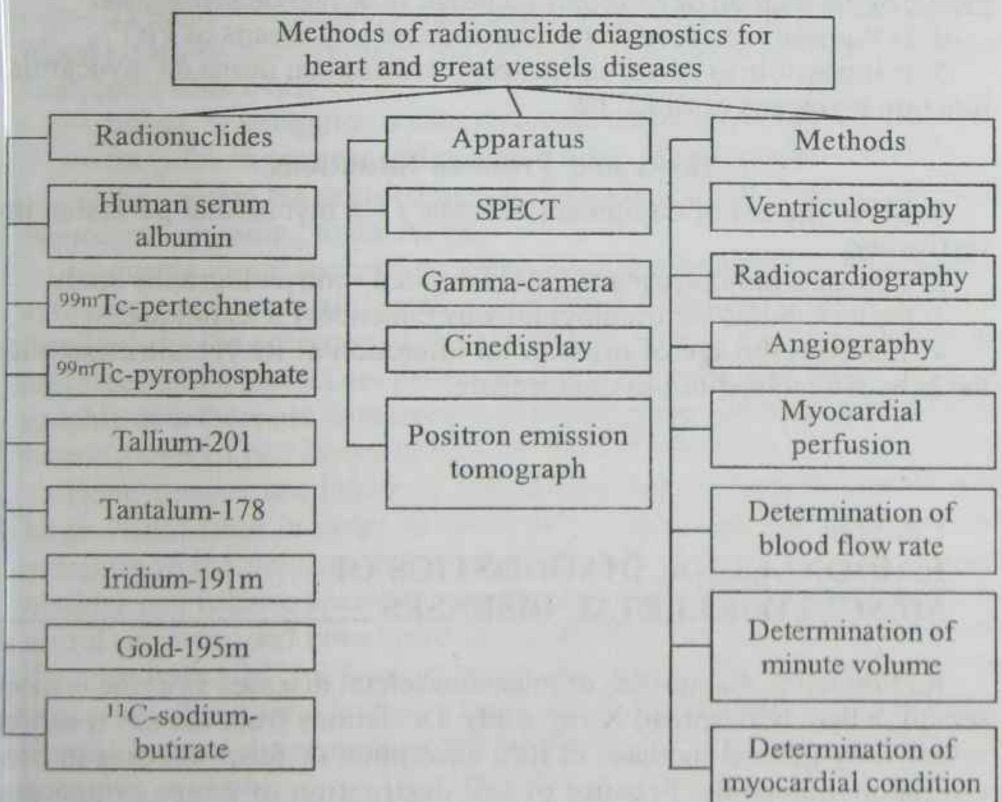
The quantitative analysis of left ventricle wall thickness with ^{99m}Tc-tetraphosmine allows obtaining additional information for diagnosis of myocardial hypertrophy. The most frequent clinical indications for administration of radionuclide ventriculography — cardiomyopathy, cardiotoxic effect test, ischemic heart disease (prognosis, remodeling, risk of dissection), defects (portal insufficiency), pharmacological testing.

Study of antianginal drugs influence on myocardial perfusion. The single-photon emission computer tomography of the heart with ^{99m}Tc-technetril can be successfully used for estimation of influence of one or another antiseptic drug on myocardial perfusion. By means of perfusion scintigraphy of the myocardium for the first time it was possible to objectively establish that under influence of antagonists some IHD patients can develop deterioration of coronary blood circulation.

Key Concepts of the Theme

Radiocardiography, gated ventriculography, radionuclide angiography, myocardial infarction imaging, a technique of ventricular function analysis, technique of portal blood flow rate determination, a technique of minute volume determination, a technique of myocardial condition analysis, a technique of studying antianginal drug influence on myocardial perfusion.

The Formalized Structure of the Theme Contents



Questions for Independent Work

1. Name radionuclides used for radionuclide study of the heart and great vessels.
2. Name methods of radionuclide diagnostics of the heart and great vessels.
3. Is there a necessity of catheterization of the heart and great vessels at radionuclide diagnostics of the heart and great vessels diseases?
4. How to determine pump function of the heart?
5. Determine the aim of bolus ventriculography.
6. Describe radionuclide method of heart investigation with exercises.
7. Use of PET for radionuclide diagnostics of heart diseases.
8. Use of SPECT for radionuclide diagnostics of heart diseases.

Alternative Test Tasks for Self-checking

1. Have all radionuclide used for diagnostics of heart and great vessels diseases been listed: technetium, human serum albumin?
2. Is it possible to determine ischemia foci of the myocardium by myocardial perfusion method?
3. Is it possible to differentiate liver cirrhosis and chronic hepatites by means of the method of cardioportal blood flow rate determination?
4. Is it possible to reveal zones of ischemia by means of PET?
5. Is it possible to reveal influence of antianginal drugs on myocardial function by means of SPECT?

Tasks and Problem Situations

1. Make the list of equipment necessary for myocardial perfusion investigation.
2. Choose a radiopharmaceutical for gated ventriculography study.
3. Perform bolus ventriculography by Oldendorf's technique.
4. Estimate the age of myocardial infarction at its visualization with the help of ^{99}technetium-pyrophosphate.

Chapter 2
RADIONUCLIDE DIAGNOSTICS OF MUSCULOSKELETAL DISEASES

Radionuclide diagnostics of musculoskeletal diseases as a rule is more sensitive than widespread X-ray study. Deviations from the norm can be revealed by general increase in RPh absorption or focal increase in concentration. Sometimes because of full destruction of bones or necrotic area, nuclide uptake doesn't take place and a "cold spot" is noted. Presence of the increased soft tissue in thick patients increases dispersion of photons and thus influencing technical quality of the image. Besides, the kidneys, urinary bladder, other normal areas can concentrate RPh at scanning bones: the nasopharynx, the oral cavity, the breast and the lacrimal apparatus. Different pathological damages of soft tissues accumulate RPh at bone scanning. Compounds of technetium-99^m with affinity to the bone tissue join mineral exchange intensively. There are two great classes of phosphor containing compounds:

1. Pyrophosphate which has two phosphate residues with a bond P—O—O.

2. Diphosphates. These compounds are organic analogs of pyrophosphate with bonds P(s)—C—P. Chemically they are more stable than polyphosphates and more susceptible to enzymatic hydrolysis *in vivo*. After intravenous injection of ^{99m}Tc complexes RPh spreads fast through the extracellular liquid. The most part of the administered dose is accumulated by the bone from there, the rest is excreted by kidneys into urine. Average cumulative six-hour excretion with urine makes out 68% for ^{99m}Tc.

Technique of the study:

— 75 ml of ^{99m}Tc-methylendiphosphate are injected intravenously, then blood clearance and uptake in the skeleton from the radiotracer have been analyzed within 2 hrs;

— before investigation a patient should empty the urinary bladder;

— they obtain anterior and posterior whole-body image;

— they obtain the detailed image of the chest if the object of the study is sarcoma spreading to the lungs;

— during visual analysis of scintigrams they estimate agent uptake in symmetric zones of pair bones and in near-by vertebras. On the basis of this analysis the presence of focal pathology, site of the process, number and sizes of lesion foci are determined. At computer processing of scintigraphic data there are compared in percentage the agent content and symmetric zones of pair bones or near-by located vertebras.

Bone images are better to obtain with use of gamma-camera with large visual field in order to cover all the skeleton. The processes developing in the pelvis and masking by residual activities in the urinary bladder can require special consideration; for example, diseases of the sacral or coccygeal bone need in visualization of a patient sitting on a detector with a lateral view of pelvis. In cases of diseases including the processes of vertebral bodies, a medially directed collimator can be used. For differential diagnostics of hidden fractures, three- or four-phase bone scanning is used.

Rise in osteotropic RPh accumulation by 40% and more at the area of 1.5–2 m^2 and more in comparison with a symmetric site of a pair bone is considered as presence of pathological process. Presence of pathology is considered to by doubtful if accumulation of the agent less than indicated values. The picture at inflammatory and tumor defeats is connected with increase in accumulation of osteotropic radionuclide, sometimes 10–15 times as much in comparison with a healthy site.

Scintigraphy allows to reveal initial symptoms of inflammation in joints of patients suffering with aseptic arthritis (Fig. 3) even at absence of clinical symptoms, manifestating diffuse increase in periarticular surface activity.

X-ray studies in such cases can show only a stretching of a capsule of a joint. Comparison of clinical and X-ray data with results of scintigraphy with ^{99m}Tc-pyrophosphate at joints study has shown that radionuclide investigation is the most sensitive indicator of inflammation activity, and the change revealed by the radionuclide method often precedes the development of clinical radiological signs of pathological processes in joints. By means of radionuclide methods one can manage to reveal the presence of subclinical signs relapse in patients suffering from rheumatoid arthritis. The scintigrams with ^{99m}Tc are more sensitive in detecting synovitis than clinical investigation of joints. One should mind that osteoscintigraphy reveals greater number of damaged joints than it was clinically suspected. But the given type of study is nonspecific for arthritis, changes take place during fractures, bone diseases.

As an example we adduce the following clinical cases:

1. A 20 year-old woman complains of slight rigidity and pain in hands. Deformation is not detected at physical examination. At the bone scan there is an average increase in radionuclide accumulation in both wrists, the second, the third and the fifth phalangial joints, the second proximal interphalangial joint of the left wrist, the second and the fifth metacarpophalangial joints of the right wrist. Diagnosis: arthritis which has involved wrists and hands.

Laboratory studies confirmed the diagnosis of rheumatoid arthritis. The patient has recovered after treatment by anti-inflammatory means.

2. A boy of 11 years old has trod on a rusty spring of the bed and wounded the right foot. A week later the pain in the right extremity developed, and he was hospitalized. X-ray investigation revealed nothing, and the boy was sent home. In 4 days the pain intensified, and he returned to the hospital. Scanning of the bone with ^{99m}Tc MDR in a frog position revealed increased blood flow in the right heel bone, which was evidence of osteomyelitis of the right heel bone. The patient was directed to treatment of osteomyelitis. Radiological investigation revealed increased X-ray transparency and irregu-

larity, which could testify to osteomyelitis. And despite the fact that growth of microorganisms in the heel bone was not detected, it was considered that the patient had osteomyelitis, and he received intravenous injections of antibiotics within 4 weeks. At the moment of discharge the infection was under the control.

3. Now we give an example of radionuclide diagnostics of polymyositis:

A patient of 49 years old complains of muscular weakness and fever, which developed two months ago. Creatinphosphokinase of serum has made 5,800 units. Myoglobulinuria and cylinders in urine were also observed. At bone scanning with ^{99m}Tc increased uptake of the radioactive indicator was observed. Muscle biopsy revealed chronic inflammation with fibers necrosis and regeneration. The patient was treated with steroids and at the moment of discharge the condition of the patient considerably improved, fever was absent.

With various forms and different stages of gout there was observed an increased concentration of a ^{99m}Tc labeled RPh. Side by side with revealing inflammatory signs of joints, various size urates accumulation were noticed both near joints, and in other soft tissues. Deeply located tofuses have accurate borders on the scan. Concentration of the agent in them exceeds the norm 5–7 times as much. At a third of patients at gamma-scintigraphy the accumulation of urates in kidneys is revealed. Renal pathology had not been diagnosed before.

Thus, scintigraphy allows revealing characteristic changes in joints, and accumulation of urates in other tissues, which is very important in making final diagnosis.

The patients suffering from psoriasis often have latent forms of arthritides or spondiloarthritides. Scintigraphy helps very much in diagnosis of defeats of joints in different terms of disease. High concentration of the agent is noticed in distal phalanxes, ankle joints, iliosacral joints and the lumbar department of a spine. In the field of sternoclavicular, iliosacral joints RPh accumulation occurred unevenly, and in the spine increased agent concentration was often found out only unilaterally. (Fig 3). In contrast to X-ray investigation at scintigraphy the inflammation foci are revealed not only in the joint itself, but also at a distance. Bone scanning reveals indistinct borders. Defeat of iliosacral joints is observed along a great extent with width of 6–7 cm. Beside of the specified joints affection, the foci of moderately raised accumulation of RPh in the middle of the sacrum and in the area of lumbar vertebrae are revealed. RPh accumulation is observed also at sites of tendons attachment. Spine affection in contrast to Bechterew's disease (Fig. 4) on a scintigram is revealed at the lateral parts, contours of vertebrae are indistinct.

Intense accumulation of RPh is observed at bone fractures, rheumatic polyarthritides and is not considered to be a specific sign of a certain disease. Osteotropic metastases are the most precisely revealed by scyntigraphy.

The diffuse increase in ^{99m}Tc-phosphate uptake usually takes place at metabolic diseases of the bone. The increased delay of ^{99m}Tc-diphosphate uptake is found out in patients suffering from renal osteodystrophy, osteomalacia or primary hyperparathyroidism. Patients with senile osteoporosis on the contrary show a normal delay of diphosphate.

The bone scanner is more sensitive than the roentgenogram at determination of primary hyperparathyroidism, renal osteodystrophy and osteomalacia, but is less sensitive than the roentgenogram at determination of osteoporosis. Osteoporosis is determined at loss of no less than 30–60% of bone weight. Intensified uptake of the osteotropic radiopharmaceutical at the site of fracture is noticed at the period between 12 and 24 hrs after the injury. The increased uptake of tracer can be observed for many years. Formation of callus takes place much earlier than at X-ray investigation.

Differential diagnosis between infection and hip joint hypermobility in patients with hip joint prosthesis is carried out with combined scintigraphy with ^{99m}Tc-leukocytes and ^{99m}Tc-MDR adjoining the prosthesis of tissues.

Use of radionuclide study at Bechterew's disease renders greater help at early and differential diagnosis of spine and joints diseases, to define more exactly the degree of local inflammatory process activity, to reveal the spine or joints affection sites for the lack of clinical signs of inflammatory process, to make evaluation of pathologic process dynamics more objective.

With use of ^{99m}Tc labeled osteotropic RPh the kidneys and the urinary bladder are also visualized because up to 40% of these compounds are washed out from an organism by kidneys. This allows to examine the kidneys at suspicion on hypernephrome. During this study anatomic-topographic features of the kidneys, the secretory-evacuation function, blood flow in the renal parenchyma, tumors and presence of metastases in system are determined in one stage.

Radionuclide studies are used at diagnosis of benign tumors. Osteoid osteoma is a frequent benign tumor of the bone. It is met in men twice more often than in women and approximately 90% of occurrence is between the age of 5 and 25 years. The local pain is often stronger at night, increases at physical activity and can be weakened by aspirin. When the spine is involved, a painful rigid scoliosis appears, which is bent inwards to the site of affection. Pathological components of osteoid osteoma are small, with high vascularization osseus trabeculae and surrounding sites of reactive bone sclerosis.

Osteoid osteoma causes intensive radionuclide uptake at the site of damage, as a result of blood flow increase and a reactive neoplasm.

We give the following example:

A 10-year old girl within 9 months was in a corset in connection with thoracolumbar scoliosis, accompanied by pains in the back. X-ray exam revealed no damages of the vertebrae or spine column. At bone scanning with ^{99m}Tc-MDR the area of intense uptake of radioactivity in an articulate surface of the body of the eighth chest vertebra is revealed. On the basis of clinical data and scanning results osteoid osteoma was supposed. Surgical removal of osteoid osteoma reduced scoliosis from 40 to 12 degrees. Pains in the back disappeared.

A unicameral bone cyst arises mainly in small children and teenagers. It is asymptomatic as a rule and is mostly located in the proximal department of the humeral bone. With absence of pathological fracture the radionuclide bone scanning mainly shows absence or minimal radioactivity increasing at the site of the cysts. Large cystic damages can be shown on the bone scans as a photon-deficient zones.

Eosinophilic granuloma of the bone is the most benign form of histocytosis. Usually bone diseases develop in patients under 10 years old. A pain in bones and restriction of mobility are the most frequent complications. These diseases are usually seldom determined on X-ray exams and mainly show increased radionuclide uptake up to bone scans.

The other benign bone tumors, such as enchondroma and osteochondroma are characterized by different uptake degree, which deviates from the intensive one, like with sarcomatous disease, till the lower one.

Approximately 50% of injected ^{99m}Tc accumulate in bones. Another 50% of the administered dose are excreted by the kidneys. The excreted radioactive substance which accumulates in the urinary bladder, can prevent visualization of pelvic bone structures. In order to decrease the influence of the urinary bladder content, it is necessary to empty it directly before the study. Intake of liquid between the contrast injection and the study stimulates reflex of urination. This procedure should decrease the radiation dose due to reduction of radioactive substance transit term.

Osteoid osteoma is characterized by intensive focal accumulation of technetium-99m methyldiphosphate mark in the image obtained in 3–4 hrs after the injection.

Both osteogenic component of the disease, and great blood flow promote considerable uptake of the mark. Osteoid osteoma covers approximately 10%

of benign bone tumors. The tumor mostly occurs in the second and third decades of the life, a half of cases develops in the hip or tibia. The defeat is more often localized by the end of a plate of long bones. The humeral bone, the spine and the wrist can be affected as well. In the spine they are usually localized in *pedicules, laminae et processus transversus*. Often they are connected with a painful scoliosis. Bone scintigraphy in osteoid osteoma, like with many other infringements, reveals the disease before it is revealed in X-ray. If this diagnosis is suspected even with normal X-ray exam, bone scan should be executed. It can improve the term of diagnosis establishment by some months or years. From 100 cases of surgically confirmed osteoid osteoma, 75% were suspected on the grounds of a usual initial X-ray examination, which helped in preoperative diagnosis. Bone scan often is not necessary at osteoid osteoma of long bones, when roentgenologically the diagnosis is often (but not always) determined. Bone scan is used with defeats of the axial skeleton, which is difficult to reveal roentgenographyically. Often children are treated for different reasons of pain in the back before the diagnosis of osteoid osteoma is established.

In structure of oncological diseases a great proportion is occupied by nosological forms of cancer which are often accompanied by multiple metastases in the bone: breast cancer (BC) (Fig 4), prostate cancer (PC) and thyroid cancer, lung cancer, etc. So, according to autopsy at breast cancer bone metastases are revealed in 40–70% of patients, and at lung cancer and prostate cancer — at 50–85%. It is established that in 18 months after diagnosing breast cancer at 8% of patients with initially normal scans bone metastases develop and in 36 months their number reaches 15%. It is necessary to take into account that 44% of patients without pain in bones have metastases in bones.

Let's give an example:

A woman, 58 years old, was developed dizziness and gait disorder 2 weeks ago. In a week the right hand and the leg became weak and painful, speech disturbances added. She was admitted to the hospital where a mobile mass of 4×5 cm was revealed in the right mammary gland. At investigation of bones with ^{99m}Tc-MDR plural areas of the increased quantity of tracks were found in the skull, neck, mediastinum, lumbar vertebrae.

Presumably: multifocal metastases of breast carcinoma to the bones. The computer tomography revealed masses in the field of left parietal bone, interfering the brain tissue. The mental status of the patient worsened, right hemianopsia developed. Brest biopsy revealed undifferentiated carcinoma of ducts. Scan diagnosed metastases.

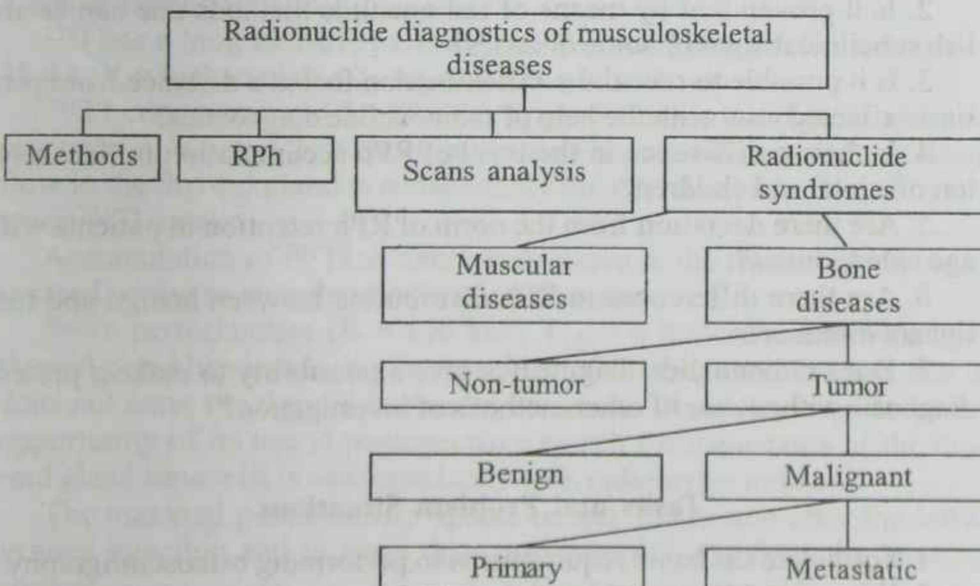
Osteosarcoma takes place at men more often than in women (2 : 1) and the peak of its detection is in the age between 10 and 25 years. The pain and swelling are the most frequent symptoms. It most often arises in the lower extremity, in particular, around the knee joint, both in the distal department of the hip, and in proximal department of tibia (Fig. 6).

On radionuclide bone scan the osteosarcoma usual reveals intense activity because of its rich vascular nature and formation by a tumor of a new bone. Bone scans are performed at osteosarcoma first of all to determine metastases.

Key Concepts of the Theme

Musculoskeletal system, a scintillation camera, radionuclides, arthritides, osteomyelitis, polymyositis, osteoscintigraphy, hyperparathyroidism, renal osteodysrophy, osteomalacia, Bechterew's disease, benign bone tumors, malignant tumors.

The Formalized Structure of the Theme Contents



Questions for Independent Work

1. What principles is radionuclide diagnostics of bone tumors based on?

2. What tumors are the most definitely revealed at radionuclide investigation of bones?

3. Is there a need in radionuclide diagnostics of bones taking into account the available X-ray studies?

4. Under what conditions are low concentrations of RPh observed in the bone?

5. Name indications to osteoscintigraphy.

6. Describe technology of osteoscintigraphy.

7. What equipment is used for osteoscintigraphy?

8. Name ^{99m}Tc compounds with affinity to bone tissue?

9. Name the reasons for possible distortions of osteoscintigraphy?

10. Radionuclide syndromes at investigation of the musculoskeletal system.

11. Name diseases of the musculoskeletal system which cause raised RPh accumulation in the body.

Alternative-Test Tasks for Self-checking

1. Is radionuclide diagnostics more sensitive than X-ray with all the diseases of the musculoskeletal system?

2. Is it proven that by means of radionuclide methods one can establish subclinical signs of some diseases?

3. Is it possible to reveal the inflammation foci at a distance from psoriasis affected joint with the help of radionuclide diagnostics?

4. Is there a difference in the level of RPh accumulation in the skeleton of adults and children?

5. Are there deviation from the norm of RPh retention in patients with age osteoporosis?

6. Are there differences in RPh distribution between benign and malignant diseases?

7. Does radionuclide diagnostics give a possibility to make a precise diagnosis without use of other methods of investigation?

Tasks and Problem Situations

1. Formulate the basic requirements to performing osteoscintigraphy.

2. What should be considered during analysis of osteoscintigraphy results?

3. What causes intense RPh uptake in bones? Formulate the mechanism of such rise in RPh uptake.

Chapter 3

RADIONUCLIDE DIAGNOSTICS OF THYROID DISEASES

Radionuclide methods of investigation as the most informative and objective, occupy a special place in diagnostics of functional and organic infringements of the thyroid gland.

The most widespread radionuclide for thyroid gland investigation is ^{131}I (on 90% β-emitter, $T_{1/2}$ phys. — 8 days, E = 364 keV).

Thyroid visualization with ^{131}I is performed 24 hrs after RPh oral intake. At this time, approximately 10.0–30.0% of injected ^{131}I are localized in the thyroid gland. The most part of iodine excretes through the kidneys or to much lesser degree — through the gastrointestinal tract. ^{131}I excretes, like iodide or protein-bound iodide thyrosin, to the breast milk.

^{123}I has a short half-life period (13.6 hrs) and E = 159 keV. ^{123}I belongs to expensive RPh.

^{125}I has a long half-life period — 60 days and low photon energy — 35.4 keV, which explains its main use as a label *in vitro*.

^{201}Tl concentration (E = 80 keV, $T_{1/2}$ = 73 hrs) in the thyroid gland is proportional to blood flow. So, in patients with toxic diffuse goiter the blood flow in the thyroid gland is considerably raised, which is reflected by intense ^{201}Tl uptake.

Accumulation of ^{201}Tl at tumor metastases in the thyroid gland is increased owing to vascularization of metastases.

^{99m}Tc pertechnetate (E = 140 keV, $T_{1/2}$ = 6 hrs) concentrates in the thyroid gland like iodide, but is not subjected to iron organification, that is does not enter the thyroid hormones structure. This feature excludes an opportunity of its use at postoperative search for metastases of the thyroid gland cancer (it is conducted only with radioactive iodine).

The maximal pertechnetate uptake occurs 10–30 min after the intravenous injection and in norm does not exceed 3–4% from the injected amount.

For search for functioning metastases of thyroid carcinoma a patient takes orally 200 mBq of ^{131}I and in 72 hrs body scanning is performed.

^{99m}Tc-pertechnetate (50 mBq) is injected intravenously and scanning is carried out in 15 min.

Scanning with pertechnetate is carried out on different distances between the collimator and the neck: 17 cm — to estimate the size of the structure and correlation to other structures, 6 cm — to determine the site of increased or decreased activity in the gland. On neck scan is noticed *cartilago thyroidea* and *incisura sternalis*. Nodes are labeled with lead rings or radioactive markers.

Anterior scan of a normal thyroid gland usually shows the lobes symmetric in relation to the middle line (Fig. 7). The right lobe is usually slightly bigger than the left one. The isthmus can be wide, thin or not to be visualized. The size, form and configuration of the thyroid gland varies considerably, even at absence of disease.

For studying radioiodine uptake by the thyroid gland the patient is given liquid iodine, or in a capsule in amount of 75–150 kBq. Values of uptake in 2–4–6–24–48 hrs after radioiodine intake are studied. The percent of uptake by the thyroid gland is calculated under the formula:

$$\frac{\text{Neck index} - \text{Hip index}}{\text{Standard}} \cdot 100$$

The hip index is considered as approximation to non-thyroid uptake in the neck.

Indications for radionuclide visualization of the thyroid gland are the following: a palpated node in the parenchyma or in the neck zone, suspicion on ectopically located elements of the thyroid tissue, goiter relapse after surgical treatment, suspicion on a tumor, metastases, growing progressively worse thyroiditis, hyperplasia of the thyroid gland, clinical hyperthyrosis.

Contraindications to radionuclide investigation of the thyroid gland are pregnancy and lactation. Lactating mothers, which received ^{131}I, should not continue breast feeding until the radioactivity in milk will not return to the normal level (approximately 6 weeks).

Temporary repeal of radionuclide examination of the thyroid is necessary after intake by the patient of some agents — for 1 week after salicylates intake; for 2 weeks — triiodothyronin, sulfanilamides, antihistamines agents, reserpin; for 3 weeks — anticoagulants, glucocorticoids, estrogens, contraceptives, androgens; for 4 weeks — mucozolol, methyluracil, iodine and bromine agents, thyroidin; for 6 months — water-soluble contrast agents; for 12 months — oil contrast agents.

The technique of simultaneous investigation of function and anatomic-topographical features of the thyroid gland is developed in radionuclide laboratory named after N. A. Semashko (the patent of Ukraine N 3796-XII). This investigation allows to determine at the same time the function, the structure and the localization of thyroid tissues by dynamic scintigraphy after intravenous introduction of a small amount of ^{99m}Tc-pertechnetate. The functional condition of the gland as a whole and each lobe separately is estimated. Insignificant radiation dose allows to carry out investigation repeatedly, and also to children. Reduction of time of investigation till 15–20 min is comfortable for patients who are examined in the outpatient setting or live at a great distance.

The method can be used both independently and as an important addition in complex inspection of the thyroid gland at patients with diffuse, nodular and mixed goiter. Use of the suppression test helps to differentiate the erased forms of thyrotoxicosis from intensification of functional activity of the thyroid gland caused by somatic diseases. Thus, repeated studies can be conducted in 2–4 days without making harm. The test with stimulation renders essential help in differential diagnosis of primary and secondary hypothyrosis.

Investigation is carried out with use of computer scintillation gamma-camera which is equipped with a system of automatic processing of the radiological information (SAPRI). After ^{99m}Tc pertechnetate intravenous introduction during 10 min the scintigraphical image of the thyroid gland, surrounding tissues and organs are recorded to the permanent memory of the computer. The kept information is subjected to program processing, and histograms which represent intensity of injected RPh uptake are made. Functional condition of the thyroid gland, its sizes and other parameters are determined by means of the application programs. The estimation of anatomic-topographical features is conducted visually and by means of base computer programs (Fig. 7).

Parameter of absorbing function of the thyroid gland is K_{10} — percent of ^{99m}Tc pertechnetate accumulation by 10-th minute of study. Thyroid gland is considered to be satisfactory at values of K_{10} from 1.4 up to 3.8%, when K_{10} is lower than 1.4% — function is deminished, at values of K_{10} above 3.8% function of the thyroid gland is increased. Parameter K_{10} can reach the level of 20–30% and more with non treated thyroiditis with the pronounced increase of the thyroid gland of IV–V degree. Intense uptake of ^{99m}Tc-pertechnetate is noted in cases of subacute and autoimmune thyroiditis, thus K_{10} can increase up to 4.0–4.4%.

The parameter of thyroid saturation rate Ks depends on its functional activity, degree of blockade by stable iodine in patients with satisfactory or diminished function. At Ks — 1.2 and more thyroid saturation rate is considered to be low.

Nodular defeats of the thyroid gland and differential diagnostics of clinically or ultrosonographycally revealed nodular formations of the neck is the most often indication to thyreoscintigraphy. The main purpose of investigation is to estimate the degree of nodes functioning, identify single or multiple formations, and determine's connection of nodes with the thyroid tissues. Depending on functional activity and degree of radiopertechnetate uptake the nodes are traditionally divided into "hot", "warm" and "cold". However, such division concerns only their scintigraphic estimation.

The term "hot" node means a situation when RPh accumulates almost exclusively in the node area and does not in the other departments of the organ. Similar findings are typical for independent thyroid tissue, toxic adenoma, autoimmune thyroiditis, congenital lobar aplasia. Absence of RPh accumulation in the tissue which surrounds the node testifies by the fact that an independent node secretes thyroid hormones which reduce TTH secretion causing suppresion of normal tissue function.

Functionally inactive ("cold") nodes are characterized by absence or sharp decrease in radiopertechnetate accumulation. This less specific finding accompanies a wide spectrum of pathology; a nodular goiter, colloid cyst, adenoma, nonspecific strumitis, in 15–25% of cases — thyroid cancer (Fig. 8).

Identification of "warm" nodes is the most difficult task. This nodes are considered to be a version of "hot" ones, but in contrast to the latter functional suppression of normal thyroid tissue is poorly pronounced of absent in them. As a result RPh accumulation in nodes can not differ from surrounding parenchyma and lead to false-negative data of scintigraphy. The most usual cause of hypofunctional solitary node in the thyroid gland is the adenomatous hyperplasia. Approximately 50–60% of all solitary hypofunctional ("cold") nodes of the thyroid gland are detected as cysts or foci of adenomatous hyperplasia. The following frequent cause of a "cold" node is a follicular adenoma and thyroid carcinoma.

"Cold" nodes of the thyroid gland are revealed in case of thyroiditis, hemorrhagia and metastatic tumors. Cancer of the mammary gland, lung and kidneys, malignant melanoma spread to the thyroid most often.

The majority of independent nodes does not lead to hyperthyroidism, or suppression of pertechnetate or radioiodine uptake by the rest part of the thyroid gland. Independent non-toxic nodes are small as a rule and most often are represented as sites of adenomatous hyperplasia which is revealed in patients with a multinodular goiter.

In some patients they increase in a course of time, but such nodes often are subject to regress: because they are pooly supplied with blood and become degenerated cyst areas which are represented on scan hypofunctional. Hyperfunctional ("hot") nodes seldom detect thyroid cancer. The history of head and neck irradiation in the childhood makes great influence. Solitary "cold" nodes in such patients can be malignant in 30% of cases, while multiple "cold" nodes — only in 4%.

Thyroid scan helps at differentiation of toxic diffuse goiter (Fig. 9) from adenoma. Hashimoto's thyroiditis, multiple adenomas and carcinomas provide the basis for multinodular goiter.

If thyroid scan shows a solitary "cold" node, it can be malignant with 15–25% probability. If there are plural hypofunctional areas, the probability of thyroid cancer decreases to less than 5%.

In the general population it is possible to expect one case of thyroid cancer by 27 thousand of examined. The probability of detection of thyroid pathology in patients who had head and a neck exposure in the childhood makes out approximately 20% and the probability of thyroid cancer in these patients makes approximately 5%. Revealing of thyroid cancer also increases with radiation dose increase. Higher doses tend to thyroid destruction and are more likely connected with hypothyriosis than with cancer. The peak of thyroid tumors rate is between 5 and 30 years after the exposure and the individuals which were less than 6 years old during the exposure are in the highest risk group. The most part of cancers is well-differentiated papillary or follicular carcinomas (or combinations of these types) which grow slowly, spread rather late and are surgically treated if diagnosed during the period before metastases appearence.

The most part of patients with plural "cold" nodes on scan without previous history of radiation exposure are old patients with multinodular goiter. Risk of thyroid cancer in such patients is low. Revealed multinodular goiter in old patients in most cases reflects degenerative changes of the thyroid gland.

Approximately 80% of all carcinomas are well-differentiated and consist of papillar and follicular cells (or both), neoplastic (15%) and medullar carcinoma (5%) make the rest 20%. Thyroid carcinoma can occur at different age, but the peak comes to the fifth decade. Women are affected with the disease more often than men. Papillary carcinoma has peak of age representation during the third decade of life and is the most usual tumor of the thyroid gland. Follicular carcinoma is the other most usual tumor. Together these two well-differentiated tumors make approximately 75% of all thyroid cancers.

The most part of metastases are found in patients with differentiated carcinoma (10–40%) both at primary cancer or they appear later. Both X-ray of the thorax and ^{131}I imaging require the adequate determination of pulmonary metastases because diseases can be revealed only with the help of scintigraphy or radiography. Cases of pulmonary metastases are higher at follicular (33%) than at papillary cancer (15%). Bone metastases are met more often at follicular carcinoma. Body imaging with ^{131}I

is preferable for determination of skeletal metastases from thyroid carcinoma.

Medullar carcinoma grows from parafollicular cells and consists of non-differentiated spindle-shaped cells. It is not encapsulated and early spreads to pulmonary lymph nodes, liver and bones. Middle age of patients during making diagnosis makes out 60 years. A 10-year survival makes approximately 90%.

The goiter is the most usual manifestation of the thyroid disease determined as gland enlargement. Patients with diffuse thyreotoxic goiter usually have diffusely enlarged gland, and the toxic adenoma is connected with a nodular goiter. The goiter at euthyroid patients is usually present at Hashimoto's thyroiditis, hypothyroidism, as well as congenital enzymatic defects of the thyroid metabolism. Hypothyroidism is the most usual in patients with endemic goiter, secondary to iodine insufficiency.

Nervousness, weakness, trembling and intolerance to hot conditions are usual complaints at hyperthyroidism. These symptoms are caused by increased amount of circulating thyreohormons at thyreotoxicosis irrespectively to the etiology. Other typical symptoms of thyreotoxic condition include weight loss (often, despite increased appetite), oversweating and fatigue. Tachycardia is the most characteristic sign at thyreotoxicosis. Other frequent symptoms include tremor, anxiety, weakness. At a complex of disorders leading to hyperthyroidism, the goiter of different degree is present.

The T_4 increased concentration in plasma and T_3 increased uptake indicate overproduction of circulating thyroid hormone and increased accumulation of T_4-bound globulin.

The most typical reason of hyperthyroidism is diffuse toxic goiter. The diffuse increasing of the thyroid gland is observed in the majority of patients with hyperthyroidism though gland is of normal size or only slightly increased in some patients.

The disease is characterized by T_3 and T_4 overproduction with manifestation of thyreotoxicosis. It prevails mainly in the third and fourth decade of life. The disease is met 4–8 times as much in women than in men. Development of diffuse toxic goiter is often preceded by emotional stresses.

Etiology of diffuse toxic goiter unknown, though there are proofs that it is autoimmune disorder. More modern studies specify that the immune phenomenon is responsible for hyperthyroidism of diffuse toxic goiter.

Scan of the thyroid gland with ^{99m}Tc pertechnetate at diffuse toxic goiter usually shows diffuse symmetric increase in the thyroid gland with the increased concentration of RPh (Fig. 9).

Visualization of the thyroid gland shows a pyramidal lobe approximately in one third of patients.

Another most frequent case of hyperthyroidism is a toxic nodular goiter, including single and multinodal forms. This pathology is manifested by hyperfunction of one or more thyroid nodes (more often adenomas or adenomatous nodes), which lead to hyperthyroidism, suppression of TTH secretion by hypophysis and to reduction of thyroid extranodular thyroid parenchyma function. A 24-hour uptake of radioiodine in patients with a toxic nodular goiter can rise, but is often in the norm. Thyroid scan shows one or more areas of the increased activity and suppression of functions in the rest thyroid. At physical investigation a separate node or multiple nodes are usually palpated.

Iodide-induced hyperthyroidism is called "iodide-Basedow's", which is revealed right after the first use of iodine for treatment of endemic goiter. However, it is also observed in the regions where deficiency of iodine is not endemic. This infringement is the most usual in patients over 50 years old and with long history of multinodular goiter. However, it is observed in patients with diffuse toxic goiter in the anamnesis or with autonomic thyroid node. Thyreotoxicosis develops after introduction of great amount of organic iodides, and also inorganic iodine. Iob-Basedow phenomenon is met after introduction of urological, cholecystographical contrast agents and antiarrhythmic drugs. Patients have increased concentration of T_3 and T_4 levels in plasma and suppressed TTH level. The mechanism of thyroid hormone overproduction is unknown. Thyroid scan reveals a multinodular goiter as a rule.

Hypothyroidism owing to decrease in hormone production can be result of primary disease of the thyroid gland or can be secondary in relation to reduced TTH production. Primary hypothyroidism is the most usual form of hypothyroidism caused by inability of the thyroid gland to produce a necessary hormone. In children the hypothyroidism is more often caused by maldevelopment of the thyroid gland (in regions with absence of endemic goiter), more rarely — by thyroiditis or a congenital syndrome of dishormonogenesis. At adults it is a consequence of chronic thyroiditis or previous radioiodine-therapy of hyperthyroidism. Secondary hypothyroidism arises as a result of insufficient production of the anterior part of hypophysis of essential amount of TTH, that can be a result of destruction of anterior hypophysis because of postnatal hemorrhagia, injuries of the head, tumor of hypophysis, surgical aneurysm or a therapeutic irradiation. Low TTH levels in plasma lead to reduction of thyroid hormone production. Tertiary (or hypothalamic) hyperthyroidism is a result of decrease of hypothalamic ability to appear in changed TTH secretion, that in its turn leads to reduction of thyroid hormone production.

Goiter cretinism is connected with disorders in all known phases of synthesis and action of the thyroid hormone. Patients can suffer from diffuse symmetric thyromegaly with high serum TTH, low serum T_4, but the increased pertechnetate uptake because of organification defect. Under the given condition the reduced levels of a circulating hormone stimulate TTH secretion which leads to thyroid enlargement.

Acute purulent thyreoditis arises rather rare and proceeds from 1 to 3 months. During an acute stage the iodide uptake falls.

Etiology of subacute thyroiditis is unknown, but there are evidences that it may be caused by virus infection. The infection of the upper respiratory ways often precedes some symptoms from 2 to 3 weeks; a prodromal phase is possible too, which is characterized by fatigue, flaccidity and myalgia. A variation of antiviral antibodies is identified in association with subacute thyroiditis.

Women fall ill almost 5 times more often than men. The peak of morbidity takes place between the 2nd and 5th decades of life, and children suffer from this disease very seldom.

Patients with subacute thyroiditis usually have a swelled thyroid gland. This disease is characterized by presence of lymphatic infiltration with granuloma and giant cells. Functional abnormalities depend on the stage and severity of disease. These patients complain of severe pain in the thyroid gland, fever. Their thyroid gland is soft; clinical and chemical symptoms of hyperthyroiditis are revealed. ^{131}I uptake is noticeably reduced at this time. After a short euthyroid phase these patients become clinically and chemically hypothyroid. The hypothyroid phase is kept for 2–7 months. Then the phase of recovery comes, when the thyroid gland comes back to its normal size, form and consistence. ^{131}I uptake often exceeds the normal levels during recovery.

Results of clinical laboratory studies represent pathological processes in the thyroid gland. At first protein-bound iodide rises in plasma as a result of release to the blood flow of thyrioglobulin and other iodinated proteins, T_3 and T_4. During the phase of hyperthyrodism circulating levels of TTH are suppressed and there is a tendency to TTH reduction. At the same time an ability of the thyroid gland to detain the iodide is noticeably weakened and leads to characteristic low level of radioiodine uptake.

Subacute thyroiditis is one of many diseases which can give rise to scintigraphically "cold" nodes of the thyroid gland. If the phase of transitory hypothyroidism develops, TTH levels rise and radioactive iodine uptake can intensify.

Chronic thyroiditis (Hashimoto's disease) is autoimmune disorders with high titers of antithyroidal (antithyroglobulin and antimicrosomal antibodies) which are typically present on both early and late stages of the disease. Histologically lymphocyte infiltration is present around the gland. It is proved that 3–5% of patients, hyperthyroidism is connected with high radioiodine uptake.

Clinical manifestations of this disease vary, but a painless goiter or hypothyrosis (or both) are the most frequent findings. Hashimoto's disease is the most frequent case of goiter hypothyrosis in adults. Hashimoto's thyroiditis usually begins with gradual painless enlargement of the thyroid gland and patients usually complain of solid, lobular goiter. Hashimoto's thyroiditis should be suspected at the patient with multinodular goiter and hypothyroidism, it should be distinguished from adenomatous goiter. Hashimoto's thyroiditis often arises in middle aged women. Children suffer from goiter rather seldom, mainly as a result of Hashimoto's thyroiditis. Symptoms of hypothyrosis are present at about 20% of patients. Many of them develop hypothyrosis in a month (about one year) after diagnostics of thyroiditis.

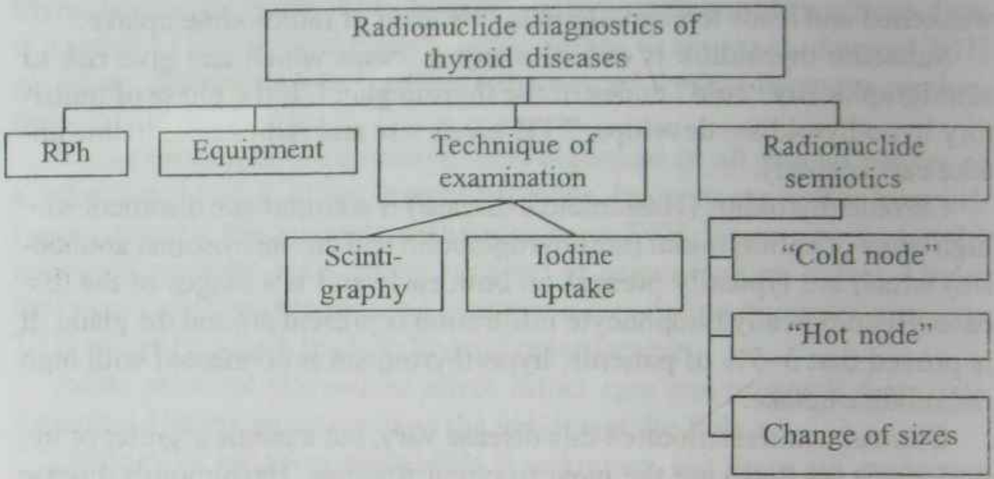
The scan can vary from normal to enlarged with diffuse absorption or with focal areas of lowered absorption. As a rule the gland is enlarged and has a multinodular structure.

The radionuclide diagnostics of differentiated thyroid carcinomas with ^{131}I is highly specific and accurate, allows to receive the objective information about process spreading. The control is carried outs both under therapeutic manipulations, and during the further prophylactic exams.

Key Concepts of the Theme

Thyroid imaging, techniques of scanning, methods of investigation of radioiodine uptake by the thyroid gland, the indication for radionuclide visualization of the thyroid gland, contraindications to radionuclide investigation of the thyroid gland, radionuclide semiotics of thyroid diseases.

The Formalized Structures of the Theme Contents



Questions for Independent Work

1. Radionuclides used for investigation of the thyroid gland.
2. Technique of investigation of the thyroid gland with ^{123}I-sodium iodide.
3. Technique of investigation of the thyroid gland with pertechnetate.
4. A method of investigation of radioiodine uptake by the thyroid gland.
5. Indications to radionuclide imaging of the thyroid gland.
6. Contraindications to radionuclide imaging of the thyroid gland.
7. What is "hot node", "cold node"?
8. Name factors which increase probability of thyroid cancer occurrence.

Alternative-test Tasks for Self-checking

1. Can ^{99m}Tc-pertechnetate been used for searching thyroid metastasis in the postoperative period?
2. Is it possible to investigate simultaneously function and somatotopographical features of the thyroid gland with the help of radionuclides?
3. Which nodes have greater probability of malignancy — solitary or plural?
4. Does thyroid carcinoma occur at different age?

Tasks and Problem Situations

1. Determine the management of preoperative investigation in patients with malignant tumors of the thyroid gland.
2. Administer examination of the patient after thyroidectomy at thyroid cancer.

Chapter 4
RADIONUCLIDE DIAGNOSTICS OF DISEASES OF THE CENTRAL NERVOUS SYSTEM

One of the first procedures of radionuclide diagnostics was brain scanning to determine its focal diseases. With introduction of gamma-camera the information on blood flow disturbances at meningioma as well as infarction became available.

By means of SPECT the patients with clinical symptoms of focal epilepsy are determined the foci of brain electric activity changes. A part of patients are revealed hyperfusion of diencephalic departments of the brain, which is also proved by EEG data. This method is more informative than CT and MRI in diagnostics of focal defeats of the brain accompanied by morphological changes of the brain tissue.

4.1. Radionuclide Methods of Diagnostics

Single photon emission computer tomography (SPECT) with brain perfusion markers reveals blood supply disturbances of the brain (the foci of ischemia and hyperemia of the brain tissue) which are met not only at neurosurgical (craniocerebral trauma, vascular and tumor processes, cervical osteochondrosis) and neurologic pathology (strokes, transient ischemic attacks, vertebrobasilar failure, etc.), but also in patients suffering from essential hypertension, renal diseases and chronic cardiovascular insufficiency. At intravenous introduction of brain perfusion markers, SPECT allows to reveal the "mute" ischemia foci (without developed clinical symptoms), examines evolution of the blood supply disturbances foci and indirectly estimates cerebral hemodynamics reserves, serves for prognosing the clinical course and outcome of the disease.

Radionuclide cysternomyelography (RCMG) reveals a pathology of liquor ways of the brain and spinal cord (change of circulation and liquor resorption). The method defines more exactly types of hydrocephaly, visualizes arachnoidal cysts (makes accurate their volume, localization and the communications with liquor ways) diagnoses basal liquoreas (nasal, nasopharingeal and ear), and also liquor fistulas in the region of the spinal cord. At given investigation RPh is entered endolumbarly. Changes of liquor dynamics is a constant sign of pathological picture at a craniocerebral trauma, vascular, tumor and inflammatory processes, as well as at congenital maldevelopments of the brain. RCMG is a method of choice and the control of efficiency after shunting operations on liquor ways of the brain and spinal cord.

Radionuclide cerebral angiography (RCA) — diagnoses blood flow disturbances in the main vessels of the head and the neck in arterial and venous phases. RPh is injected intravenously, allows estimating the blood flow in carotid and vertebrobasilar systems, as well as in large venous sinuses and jugular veins. It can be used at vascular and post-traumatic processes, cervical osteochondrosis; it reveals arteriovenous shunting at epileptic syndrome; it defines exactly presence of thromboses of venous collectors with inflammatory processes.

Brain scintigraphy (BS) reveals space-occupying lesions of tumor and non-tumor genesis (Fig. 10, 11).

The method of brain scintigraphy is based on RPh ability to concentrate in brain tumor tissue in greater amount than in the normal brain tissue. As RPh Tc (pertechnetate) without a tracer, 500–700 mBq are injected intravenously. In an hour after RPh intravenous introduction, the investigation is carried out on gamma-camera in five projections: anterior direct, posterior direct, lateral left, lateral right, parietal projection.

Such histologic groups as meningeomas, glyoblastomas, metastases are early revealed during examination almost in 100% of cases.

Positron-emission tomography (PET). Positron-emission RPh are obtained in cyclotrons directly in the hospital or close to it. Epilepsy, brain tumors, stroke are among diseases which can be detected by means of PET. For identification of the site for PET study, X-ray CT is performed.

PET extends brain study considerably. The knowledge of the functional organization of a human brain is discovered with the help of PET studies, and these functional visualization diagnose pathological disturbance earlier than usual anatomically directed technologies. PET gives more precise picture of damage spreading, since all the brain diseases are consequence of biochemical defeat.

Discrepancy between structural and functional infringements can be observed in patients with apoplectic infringements, dementia, neurodegenerative diseases and acute cerebral strokes. Besides, PET also provides studying local sensitivity, motor function, memory, cognitive function at normal individuals *in vivo*. Studying with ^{15}O-labeled water for measurement of brain blood flow or with ^{18}F-labeled fluorodesoxyglucose (FDG) for measurement of glucose utilization level, discovered some normal physiological reactions of the visual and acoustical cerebral cortex. At patients with cerebral infringements PET serial investigation helps to identify pathophysiologic sequence of events, observed during syndrome manifestation. At PET studies with FDG all the patients with Hantington's disease develop a noticable reduction of glucose in the striate body.

In group of asymptomatic individuals subjected to risk of this disease, about half demonstrate taxis from soft up to the moderate reduction of glucose utilization in *nucleus caudatus*. Measurement of oxygen extraction and utilization is a more real predecessor of tissue degeneration than the blood flow in intense development of cerebral ischemia and infarction.

United indices of energy of metabolism and protein synthesis for determination of metabolism rate and tumor growth before and after therapy can be investigated by PET. The increase in malignization degree is connected with increase in glucose utilization rate at measurement with FDG.

Now looking at PET-scan, it is possible to say: "Yes, it is a part of the brain where epileptic attack begins", or "Yes, it is Alzheimer's disease", or: "Yes, this schizophrenia patient receives a correct dose of a neuroleptic", or "Yes, this amount of methadone is a sufficient dose for this former chronic alcoholic".

Epilepsy, brain tumor, stroke are the diseases which can be studied with positron emission tomography to obtain clinically useful information.

When ^{99m}Tc-pertechnetate is used for studying brain or brain perfusion, the patient should receive 200–400 mg of potassium chloride before the study. This drug slows down radiopertechnetate uptake by choroid plexuses. Radioactivity in plexuses can distort scan results because of interference. Perchlorate is usually administered in the form of liquid for oral intake or in capsules 10–30 min before pertechnetate introduction.

As pertechnetate accumulates in salivary glands also, 0.4 mg atropin sulfate is recommended to inject preliminarily in order to slow down saliva secretion. Without this manipulation it is difficult to interpret the received data because of presence of radioactive saliva in the zone of the face.

Perchlorate and atropine are not required when ^{99m}Tc-diethylenetriaminepentacetic acid (DTPA) or ^{99m}Tc-gluceptate are used for brain scintigraphy. These two radioactive indicators insignificantly accumulate by vascular tunica or salivary glands and consequently are the alternative to radiopertechnetate at patients who cannot swallow perchlorate.

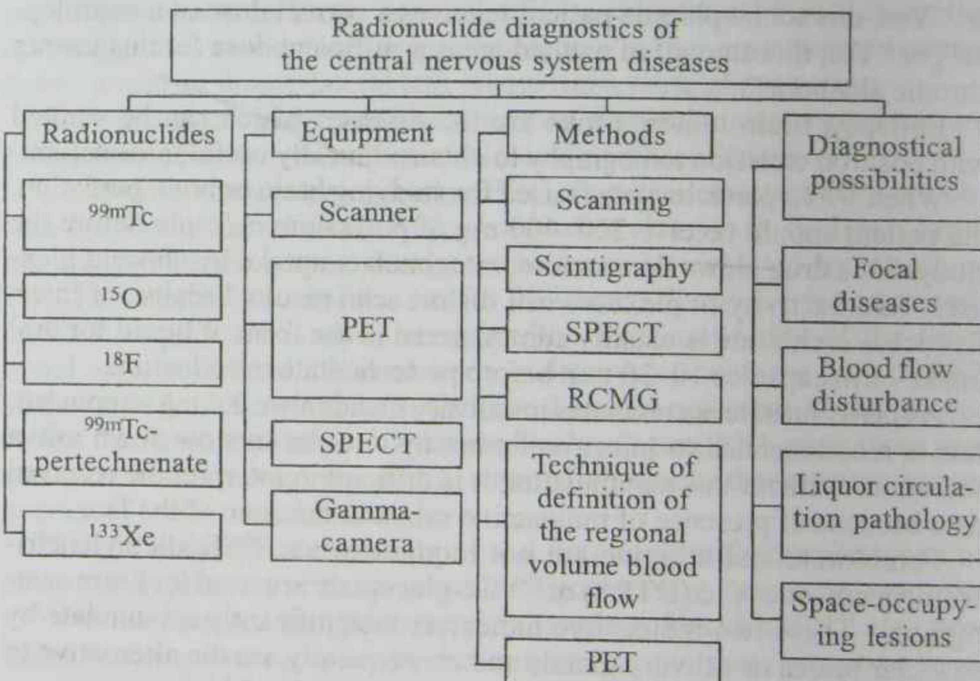
Technique of determination of regional brain blood flow. The method is based on Fick's principle and consist in washing out of radioactive gas by a certain volume of blood. A patient is injected 10–20 mBq ^{133}Xe dissolved in 2 ml of NaCl isotonic solution into the carotid. Radioactivity is recorded within 10 min above the affected and closely located sites of the brain by a radiometer URI-3, which allows to receive 4–5-zonal radiocirculogramm. The steepness of the curve fall is in direct dependence on intensity of blood flow in a certain department of the brain.

In the norm volume of regional brain blood flow is 50–55 ml on 100 g of brain substance by 1 sec. At malignant tumors blood flow rate slows down in connection with edema around the tumor and vasoparalysis of vessels of the tumor. At benign vascular tumors speed of washing out increases, and the exchange blood flow increases.

Key Concepts of the Theme

Diagnostic opportunities of SPECT, RCMG, RCA, BC, CT; positron-emission tomography; technique of determination or regional brain blood flow.

Structure of the Theme Contents



Questions for Independent Work

1. Is it possible to reveal "mute" ischemia foci with the help of SPECT?
2. Diagnostic opportunities of radionuclide cysternomyelography.
3. Diagnostic opportunities of radionuclide cerebral angiography.
4. Diagnostic opportunities of brain scintigraphy.
5. Diagnostic opportunities of PET.

Alternative-test Tasks for Self-checking

1. Are CT and MRI more informative methods than SPECT study?
2. Is the following statement correct: SPECT with markers of brain perfusion allows to reveal infringements not only in brain blood supply, but also in neurosurgical and a neurological practice?
3. Is it possible to use SPECT at dynamic supervision?
4. Is it possible to inject RPh intravenously for revealing a pathology of liquor ways of the brain and spinal cord?
5. What is scintigraphic diagnostics grounded on?
6. Can RCA be used for post-traumatic processes diagnosing?

Chapter 5

RADIONUCLIDE DIAGNOSTICS OF LUNG DISEASES

Radionuclide study turned out to be rather effective for definition of lungs affection severity and became widely practiced at determination of indications to surgical treatment. According to perfusion pulmonoscintography data it became possible to determine a zone of spread and extent of capillary network defeat and in some cases to establish extent of intervention without angiopulmonography application.

5.1. Radiopharmaceuticals

Xenon-133 (^{133}Xe) is a widely used gas for studying regional ventilation, despite its low energy and solubility in blood and fat. Xenon-127 has higher gamma-energy peaks.

Aerosol inhalation scanners are used as indicators of regional ventilation. Deposition of aerosols depends on many factors, including the size, the form, density, an electrostatic charge of a particle, pulmonary geometry and ventilation character. Only about 10% of this RPh reach lungs.

Other agents recommended as substitutes for ^{133}Xe at studying ventilation, include gases ^{127}Xe and ^{81m}Kr and ^{99m}Tc labeled aerosols. ^{127}Xe is exposed to smaller dispersion in the body than ^{133}Xe since ^{127}Xe allows imaging ventilation after ^{99m}Tc perfusion scanning. However, usage of ^{127}Xe is limited because of its high cost.

Kripton-81m

^{81m}Kr is of great interest, because it is not distributed in the inner gas volume, and its distribution changes with lung volume.

Inert gas ^{81m}Kr has a 13 second half-life period. Due to such a short half-life period ^{81m}Kr provides a stable stage of visualization in which activity is proportional to regional ventilation. The drawback consists in its inability to determine the phase by a washing out by a standard ventilating visualization.

5.2. Radionuclide Methods

1. *Routine visualization* in anterior, posterior and lateral visual fields shows even borders of lungs with rather smaller activity in tops. The posterior oblique position reduces the frequency of ambiguous interpretation from 30% to 15%, improves the image of small defects, and identifies many defects around the *radix pulmonis*.

Costal-diaphragmal angles get dull usually in thick patients. Patients injected in position on the back are usually asked to make 2–3 deep breaths during the injection to distribute the drug evenly. When the injection is carried out in a sitting position, the pulmonary blood flow gravitational effect counts often.

2. *Radionuclide angiocardiography*

The atria radionuclide angiocardiography is an indirect method of detection of greater pulmonary emboli. Occlusive portion of pulmonary vessels reduces efficiency of circulated pulmonary blood volume in patients with emboli. First of all, time of radionuclide transit from the right to the left ventricle will increase while cardiac output remains unchanged. Thus, the index determining the time of pulmonary transit and cardiac output will be essentially reduced in patients with pulmonary embolism.

3. *Studies with dioxide carbon*

Inhalated carbon dioxide diffuses fast through the alveolar-capillary membrane in blood and it is cleared from lungs within some seconds. Clearance rate is directly proportional to pulmonary blood flow. If dioxide of radioactive carbon is inhalated to the area with reduced pulmonary arterial perfusion as a result of pulmonary embolism, clearance occurs much more slowly or is absolutely absent and the "hot spot" of the kept activity will be visible with positron visualization.

4. *Studies with methyl iodide*

During inhalation of gaseous ^{131}I-labeled methyl iodide the radioactivity instantly delivers from alveoli to lung capillaries. Due to pulmonary circulation, RPh delivers to the system circulation, but in the field of blood stasis a transitory pulmonary "hot spot" is kept. Methyl iodide is not expensive, but radiation danger of ^{131}I limits execution of this technique.

5. *Perfusion scintigraphy of lungs*

The purpose of the given technique is to investigate the capillary blood supply at the account of timely embolization of the capillary channel of lungs. As a radionuclide 1-131, In-113m and In-99m are used, which enter the RPh. A radiopharmarmaceutical in the form of macroaggregate condition or as microspheres of HSA, which particles have the size 15–30 mcm in 90%, is intravenously injected. These microparticles detain in capillaries of smaller size, giving radiation emitted by scintilation detectors.

At perfusion scintigraphy in the norm, even, enough intensive image of the blood channel of lungs in four projections is obtained: anterior, posterior and two lateral. At obstruction of pulmonary vessels in corresponding zones, the amount of deposited particles decreases, and the image of lungs on scintigrams has the lowered intensity.

6. *Aerosol scintigraphy* allows to determine localization, character and prevalence of ventilation disorders of lungs and bronchial obstruction. RPh are administered into the bronchial tree by inhalation. RPh sediments on walls of the bronchial tree and alveolar channels.

7. *Radiopulmonography* — a complex method of successive investigation in the beginning regional ventilation, and then a capillary blood flow:

— 1st stage is conducted with use of Xe-133 labeled RPh, which practically is not absorbed inhalation, does not bind with elements of blood at intravenous injection, diffuses fast in the alveolar lumen and is quickly excreted.

— 2nd stage — investigation of the capillary blood flow by perfusion pulmonoscintigraphy technique.

At investigation with gamma-camera, after xenon introduction it is possible to obtain the lungs image in the deep breath phase and at exhalation with visualization of low ventilation departments.

8. *The method of radionuclide estimation of permeability of pulmonary epythelium* (PPE) consists in registration of inhalated RPh (most often ^{99m}Tc-DTPA) transition from pneumatic ways to blood. Clinical value of PPE study is caused by ability to establish activity of pathological process. Determination of ^{99m}Tc-DTPA pulmonary clearance velocity can be useful at differential diagnosis of initial forms of interstitial diseases, a pulmonary edema. PPE investigation is capable to replace the invasive procedures at the intermediate control of treatment efficiency.

Advantages of the method are noninvasiveness, rather low radiation dose, simplicity of performance and availability of applied RPh.

Lung scintigraphy despite of a plenty of indefinite results remains the most often applied means of ray diagnostics at suspicion on pulmonary embolism after traditional chest X-ray (Fig. 12). A new technique of scintigraphic diagnostics of pathology of pulmonary blood circulation at acute destructive-pneumonia is executed with ^{99m}Tc-macroaggregates of albumin in the doses which do not exceed age specifications (from 0.54 up to 3.3 mBq/kg of the body weight). Regional hypoperfusion is estimated by specific activities — amount of impulses on a standard site of a matrix of 100 units on the display in 3 zones of each lung and in zones of a contralateral lung. The normative parameter of the regional specific activity makes 16.6%.

There are three degrees of reduction of pulmonary blood flow along the arteriolar capillary channel: moderate, pronounced and severe. The reduction of the pulmonary blood flow in departments of lungs that are borders with a damage focus in which X-ray exam does nor reveal pneumatization decrease, which is evidence of generalization of purulent inflammatory process and such patients make group of risk and need more intensive therapy. At ventilation-perfusion scintigraphy of lungs with the purpose of pulmonary thromboembolism diagnostics it is necessary to use only quantitative estimations of thromboembolism probability.

9. The sensitive indicator of inflammation or damage, which touches the interstitial space of lungs and alveoli is *pulmonary clearance rate* (PCR) with ^{99m}Tc-DTPA. Advantage of the method is non-invasiveness, rather low radiation dose, simplicity of performance and availability of applied RPh.

Using complexes of RIA, such as cortisol, general and specific immunoglobulins it is possible to reveal atypical forms of bronchial asthma, especially when execution and analysis of routine allergic tests are impossible (for example, at neurodermatitises), as well as to supervise over the immunological reactivity condition during treatment.

Key Concepts of the Theme

Advantages of radionuclide diagnostics of lung diseases, radiopharmaceuticals for radionuclide diagnostics, radionuclide techniques, indications to radionuclide diagnostics of lung diseases, estimation of results of radionuclide study of lungs, radioimmunological studies.

Formalized Structure of the Theme Contents

Radionuclide diagnostics

Methods	Radiopharmaceuticals
Routine imaging	Xenon-127
Radionuclide angiography	Krypton-81m
Perfusion scintigraphy of lungs	^{11}C-radiocarbon
Aerosol scintigraphy of lungs	^{131}I-methyl iodide
Radionuclide estimation of lung epithelium permeability	^{113m}In
Pulmonary clearance rate	^{99m}Tc-DTPA
Radionuclide methods	Human serum albumin

Questions for Independent Work

1. Advantages of radionuclide methods of lungs examination.
2. Radionuclide pharmaceuticals used for studies of lungs.
3. Methods of radionuclide studies of lungs.
4. At what position of the patient is gravitation effect of the pulmonary blood flow revealed?
5. By means of what method is it possible to reveal pulmonary emboli?
6. Indications to positron visualization of lungs.
7. A method of investigation of the capillary channel of lungs.
8. At what method of radionuclide study of lungs is human serum albumin used?

Alternative-test Tasks for Self-checking

1. Is it possible by means of the method of radionuclide estimation of pulmonary epithelium permeability to reveal initial forms of interstitial diseases of lungs?

2. Should radionuclide study be used for determination of indications to surgical treatment?

3. Does functional condition of lungs worsen at the time of embolisation of capillary channel of lungs at carrying out perfusion scintigraphy of lungs?

4. Is radiation dose high at investigation of pulmonary clearance rate with ^{99m}Tc-DTPA?

Tasks and Problem Situations

1. At positron visualization of lungs with ^{11}C-labeled radiocarbon-dioxide, a "hot spot" is visible on the scan. What does this phenomenon speak about?

2. Study of lung capillaries with ^{131}I-methyl-iodide is rather informative. What limits application of this method?

3. What method do you use at determination of the pulmonary blood flow reduction degree?

4. Formulate groups of risk on the basis of results of radionuclide estimation of pulmonary epithelium permeability.

Chapter 6

RADIONUCLIDE DIAGNOSTICS OF HEMATOLOGICAL AND INFECTIONAL DISEASES

Clinical use of scintigraphy of the bone marrow includes its cartography, determination of bone brain loss and identification of the bone marrow site for biopsy.

Loss of the bone marrow is typical for aplastic anemia, myelofibrosis, a number of cancer tumors, condition after radiotheraphy (at the radiation dose more than 3,000 rad).

6.1. Radiopharmaceuticals and Methods

Radiopharmaceuticals for marrow imaging are divided into radiocolloid and nonradiocolloid. Radionuclides are phagocytized by the reticuloendotheial system.

^{99m}Tc-colloid of sulfur is more often used today because of its low radiation dose. However, only 1–5% from the introducted activity are absorbed by the marrow, while 80–85% — are absorbed by the liver and 10–15% — by the spleen.

The technique of investigation consists in intravenous injection of 370 mBq of ^{99m}Tc colloid-sulfide; the marrow image is obtained in 10–20 min.

Non-colloid radiopharmaceuticals for the marrow image contain radioactive iron and indium, both elements form a complex with transferrin.

6.2. Results of Radionuclide Study

Marrow hypoplasia is revealed in 10%–20% patients with polycythemia.

Replacement of the marrow with myelofibrosis leads to reduction of the central part of the marrow and to a peripheral marrow hyperplasia.

With a plastic anemia a full loss of marrow cellularity is observed. After recovery a normal RPh uptake in the marrow renews with compensatory hyperplasia symptoms.

At chronic hemolytic anemia (by a sickle-cell type), marrow site extension at the periphery is observed.

Hypoplasia of the central part of the marrow is the most often met with Hodgkin's and other lymphomas.

The marrow investigation can be used for biopsy with the purpose of detection of malignant tumors metastasis to the bone since the marrow contains 40% of all the bone blood volume.

The marrow infarctions at sickle-cell anemia crises are detected as "cold" areas surrounded by increased uptake in the surrounding active marrow.

^{111}In-chloride and ^{67}Ga-citrate accumulate in abscesses.

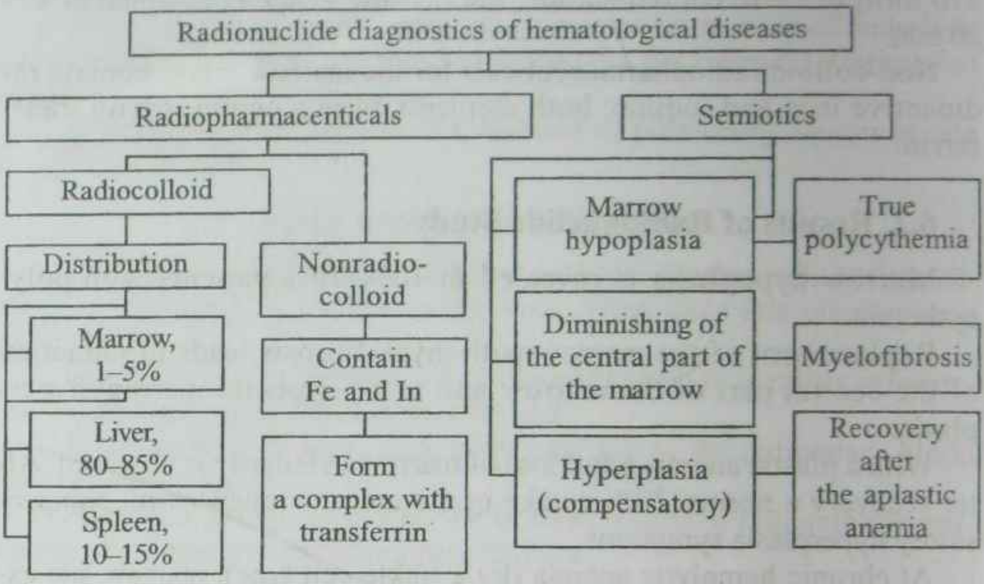
Studies with ^{67}Ga are used for detection of abscesses, limited peritonites, pneumocystic pneumonia *(Pneumocystis carinii)*, for search of infection foci in case of unknown genesis fever.

^{67}Ga is used to diagnose vertebral osteomyelitis owing to the chronic nature of such infections. ^{67}Ga-labeled leukocytes are applied at suspicion on infectious complications after prosthetics. ^{67}Ga-scanning is useful for diagnostics of various infections and malignant neoplasms in HIV-positive patients.

Key Concepts of the Theme

Marrow scintigraphy, radiopharmaceuticals, technique of marrow study, marrow hypoplasia, myelofibrosis, marrow hyperplasia.

The Formalized Structure of the Theme Contents



Questions for Independent Work

1. What purpose is marrow scintigraphy applied with?
2. What agents are applied for marrow image?
3. Scintigraphic picture of the marrow at myelofibrosis.
4. Scintigraphic picture of the marrow at aplastic anemia.
5. Scintigraphic picture of the marrow at sickle-cell anemia.

Alternative-test Tasks for Self-checking

1. Is loss of the marrow possible at multiple cancer tumors?
2. Can noncolloid RPh be used for marrow scanning?
3. Has marrow hyperlasia been met at aplastic anemia?
4. Has a marrow site expansion been revealed at chronic sickle-cell anemia?

Tasks and Problem Situations

1. Calculate the amount of RPh in the marrow after an intravenous injection of ^{99m}Tc-sulfide colloid 10 mg.

2. A patient is revealed multiple malignant tumors for the first time. Is there a necessity in marrow scintigraphy?

3. A patient is executed radiotheraphy. Is he indicated marrow scintigraphy?

Chapter 7

RADIONUCLIDE STUDY OF THE LYMPHATIC SYSTEM

As the lymphatic system is an important way of malignant tumors spread, evaluation of lymphatic system function is important for optimization of radiation therapy planning or surgical treatment, for estimation of disease growing progressively worse and quality of treatment.

The first clinical work about studying gold radiocolloid usage was conducted by Hultborn (1955). Standardization of radioisotope limphography was initiated by Sage (1958), Smith and co-authers (1960). Sage (1964) studied colloid distribution among sick and healthy individuals, impulses number dependence on the detector-source distance.

Radionuclide limphography can be direct and indirect. Indirect limphography is more widely used in clinic (Fig. 13) as its technique is more simple. Gold radiocolloid (^{198}Au), technetium (^{99m}Tc) are subcutaneously injected to different sites. It allows studying circulatory and phagocytic functions of the lymphatic system. Use of gallium-67-citrate and traced bleomycine injected intravenously, allows to investigate metabolism in the lymph nodes (metabolism at tumor defeat is considerably increased).

The indirect lymphography method is based on the fact that particles, penetrated the tissue, because of their size cannot be absorbed by the blood capillaries; transported to the regional nodes by the lymph (refer to Fig. 13). The experiments with torotrust demonstrated that colloid accumulate mainly in marginal, intermediate structures and sinuses, but follicles remain unchanged.

Advantages of non-direct lymphography:

1. Simple technique of radionuclide introduction.
2. It is possible to execute any number of control inspections.
3. It is possible to receive the functional information about lymphatic system.
4. It is applied for searching metastases of solid tumors and system diseases.
5. An opportunity of the continuous control of therapy results.
6. The heighted diagnostic value when combined with direct limphography.

Drawbacks of radionuclide lymphography:

1. In comparison with radio-opaque lymphography it is impossible to reveal details of vessels and nodes structure.
2. Inflammatory complications at the site of introduction.

Scintigraphy at edema of extremities. Indirect lymphography (scintigraphy with radiocolloid) helps to distinguish various edemas of the upper and lower extremities, such as:

— venous;
— systemic;
— lymphatic: a) primary b) secondary.

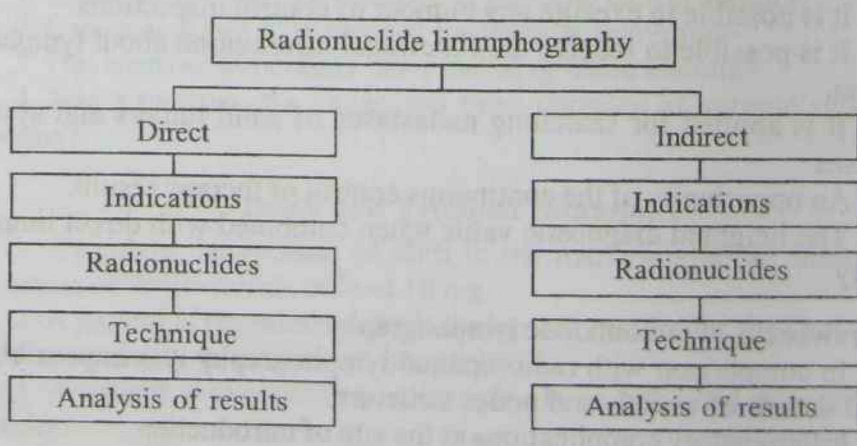
At interpretation of lymphoscintigrams of extremities, the level of activity in extremities and regional nodes is compared. A normal picture is caused by the level of activity at the site of radiocolloid retention and in other part of extremity. In the norm radiocolloid doesn't accumulate in the extremity, hence, it is equal to a background. Exception is linear accumulation in a bunch form on the medial side of extremity in case of ^{99m}Tc-sulfide colloid use.

Lymphoscintigraphy is used in children with pronounced edemas. In adults it is used as a method of screening in an out-patient practice when the puncture of the vessel for direct lymphoscintigraphy is impossible.

Key Concepts of the Theme

Direct radionuclide lymphography, indirect radionuclide lymphography, advantages of direct and indirect lymphography, disadvantages of direct and indirect radionuclide lymphography, technique of radionuclide lymphography, estimation of radionuclide lymphography results.

Formalized Structure of Theme Contents



Questions for Independent Work

1. Value of radionuclide diagnostics of lymphatic system.
2. Types of radionuclide lymphography.
3. Radionuclides used for lymphography.
4. Advantages of radionuclide lymphography.
5. Drawbacks of radionuclide lymphography.
6. Technique of radionuclide lymphography.
7. Interpretation of lymphoscintigrams of extremities.

Alternative-test Tasks for Self-checking

1. Is it necessary to carry out radionuclide investigation at planning radiation therapy?

2. Is it necessary to carry out radionuclide investigation at planning surgical treatment?

3. Is it possible to estimate that disease grows progressively worse by means of radionuclide study of lymphatic system?

4. Is it possible to estimate the quality of treatment by means of radionuclide study of lymphatic system?

5. Is the reactive hyperplasia of the lymph nodes a specific parameter of early stages of tumors?

6. Does radionuclide lymphography allow to make constant control over therapy results?

Tasks and Problem Situations

1. Make instructions for radionuclide diagnostics laboratory on technique of direct lymphography.

2. A child of 5 years old has pronounced edema of lower extremities. Offer the method of radionuclide diagnostics of a lymphatic system disease.

3. Choose the method of radionuclide lymphography suitable for a continuous control of therapy results.

Chapter 8
RADIONUCLIDE DIAGNOSTICS OF DISEASES OF THE GASTROINTESTINAL TRACT, LIVER, SPLEEN, PANCREAS

8.1. Radionuclide Diagnostics of Gastrointestinal Diseases

On the whole, diagnostics is directed on determination of a functional condition of digestive system at some diseases. It can be performed for quantitative estimation of motor-evacuator function of the stomach and duodenum, and for estimation of a surgical operation efficiency. Radionuclide visualization yields good results in diagnosis of intestinal obstruction and venous blood flow disturbances, gastro-esophageal reflux. By means of radionuclide techniques processes of absorption in the small intestine are studied, the reason of steatorrhea is found out, gastric mucosa infection is diagnosed.

The technique of determination of gastric mucosa infection by *Compilobacter pylori* is based on introduction of the urea water solution labeled by radiocarbon with its decomposition under influence of allocated by bacteria urease on labeled carbon dioxide and ammonia, carbon dioxide absorption in blood, its transfer to the lungs and carbon dioxide excretion with exhaled endogenic carbonic gas. Samples of exhaled gas are investigated on a spectrophotometer and atomic-absorbing spectrometer. It is proved that radiocarbon concentration in infected patients rises up to the 15th minute, reaching maximum — 27% whereas in the norm a similar parameter makes 3%.

8.2. Radionuclide diagnostics in hepatology

The liver diseases are revealed by the following techniques:
— hepatoscintigraphy (Fig. 14);
— radionuclide hepatobiliary imaging.

Hepatoscintigraphy is used for studying anatomical-topographical condition of the liver and spleen. Clinical indications for hepatoscintigraphy are the following: hepatomegaly, hepatolienal syndrome; necessity in revealing or exception of primary and metastatic tumors related to the liver, the dynamic control of liver condition after surgical interventions; relaxation of the right cupula of diaphragm.

^{99m}Tc and ^{113}In labeled colloid solutions are used as RPh. All colloids after intravenous injection accumulate in cells of reticuloendothelial system of the liver and the spleen. The mechanism of colloid accumulation in the liver is determined by two factors: blood mass delivered to each organ and functional activity of the reticulo-endothelial system. For detailed studying of RPh uptake it is necessary to make the scintigraphy in three projections: direct, posterior and right lateral.

Radionuclide hepatobiliary imaging is a technique of radionuclide study with RPh, passing as transit through the polygonal cells of the liver and bile-excreting system to the intestines. Now the RPh with a trade mark SIDA, LIDA are used, which are mixed up with ^{99m}Tc-pertechnetate directly before the introduction. The process of bile excretion depends on the phase of digestion, radionuclide hepatobiliary imaging is executed obligatory on an empty stomach. The program of registration on the computer consists of 30 successively executed shots, the exposition of each one is 1 min. In the norm RPh reaches the maximal accumulation in the liver in 10–15 min. By the 14th–15th minute RPh reaches the gall bladder and the common bile duct. The paint gets the intestine by the 15th minute. After obtaining a good image of the gall bladder, but not earlier than 30th minute after injection, the patient is turned to a standing position. Under the gamma-camera detector a patient has a standard breakfast consisting of 2 yolks. Right after the breakfast a continuous record of gall bladder and intestine condition is carried out for 20 min with an exposition of the shot 1 minute. In the norm, 2 min after the breakfast a motor reaction of the gall bladder is observed and since the 3rd–4th minute its fast emptying occurs, so RPh activity containing in the gall bladder decreases by 40–60% by the 20th minute.

Disorders of accumulation and excretory function of the polygonal cells is observed in patients suffering from chronic hepatitis, cholestasis and manifests itself in the form of retention, as a rule, the maximal concentration of radionuclide.

Radionuclide hepatobiliary imaging (dynamic scintigraphy of the liver) allows to estimate in a complex the absorption-secretory function of the liver, concentration and motor function of the gall bladder, passability of the biliary tracts, to reveal attributes of organic changes, to detect different by character and localization biliary dyskinesia. Radionuclide hepatobiliary imaging is carried out only on an empty stomach, after 10–14-hour starvation. Investigation is conducted in two stages more often: in horizontal position of the patient until the gall bladder is precisely visualized, then its evacuation function is investigated in a vertical position as a more physiologic one. The program of registration on the computer consists of 30–40 successive shots with a minute exposition for the first stage and 20–40 shots — for the second stage.

High enough concentration of agent in bile allows obtaining a distinct image of the liver, gall bladder, bile ducts and the intestine. Maximal accumulation of the agent in the liver comes by the 10th–13th minute. At this time one estimates the sizes, the form and functional structure of the liver that allows to reveal space-occupying lesions in the parenchyma located more close to the anterior surface. At the 14th–15th minute the gall bladder can be visualized, the level of its radioactivity intensifies, reflecting concentration function, and reaches the maximum by the 30th – 40th minute. A part of the agent taken on an empty stomach, within the first hour in regular time intervals delivers to the intestine, but no more than 10%.

The second phase of study begins with a standard cholagogic breakfast of two egg yolks. The Oddi's sphincter opens in 2–3 min and duct fragment of bile leaves for the duodenum. The liver of adults with the height of more than 17 cm and the width of more than 18 cm is evidence of hepatomegaly.

Different factors can produce unusual variants and artifacts in the hepatic image. The weakening caused by the mammary gland or covering fat is frequently observed. Residual barium in the large intestine is the reason of defects visible only on one image. The liver removes downwards to medially-planes cupules of the diaphragm with pleural exudate, emphysema and diaphragmal abscess. A noticeable removal of the liver also takes place at eventeration or diaphragm rapture.

Before cholescintigraphy with an imidodiacetic acid (IDA) a patient should starve for 3 hrs, since the gall bladder can not be visualized when the stomach is filled with food. If patients starve, cholecystokinin release can make gall bladder contraction and Oddi's sphencter relaxation, which promotes bile outflow to the duodenum. Approximately ^{185}mBq of fresh prepared ^{99m}Tc labeled IDA compound are intravenously injected to the patient. If the gall bladder is not visualized, morphine sulfate (0.3 mg/kg of the body weight) is dissolved in 10 ml of a physiological solution and injected within 3 min.

IDA compounds are quickly removed from the blood by hepatocytes. The gall bladder, the general bile duct and duodenum are usually visualized within the first 30 min. Renal excretion of IDA compounds is visible to a certain extent at the majority of healthy people.

Results of the study are displayed as many-coloured image of the hepatobiliary tract (Fig. 14). Bile-forming and bile-excreting functions of the liver, concentration and contraction ability of the gall bladder, passability of the biliary tracts are estimated with the help of histograms and visual observation. The activity/time histograms reflecting RPh redistribution in definite sites are displayed. Areas of the heart, the right lobe of the liver, the gall bladder and the intestine are chosen as zones of interest. At decrease of the liver function, presence of intra- and extrahepatic cholestasis, the steepness of rise and fall of the hepatogram is less pronounced, the time of the maximal accumulation (T_{max}) increases.

Though the size of ducts is hardly revealed, an expanded duct system can be evaluated visually, i.e. noninvasive visualization can be used early at biliar obstruction. Nuclide hepatobiliar visualization is also used for monitoring postoperative patients and diagnostics of retrograde bile reflux, as well as cyst visualization in the general bile duct.

Presence in the liver of space-occupying lesions: cysts, metastases, hemangiomas, abscesses creates focal heterogeneity of radioactive colloid distribution in the liver, i.e. defects of accumulation of different size with decrease or full absence of RPh accumulation — "cold zones" (Fig. 15).

The focal pathology of the liver is sometimes accompanied by deformation and change of organ sizes. Reduction of scintigraphic images of the liver is observed at location of a tumor in the lower departments of the right lobe (V and VI segments). Defects of RPh accumulation on scintigrams of the liver as large focus heterogeneity are observed at spreading of stomach or right kidney cancer, especially its upper pole (Fig. 16).

Revealing of the focus of destruction in the liver less than 2 cm in diameter is difficult as such small tumors often have asymptomatic clinical course and patients do not go to the doctor.

There are 3 pathological types of tumor growth. Almost two thirds of all hepatomas are multinodular, this type is more spread than diffuse one.

Usually hepatoma is revealed at radionuclide scanning as an ovoid focal defect (or defects) among hepatic parenchyma.

Hepatomas are displayed as cold defects on scannograms of the liver, obtained by ^{99m}Tc-colloid.

Hepatic adenomas are of the same size, smooth, incapsulated tumors with focal hemorrhage, with or without necrosis. They consist of layers of normal or slightly atypical hepatocytes, but without Kupffer's cells and bile ducts. Therefore they are revealed as a focal defect at liver imaging by means of ^{99m}Tc colloid sulfur (refer to Fig. 16).

Cavernous hemangioma is the most wide-spread benign tumor of the liver, usually solitary (90%) and often has subcapsular localization. Cavernous hemangiomas consist of endothelium lined and blood filled space.

Hepatic cysts are classified as congenital or acquired. The acquired cysts arise as a result of traumas, inflammation, parasitic invasion. Polycystic hepatic diseases are the hereditary infringements inherited as an autosomal dominant sign. The cysts cause hepatomegaly in 2/3 of patients. 25% of patients have small cysts — less than 1 cm in diameter, but near 40% of all patients have 1 cyst with a diameter more than 4 cm.

The cysts spread outside the liver in 60% of patients. Scanning of the liver with ^{99m}technetium-colloid usually reveals rounded intraparenchymal defects. Approximately 50% of patients suffer both from polycystic hepatic disease and polycystic renal disease. Congenital hepatic cysts connect with the bile tree seldom.

Occlusion of the vena cava inferior can lead to a "hot spot" in the liver if a radionuclide is injected into the lower extremity.

Amoebic abscesses of the liver are usually solitary, localized on the posterior surface of the right lobe (probably, as a result of blood drainage of the ascending part of the large intestine joining the portal venous blood flow). It looks like a defect of radionuclide visualization. The hepatic defect with colloid investigation includes both the abscess cavity and adjoining zone of the inflammatory hepatic tissues. The actual size of the abscess cavity is more accurately determined with the help of reduced activity at visualization with ^{67}Ga-citrate.

A more real indicator of *diffuse disease of hepatic parenchyma is* nonhomogeneous distribution of ^{99m}Tc colloid sulfate absorption. Approximately 80% of patients suffering from cirrhosis have non-uniformity from moderate to pronounced. Increased spleen activity (Fig. 17) relatively to that one in the liver and increased colloid uptake by the marrow correlate well with presence of parenchymal hepatic disease.

However, the increased absorption of colloid by the spleen and marrow can take place at anemia even at absence of a hepatic parenchymal disease.

Hepatomegaly, moderate increase in both lobes or mainly left lobe are revealed on the liver scintigram of a patient suffering from *chronic hepatitis*. The liver shape is changed as a rule, contours are insufficiently accurate, RPh distribution in parenchyma is diffusely uneven. A usual or slightly increased spleen and RPh non-intensive inclusion is typical for a chronic hepatitis with low activity. The hepatolienal coefficient (ratio of RPh accumulation in the spleen and the liver) is raised, and increases up to 15% and more. Thus the effective hepatic blood flow is within the limits of the low border of the norm or is a little bit reduced. During the periods of hepatitis exacerbation, decrease in the level of blood flow of the liver and increase in its sizes is marked.

The chronic hepatitis with a high degree of activity is accompanied by moderated hepatomegaly and splenomegaly. The level of RPh accumulation in the spleen increases up to 30%. However, a considerable inclusion of radiocolloid in the marrow is not observed. Clearness of contours is a little bit lowered, heterogeneity of RPh distribution amplifies, accumulation in the left lobe is moderately raised. The effective hepatic blood flow decreases to 1.0–0.8 L/min.

Both increase and reduction of the sizes of liver imaging (depending on a cirrhosis form) and its deformation are observed at *cirrhosis*. As a rule, the sizes of the right lobe decrease to some extent (depending on a disease stage), and of left one — increase. Inclusion of colloid RPh in the left lobe is more intensive. Decrease in radiocolloid accumulation along the right lateral and lower edge of the liver causes deformation of contours. At the same time diffuse non-uniformity becomes more expressed, and at a large-nodular cirrhosis RPh distribution is getting a focus-irregular character. The scintigraphical sign of liver cirrhosis is spleen enlargement with an active RPh inclusion. The level of an effective hepatic blood flow is moderately or considerably lowered (less than 0.75 l/min) in dependence on the cirrhosis stage and portal hypertension. Hepatolienal coefficient increases up to 50% and more. It is considered that radionuclide accumulation in the spleen is consequence of hypertension in the portal vein system developing as a result of intrahepatic block of this system. Intensive uptake of RPh by the spleen and splenomegaly sometimes are marked in patients with cirrhosis of the liver without clinical signs of hypertension. It is connected with the fact that at liver cirrhosis functional activity of reticuloendothelial system decreases and its volume decreases too. At the same time reticuloendothelial hyperplasia in the spleen — the hyperspleenism is observed. A characteristic sign of cirrhosis is the spine marrow imaging, better revealed in the posterior projection.

Fatty infiltration of the liver at radionuclide investigation of the liver is characterized by diffuse irregular distribution of colloid RPh. Unlike with chronic hepatitis and cirrhosis the radionuclide signs of splenomegaly do not reveal. The liver is evenly enlarged, the border between the left and right lobe is absent, contours are rounded, precise, sometimes the sizes of the liver are within the limits of the norm. The effective hepatic blood flow is present or slightly lowered.

Visualization of the spleen on the scintigram is observed at a number of other diseases too (Fig. 17). At spleen vein thrombosis the liver image is usually unchanged, the image of the spleen is sharply increased, RPh inclusion intensity is raised. At combination of chronic diffuse process in the liver and spleen thrombosis accumulation of RPh in the spleen amplifies very much. Visualization of the enlarged spleen is observed with innidation of the pancreas tumor to the spleen vein. Splenomagaly is revealed also at presence of metastases spread to the liver gates when the enlarged lymph nodes cause the compression of the portal vein. At the same time RPh accumulation defects may be revealed in the liver parenchyma, which are typical for metastases.

Blood diseases are often accompanied by splenomegaly, the liver can be enlarged, radiocolloid distribution is even or has a focal character at presence of zones of extramedullar hemopoiesis (leukoses, true polycythemia). At the same time positive dynamics of radionuclide picture is oserved at purposeful treatment of the basic disease.

In contrast to fatty infiltration of the liver caused by alcohol which quickly resolves after abstinence from alcohol, the *acute alcoholic hepatitis* often progressively develops up to cirrhosis.

At 80% of these patients image with colloid ^{99m}Tc-sulfate shows the liver-spleen noticable abnormalities, including single or plural defects in the liver and shifts of colloid to the spleen and marrow. In the most serious cases, hepatic absorption is so little that the liver is hardly visualized, splenomegaly is present.

Radionuclide visualization is usual in diagnostics of a *blunt hepatic trauma*. A closed injury, such as rapture or subcapsular hematoma of the liver or spleen can be identified. Scan can determine localization and extent of rapture and to specify the surgical approach. Injuries in the anterior-posterior quadrant of the right lobe of the liver is difficult for determination during surgical opening of the abdominal cavity. In addition, the scan is necessary at severe injuries, treatment, dearterialization or other surgical diseases. Results of hepatic scintigraphy in patients with a trauma are of great value.

After hepatic lobectomy, the liver regenerates, but full regeneration occurs usually in some months. The earliest complication is liver enlargement after lobectomy caused by hypostasis.

Long cholestasis as a result of Oddi's sphincter function disorders, either presence of stones or fibrosis in the general bile duct, leads to liver enlargement, mainly of its left lobe. At the same time the following processes take place: increase in plateau time and delay of an agent excretion from the liver, long visualization of lobes, general hepatic and bile ducts, decrease in concentration and contractile functions of the gall bladder, slow and irregular delivery of labeled bile to the small intestine. An expanded general bile duct, which visualizes long and precisely, slow drainage is sometimes revealed. Nitroglycerine administration does not render a proper effect, which is evidence inflammation-fibrous changes.

Concentration dysfunction of the gall bladder is displayed by late visualization and slow filling of the gall bladder (T_{max} > 40 mines). Contractile dysfunction of the gall bladder is accompanied by increase half-empting period till 90–180 min and more. The gall bladder is visualized in some patients only after administration of nitroglycerine, the gall bladder fills up very slowly. Absence of visualization during all the time of study even after nitroglycerine intake is typical for a non-functioning gall bladder. Bile scintigraphy allows to reveal duodenostases and duodenogastric refluxes and to evaluate them both qualitatively and quantitatively.

High informational value of scintigraphical studies at patients with damage of bile-excreting tract allows to characterize the pathological process more completely.

At patients with acute abdominal pain (i. e. during 4 hrs) absence of visualization of the gall bladder in a combination with normal visualization of the gall tree and the large intestine is characteristic for acute cholecystitis.

Besides, absence of visualization of the gall bladder is observed in patients without cholecystitises which receive parenteral feed (92%), at alcoholics (60%), and also in patients with long-time immobility.

The jaundice can be a result of a perenchymal disease of the liver or extrahepatic obstruction. RPh delivery to the duodenum can proceed within 30 min. If the large intestine is visualized more than for 60 min after the hepatocytes saturation phase, a partial obstruction of the general duct caused by gall stones, mucus, extrahepatic tumor, edema, etc. can be observed. Besides, lack of complete visualization activity in the gastrointestinal tract can be caused by serious hepatocellular disease. The exact mechanism of this excretion is unknown, but disturbance of normal hepatocellular function can lead to considerable change of secretion, i. e. to visualization disorders.

8.3. Radionuclide Study of the Spleen

Spleen scintigraphy can be executed with several radiocolloids, but as a rule — with sulfur ^{99m}Tc-colloid.

After sulfur ^{99m}Tc-colloid injection, image is obtained with an interval from 1 to 5 sec. This dynamic procedure of display helps to estimate the anatomic configuration of greater abdominal arterial and venous channels, as well as to estimate vascularization of damages. Static images are obtained in anterior, posterior and lateral projections in 15 min. Normal display of the liver with sulfur colloid shows homogeneous accumulation of lesser intensity than in the liver on the posterior projection. Greater colloid particles tend to be distributed mainly in the spleen as compared with smaller ones. Increased accumulation in the spleen or spleen enlargement are associated with many conditions, including different diseases of the liver, anemia, sepsis and melanoma.

Spleen scan helps to determine its size. Many methods have been suggested to calculate the spleen volume. Researches based on the fact that the spleen configuration is rather similar in all patients. However, by changing from laying on the back position to the knee or elbow position, the spleen can move or compressed by next organs. If the spleen is 15 cm in length, it is possibly increased. Massive splenomegaly (over 1000 g) can associate with chronic myelocytar leukaemia, myelofibrosis. Pronounced splenomegaly (500–1000 g) is revealed with acute leukemia, malignant lymphoma, splenomegaly, true polycytemia, or infectious mononucleosis. Moderate splenomegaly (under 500 g) is usually caused by infection, malignant melanoma, sarcoma and idiopathic thrombocytopenic purpura.

The reduced spleen size is found in adult patients suffering from sickle-cell syndrome. Family spleen hypoplasia is discovered in children with severe course of bacterial infections. The spleen atrophy was noted in different diseases, including ulcerous colitis, thyreotoxicosis, sickle-cell anemia.

Cases of polysplenia, basically, are met in women with unpaired bound *vena cava inferior*.

The term "functional asplenia" is used to describe patients with sickle-cell anemia, in which the spleen was anatomically present, but has lost an ability to absorb sulfur ^{99m}Tc-colloid. Functional asplenia cases are divided into 2 groups:

1) disorders of circulation;
2) effects of various conditions of spleen reticuloendothelial cells.

A postsplenectomic sepsis can occur in many days and even years after removal of the spleen. The death from postsplenectomic sepsis is met 200 times as often as death from sepsis in population as a whole.

Children suffering from sickle-cell anemia and hyposplenism are predisposed to pneumococcal sepsis.

Damages of the spleen occur approximately twice more often than damages of the liver. The spleen is most often injured by a blunt trauma. The most usual damages — spleen rapture and a subcapillary hematoma. The risk of spleen hematomas is increased at patients with thrombocytopenia. Radionuclide images of the spleen has approximately the same accuracy as arteriography. Imaging usually reveals the central defect within the limits of the spleen or adjacent to it.

8.4. Radionuclide Diagnostics of Pancreas Diseases

Radionuclide diagnostics of pancreas diseases because of enough high radiation dose, especially at the traditional technique, is applied seldom or is not applied at all. The most effective method of pancreas investigation is scintigraphy. A patient is injected intravenously ^{99m}Tc and ^{75}Se-methionin, which accumulate in the pancreas only by 10%. At diseases of the gland scintigrams show deformation of the gland image and change of intensity according to defeat focus localization.

Key Concepts of the Theme

The purpose of application of radionuclide diagnostics at diseases of the gastrointestinal tract, the liver, the spleen, the pancreas; techniques of radionuclide diagnostics of diseases of the gastrointestinal tract, the liver, the spleen, the pancreas; scintigraphical semiotics of diseases of the gastrointestinal tract, the liver, the spleen, the pancreas.

The Formalized Structure of the Theme Contents

Indications to radionuclide diagnostics of the diseases the gastrointestinal tract, liver and spleen

The gastrointestinal tract	*The gall bladder*	*The spleen*	*The liver*
1. Functional conditions of the gastrointestinal system 2. Evaluation of surgery efficacy 3. *Campylobacter pylory* infection	1. Gall bladder dyskinesis 2. Cholecystitis	1. Anatomic-topographical conditions 2. Hepatolienal syndrome 3. Functional asplenia 4. Injuries 5. Postsplenectemic sepsis 6. Tumors	1. Anatomic-topographical conditions 2. Hepatomegaly 3. Primary tumors 4. Metastatic tumors 5. Cysts 6. Post-operative conditions

Questions for Independent Work

1. Indications to radionuclide diagnostics of diseases of the gastrointestinal tract, the liver, the gall bladder, the spleen.
2. Radiopharmaceuticals used for gastrointestinal diseases diagnostics.
3. Methods of radionuclide diagnostics applied in hepatology.
4. Scintigraphical semiotics of diseases of the gastrointestinal tract, the liver, the spleen, the gall bladder.

Alternative-test Tasks for Self-checking

1. Is it possible to carry out quantitative estimation of motor-evacuatory function of the gastrointestinal tract by means of radionuclide diagnostics?
2. Is it possible to study the processes of absorption in the small intestine with the help of radionuclide methods?

3. Does the radionuclide method help to reveal presence of *Campylobacter pylori*?

4. Is it enough to use one projection for studying radiopharmaceutical uptake by the liver?

5. Should a patient starve before cholescintigraphy?

6. Can cysts cause liver hepatomegaly?

7. Can splenomegaly accompany chronic hepatitis?

8. Is the liver scintigraphical image deformation observed with cirrhosis?

Tasks and Problem Situations

1. A medical lorry delivered to the hospital a patient with a blunt abdominal trauma and the preliminary diagnosis "gastrointestinal bleeding". Is it necessary to administer hepatic scintigraphy for specification of the diagnosis?

2. A woman, 40 years old, during 10 years suffers from gallstone disease with recurrent attacks of hepatic colic. Which hepatic lobe can be found enlarged during scintigraphical investigation of the liver?

3. Give your idea about possible reasons of absence of gall bladder visualization.

4. Specify the reasons of functional asplenia.

Chapter 9
RADIONUCLIDE DIAGNOSTICS IN NEPHROLOGICAL PRACTICE

Non traumatic studies for patients, a relative simplicity of performance in a combination with high efficiency of received results provided inclusion of these methods in an obligatory complex of modern inspection. Quantitative estimation of received results is of special value in radionuclide study.

The rate of labeled compounds pass through the renal bloodstream, intensity of tubular secretion and glomerular filtration, the rate of agent excretion from the kidneys and the urinary bladder are calculated by special mathematical methods with the help of computer. Among radionuclide methods, scanning, renography (two variants), nephroscintigraphy (dynamic and static scintigraphy) are the most wide spread in the nephrological practice *in vivo*.

At making the morphological diagnosis radionuclide methods play an additional role in relation to radiological studies, ultrasonography and computer tomography. Radionuclide scanning allows determining the sizes, form, location of the kidneys, intensity and regularity of RPh inclusion into the renal tissue.

Renography is directed on investigation of active tubular secretion of a labeled agent and its excretion along the upper urinary tract.

The obtained curve is called renogramm, and consists of 3 sites: vascular, secretory and descending (evacuatory) (Fig. 18). The first site reflects agent distribution in the renal bloodstream, the second one — a process of selective and active accumulation of hyppurate by epithelium cells of the proximal renal tubules, the third one — agent excretion from pelvic-calyceal systems through the ureter.

The most frequent renographical symptoms of renal diseases are the following: decrease in cleansing ability of tubular apparatus of the kidney; delay of speed of RPh excretion from the kidney and a combination of these two symptoms. Persistent registration is also conducted at the gamma-camera within 15–20 min.

The received curve consists of 3 sites. The first site reflects the process of agent about-passage through the renal bloodstream, the second one — the process of glomerulus filling with a labeled complex, the third one — filtered RPh excretion from the kidney with urine. In the norm this value coincides with total renal clearance.

Dynamic nephroscintigraphy is based on investigation of a functional condition of kidneys by way of registration of uptake by renal parenchyma of labeled nephrotropic RPh DTPA with ^{99m}Tc, also intravenously injected. Investigation is conducted also on special gamma-cameras. The received information is registered at the computer and displayed as imaging of various stages of RPh (DTPA) passage through the kidneys. In the norm in 3–5 min after RPh introduction there appears the image of renal parenchyma, accumulating the agent intensively. Accumulation by renal parenchyma decreases in 5–6 min. RPh fills the pyelocalicular system, and then, in 11–15 min, accumulates in the urinary bladder distinctly. At dynamic nephroscintigraphy, renal parenchyma dysfunction (total and regional) as a result of decrease in RPh accumulation or delay of its excretion are revealed. Indications for nephroscintigraphy are the following: suspicion on congenital maldevelopments, on renal tumor, substantiation of surgical intervention, specification of its functional condition and some other indications. Static nephroscintigraphy is directed on investigation of function and structure of renal parenchyma. The technique consists in registration of radioactivity above the renal zone in 2–3 hrs after intravenous introduction of RPh dimercaptosuccinic acid (DMSA).

These two variants are combined in modern gamma-cameras at present, and consequently there is an opportunity to study simultaneously static and dynamic condition of kidneys and to receive renographic curves.

In contrast to changes of secretory-excretory function of kidneys, the changes revealed at RPh DMSA reflect adequately the character of pathological process, and severity of defeat of cortical layer of the kidney, and as a rule, are evidence of irreversible changes in parenchyma. By results of nephroscintigraphy it is possible to determine renal function up to 5% (at renography up to 10%).

Besides of advantages, radionuclide renography has drawbacks:

1. Detectors above the kidneys are installed according to standard anatomic sites, which sometimes considerably reduce accuracy of investigation (specific features of kidneys location are not taken into account).

2. There is no opportunity to distinguish precisely secretory and excretory stages, therefore division of the renographical curve into the used stages is conditional;

3. The renographical curve reflects change of activity not only in the kidney, but also in surrounding tissues;

4. Inspection of small children is difficult in connection with small distance between the kidneys.

Scintigraphy of kidneys has a number of doubtless advantages as compared with usual renography:

1. Performance of scintigraphy doesn't yield mistakes caused by wrong installation of detectors as almost without exception, all the area of a possible kidneys location is in the gamma-camera's crystals field vision.

2. At scintigraphy there is an opportunity of scintigraphical renogramm correction with taking into consideration contribution of irradiation of the around kidneys soft tissues.

3. At scintigraphy not only RPh transport through the kidney but also outflow disorders from calices, renal pelvis and at all levels of the ureter are estimated.

4. Scintigraphy gives an opportunity to receive the image of kidneys sufficient for determination of their anatomical-topographical condition, to estimate filtrational role of the kidney by segments.

5. Both scintigraphy and renal function study give a picture of central and interrenal hemodynamics, allows to define more exactly the arterial hypertension genesis.

6. The study consists of 20–30, sometimes more successive shots with 30- or 60-second exposition.

Renal imaging (dynamic renoscintigraphy) is a simple and exact method of simultaneous estimation of a functional and anatomical-topographical condition of the urinary system (refer to Fig. 18).

It is grounded on registration of nephrotropic RPh transport and a subsequent calculation of parameters, which make the two successive stages objective. The analysis of the vascular phase (angiophase) is directed on estimation of symmetry of "bolus" transit along the renal arteries and relative blood volumes delivered to each kidney in the unit of time. The analysis of parenchymatous phase provides the characteristics of a relative function of kidneys (the contribution to total cleaning ability) and time of RPh transit through each kidney or its departments. Clinical interpretation is considerably determined by the RPh elimination method. Two types of RPh can be used for dynamic visualization:

— gllomerulotropic (DTPA derivatives) are practically completely filtered with glomerules and reflect the condition and rate of glomerular filtration;

— tubulotropic (hyppurate analogues) are secreted by the epithelium of proximal tubules, reflect the condition of tubular secretion, as well as effectiveness of the renal blood flow.

Indications to the study include urologic and nephrological pathology, as well as diseases which involve the kidneys.

At different clinical situations both shape of curves and their quantitative characteristics can vary. It is necessary to emphasize, however, that character and values of changes are non-specific for a concrete pathology and first of all reflect the severity of the pathological process.

The greatest informational value of renoscintigraphy is shown at differentiation of uni- or bilateral defeat of kidneys. The main sign defining the side of defeat — asymmetry of amplitude-time characteristics of angionephroscintigrams. Asymmetry of vascular parameters, and first of all the expressed difference of time of RPh delivery to the renal arteries is one of criteria of renal arteriostenosis. Symmetry of parenchymal function changes is more typical, in particular, for glomerulonephritis; asymmetry — is a rather popular sign of pyelonephritis not only with the unilateral but also with the bilateral process. Similar changes may accompany various variants of abnormalities of kidneys and upper urinary tracts (nephroptosis, hydronephrosis).

$T_{1/2}$ excretion delay is observed at presence of stones, stricture of the ureter and other changes of the upper urinary tracts leading to hydronephrosis.

The renal colic is presented by the obstructive type of a curve on the side of defeat (refer to Fig. 19). Depending on the terms of colic onset and obstruction level, the curve of renogram will change. The long violation of urine outflow results in deterioration of renal function and decrease of the renogram amplitude. The renal image can be absent or unclear. Delayed scintigrams allow to reveal the remaining functioning of the kidney and define the blockade level. However, scintigraphy, in contrast to roentgenologic studies, does not allow to visualize a concrement directly, but often allows to detect the level and degree of ureter obturation.

Large stones in the renal pelvis can be visible as expanded RPh accumulation defects.

The use of dynamic scintigraphy of kidneys at the clinical observation of patients suffering from chronic glomerulonephritis allows to estimate the degree of renal function condition, and also finding out the sclerotic and degenerative changes in them. Efficiency of nephrolythiasis treatment by the stroke-wave lypotripsy is estimated by the index of parenchymatous and pelvic average time of RPh transit (ATT) through the kidney on the whole and separately — through its parenchyma and renal pelvis.

Radionuclide diagnostics of vesicoureteral reflux is executed by indirect and direct radionuclide scintigraphy.

Indirect (intravenous) radionuclide scintigraphy. Dynamic renoscintigraphy is conducted by the generally accepted method, as a result information is got about renal morphology, urinary tracts, renal function. At the next stage after the physiological filling of the urinary bladder a patient urinates, and the image is recorded at this time. The curves "activity-time" are built above the zones of interest: kidneys, ureters, urinary bladder. The pronounced curve lifting over the kidney or ureter, synchronous to urination act, is evidence of the presence of vesicoureteral reflux.

At bilateral vesicoureteral reflux activity above both ureters and both kidneys grows simultaneously with the beginning of the urination act.

Direct (retrograde) radionuclide cystography. The method of study includes urethral catheterization, retrograde filling of the urinary bladder by physiological solution of sodium chloride mixed with a mark, and obtaining of images of the urinary tracts region during filling of the bladder, at the moment of urination and after it.

Key Concepts of the Theme

Renography, nephroscintigraphy, renal scanning, indirect radionuclide cystography, retrograde radionuclide cystography.

The Formalized Structure of the Theme Contents

Radionuclide diagnostics in urology

Methods:
- Scanning
- Renography
- Nephroscintigraphy
- Indirect radionuclide cystography
- Retrograde cystography

Radiopharmaceuticals:
- Hyppurate
- ^{99m}Tc-DTPA
- ^{99m}Tc-DMSA

Questions for Independent Work

1. Advantages of radionuclide diagnostics of renal diseases.
2. Which disturbances and diseases can be revealed by radionuclide renal scanning?
3. Radiopharmaceuticals used for radionuclide diagnostics of renal diseases.
4. The equipment used for radionuclide diagnostics of urinogenital diseases.
5. Which method is used for screening study of patients with suspected pathology of the urinary system?
6. Renographical symptoms of renal diseases.
8. Indications for nephroscintigraphy.
9. Drawbacks of renography.
10. Advantages of kidneys scintigraphy.
11. Symptoms of vesicoureteral reflux.

Alternative-test Tasks for Self-checking

1. Are peculiarities of kidneys localization taken into consideration at radionuclide renography?
2. Does renographic curve reflect the change of activity in the tissues surrounding the kidney?
3. Which pathology is characterized by parenchymatous function changes symmetry?
4. What type of the curve is typical for renal colic?

Tasks and Problem Situations

1. Choose the device for simultaneous studying static and dynamic condition of the kidneys.
2. Dynamic renoscintography revealed asymmetry of amplitude-time characteristics of scintigrams. Is it possible to determine the side of defeat on the basis of obtained data?
3. What does renoscintigraphy allow to reveal at kidney colic: to visualize a stone or to reveal the level and degree of ureter obturation?

Chapter 10
RADIONUCLIDE DIAGNOSTICS IN ONCOLOGY

At use of any diagnostic methods, for successful treatment of oncological patients, one should solve the following problems:

— to reveal a tumor (early diagnostics of tumors);

— to answer the question whether tumor is malignant or benign (differential diagnostics of tumors);

— to determine the disease stage by TNM system:

a) sizes of a tumor (T_{1-4});

b) metastases to regional lymph nodes (N_{0-3});

c) metastases to other organs (M_{0-1});

— to estimate functional condition of other organs and systems;

— to make control over efficiency of the conducted treatment;

— to organize early diagnostics of relapses and metastases of a tumor.

Many of the listed-above problems are solved by methods of radionuclide diagnostics, connected with visualization of tumors. Visualization of malignant neoplasms is based on distinction of agent accumulation in the tumor and the tissue surrounding it. Groups of radiopharmaceuticals used for tumors imaging are called "tumorotropic" and "organotropic". In one case tumors get an ability of increaseed uptake of agent in comparison with healthy tissue (such formations are revealed in the form of the "hot spots"; in the other — the tissues lose an ability to accumulate one or another agent — these tumors are determined as "cold spots". Accordingly groups of radiopharmaceuticals used for visualization of tumors refer to "tumorotropic" and "organotropic".

There is an opportunity of direct tumor imaging on scintigrams by means of tumorotropic RPh with gallium citrate. Specificity of the agent is estimated not in relation to a certain organ but to a tumor process.

Gallium citrate-67 belongs to specific tumorotropic agents. With this agent it is possible to receive the image of tumors as "hot" foci of the majority of organs (the maxillofacial area, pharynx, esophagus, lungs, soft tissue, liver, mammary gland). This method is especially valuable in diagnostics of lymphoid tissue diseases (lymphogranulomatosis, lymphosarcoma). It is connected with the fact that at system disease it is necessary to estimate the condition of all groups of lymph nodes above and under the diaphragm.

The given problem is solved only at use of gallium citrate when after a single introduction of the agent only affected lymph nodes, irrespective of their localization, are visualized. Other methods of investigation (mediastinoscopy, direct and indirect lymphography, tomography, ultrasonic diagnostics) allow to investigate only separate groups of lymph nodes. Besides, at investigation with gallium citrate in some cases it is possible to determine damage of the stomach, liver, lungs.

Investigation with gallium citrate is effective for the control over the conducted treatment. Unfortunately the agent does not allow to diagnose authentically abdominal tumors because the agent excretes through the intestine and RPh activity in the intestine masks its increased accumulation in the tumor.

Labeled monoclonal antibodies were put in use for visualization of tumors. These agents have specificity not only to the tumor process but also to a definite organ. For example, CA-125 allows to detect ovarian tumors.

Nonspecific tumorotropic agents allow to visualize the tumors of only separate organs, at the same time intensive agent uptake in them is associated not with a tumor process, but by other reasons. The ^{131}I-labeled sodium iodide, used for diagnostics of thyroid cancer metastases to other organs: the lungs, bones, etc., is a typical example of such agents. The reason of intensive RPh accumulation in metastases occurs in this case due to their ability to execute the function of maternal tissue, i.e. synthesize hormones which need in iodine. Before investigation it is necessary to inhibit the function of the thyroid gland itself (by a surgical, radiation or drug way) and stimulate metastases function by TTH introduction. The tumors of the brain, bones, retroperitoneal tumors are visualized as "hot" foci. Visualization of tumors of skeleton has advantage over other methods, as visualization is possible at the level of mineral metabolism disorders instead of bone destruction. Therefore the radionuclide method is ahead of the roentgenologic one from 3–6 months to 1 year.

^{32}P-labeled Na_2HPO_4 may be considered as a tumorotropic agent. However, disintegration of radioactive phosphorus-32 is accompanied by only beta-particles irradiation, therefore can not be used to conduct visualization of tumors and even for radiometry the transducer should be brought directly to the tumor. On this account radiophosphoric diagnostics studies suspicious formations of the skin and some cavital organs (the esophagus, oral cavity, nose, larynx, rectum, uterus) for differential diagnostics. Presently this method is unique for differential diagnostics of melanomas of the skin, the eye.

With the help of gamma-cameras, scintigraphy is carried out — RPh distribution defects are detected. The similar information is obtained also by scanning. Absence of radioactive substance accumulation in the organ is not an evidence of the malignant formation presence. Any pathological processes which are able to result in dysfunction or sharp decline in parenchymal function of organ (inflammatory processes, cysts, benign tumors, cicatrices, etc.) hinder the normal RPh uptake at a corresponding region. This accounts for large percent of false-positive results of the negative scanning, which can be improved due to application of additional methods of study and careful analysis of clinical data of a patient.

More reliable are condisered the methods of radionuclide diagnostics based on the principle of selective (electoral) RPh accumulation in malignant formations — a so-called tumorotropic RPh.

RPh tumorotropism is determined by different factors. Some of them selectively enter the tumor by a metabolic way in connection with the intensive utilization by the tumor of certain substances, because of change of its metabolism and higher need in these substances as compared with normal tissues (microelements, some proteins, amino acids, etc.). Other agents can retain in the tumor by a mechanical way due to tumor vessels change, in particular, their permeability disturbances, along with considerable vascularisation of some tumors. Introduction of radionuclide to the tumor by the labeled antibodies to the known tumor antigens is possible also. The labeled monoclonal antibodies are used with this aim.

Positive scintigraphy to a great extent improves diagnostic information. However, absence of a specific substance tropic only to the malignant tumors causes a certain percent of diagnostic errors. The false-positive results take place less often than false-negative. It is explained by the fact that tumorotropic substances do not enter benign tumors, cysts, cicatricle tissues, as well as do not accumulate in the necrotized parts of the tumor and, vice versa, are able to fix in active inflammatory foci. The

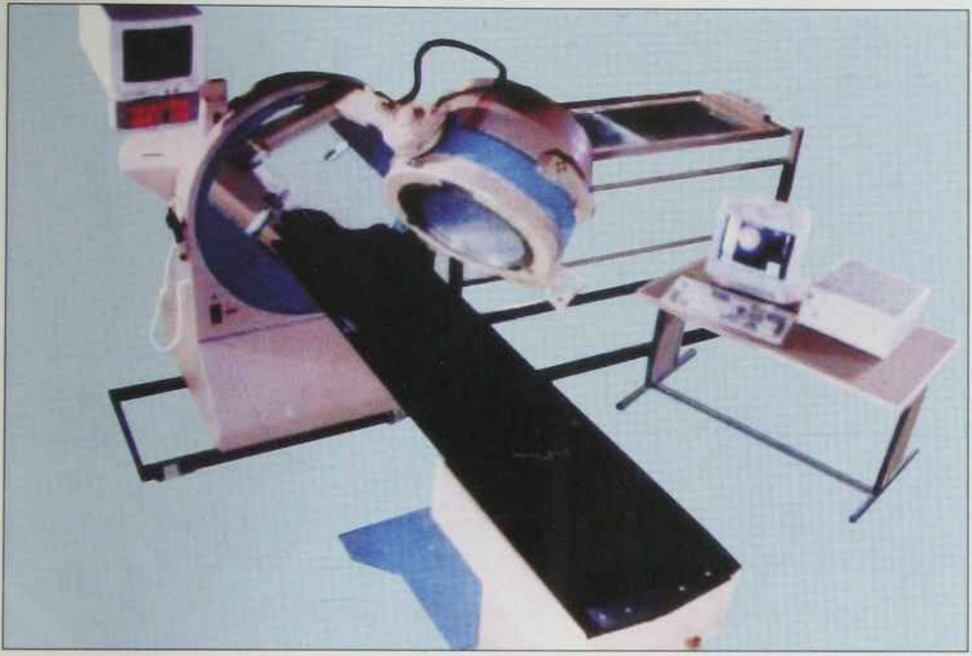


Fig. 1. Rotating tomographic camera

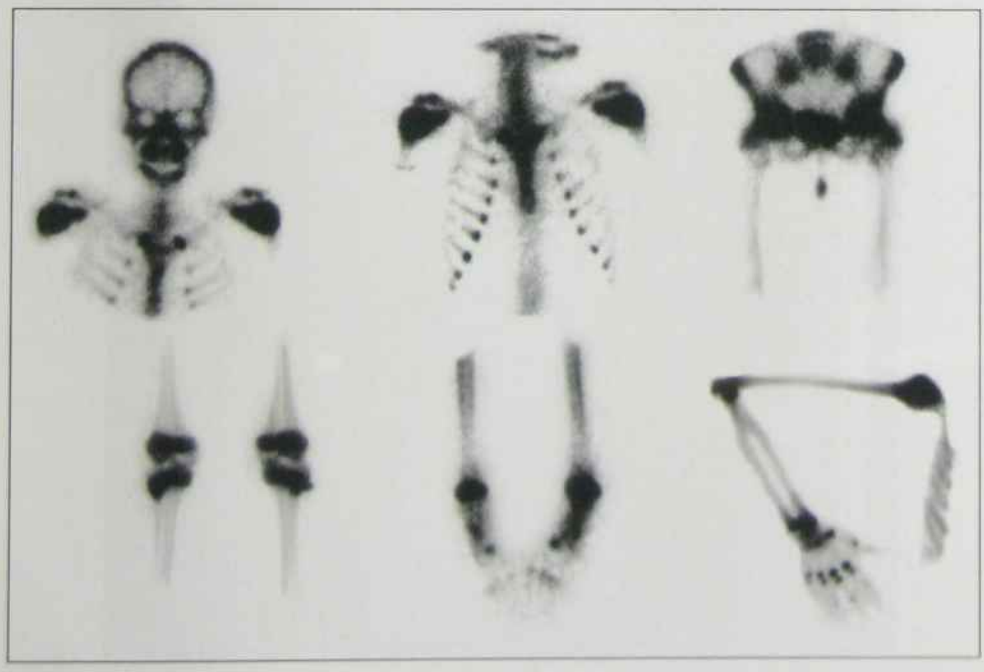


Fig. 2. Scintigram of a normal skeleton

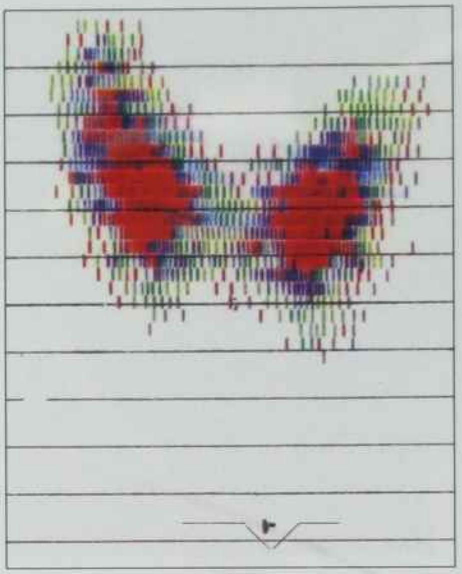


Fig. 7. Scan of a normal thyroid

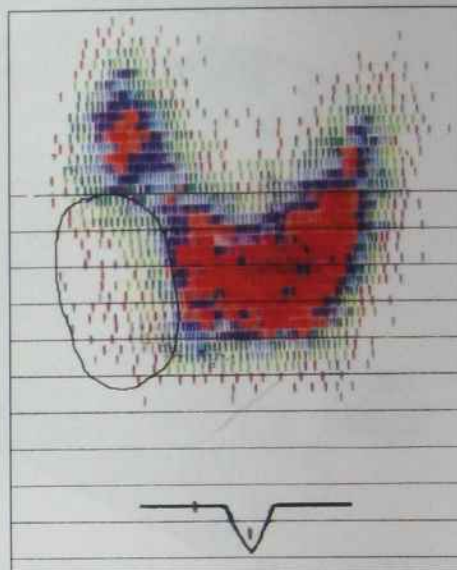


Fig. 8. Scan of the thyroid with the presence of a "cold node" (with ^{131}I)

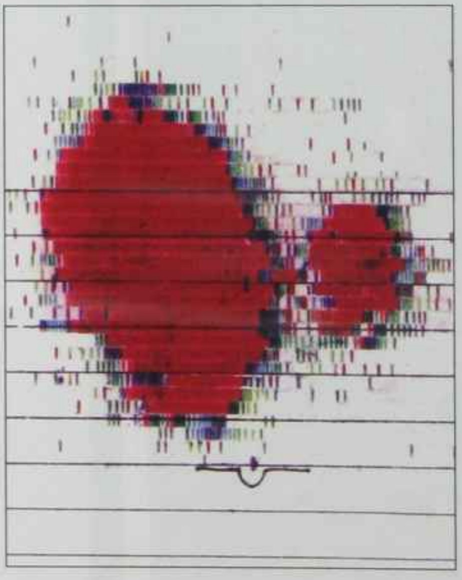


Fig. 9. Scan of the thyroid (with ^{131}I). Diffuse toxic goiter

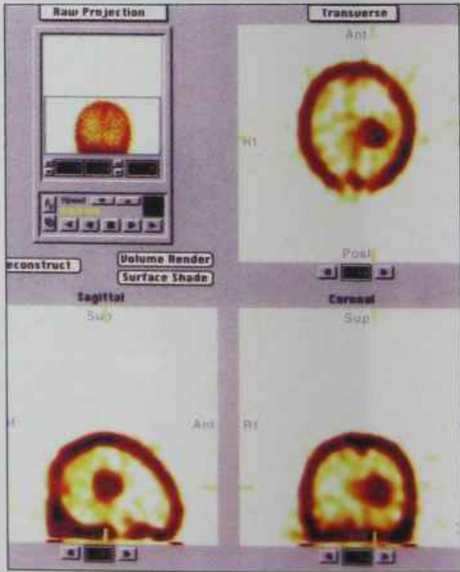


Fig. 10. Brain scintigram in a patient with brain tumour (pertechnetate ^{99m}Tc)

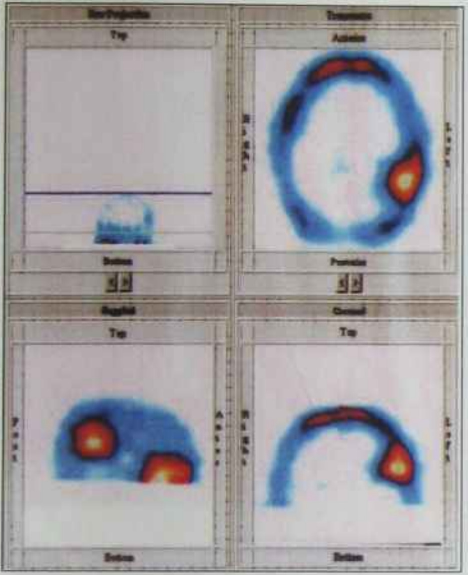


Fig. 11. Brain SPECT with ^{99m}Tc-MIBI. Meningioma of the left parietal part

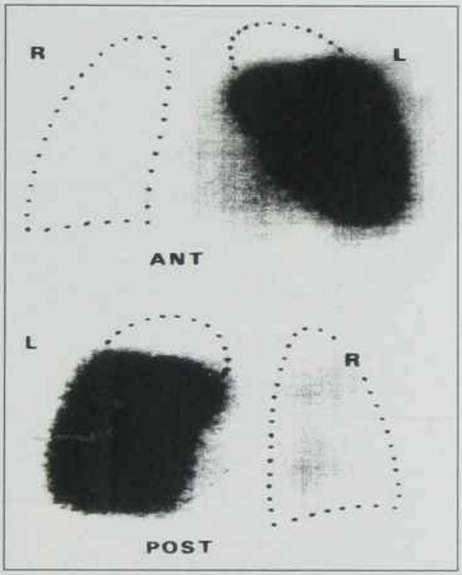


Fig. 12. Lack of perfusion in the whole lung and apex of the left lung

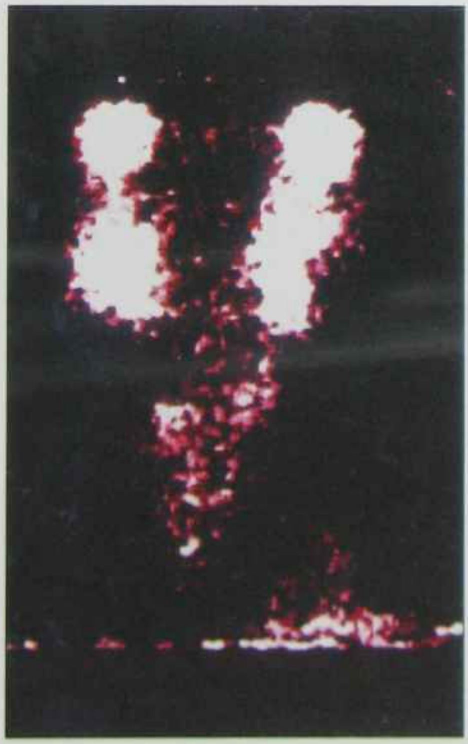


Fig. 13. Indirect lymphoscintigraphy of axillary and para-aortal nodes

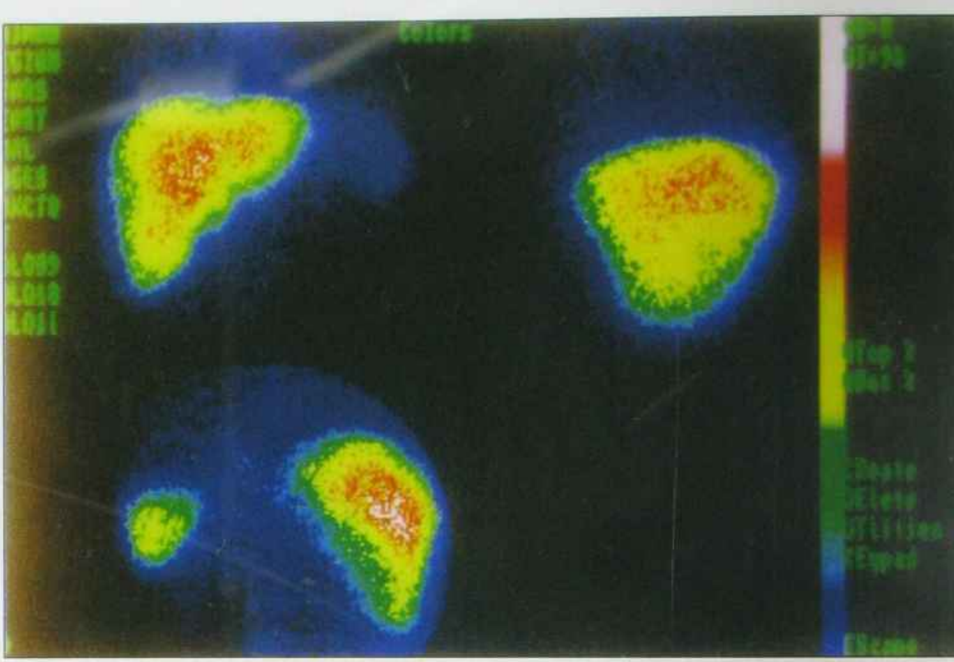


Fig. 14. Scintigram of a normal liver

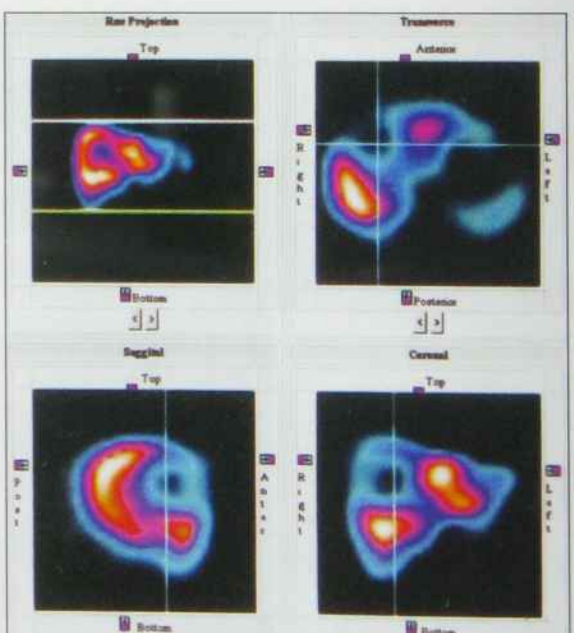


Fig. 15. SPECT of the liver with radionuclide.
A "cold node" in the right lobe

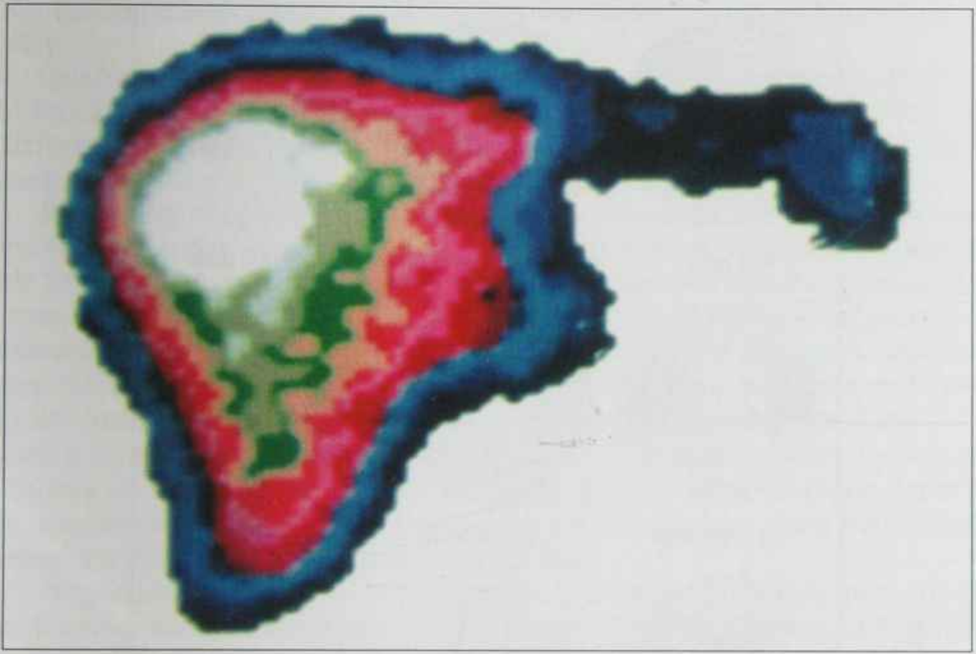


Fig. 16. Hepatoscintigram.
Focal pathology of the liver (99^mTc-colloid)

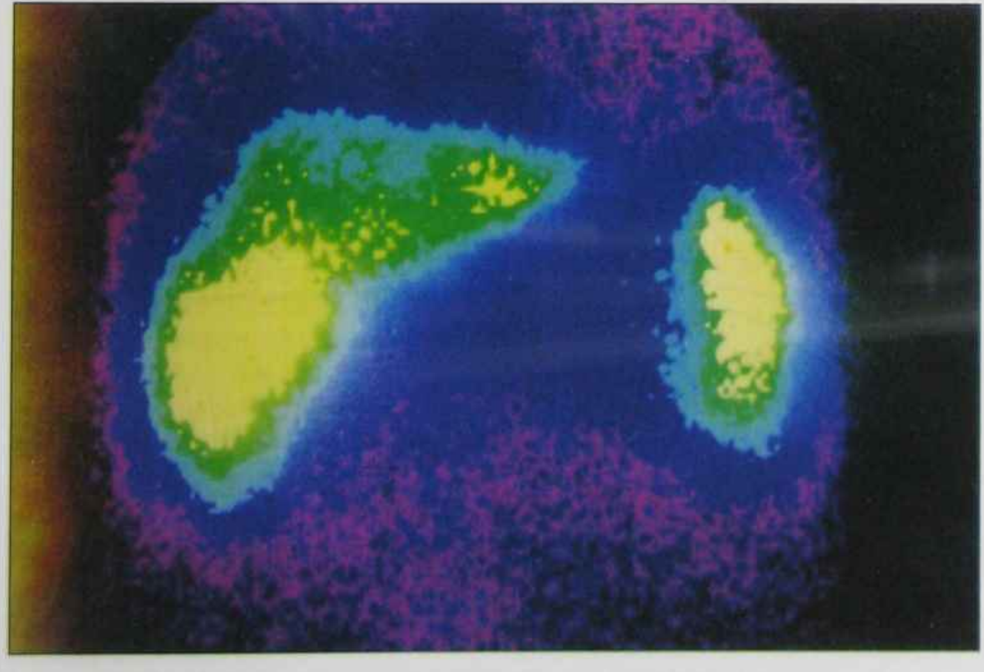


Fig.17. Spleen imaging

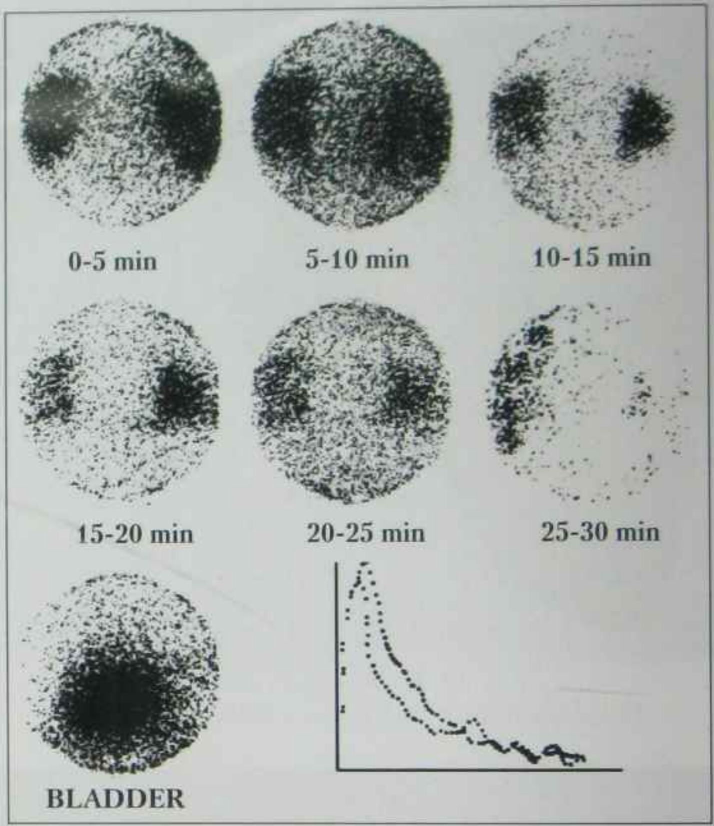


Fig. 18. A normal bilateral renogram executed with iodohippurane

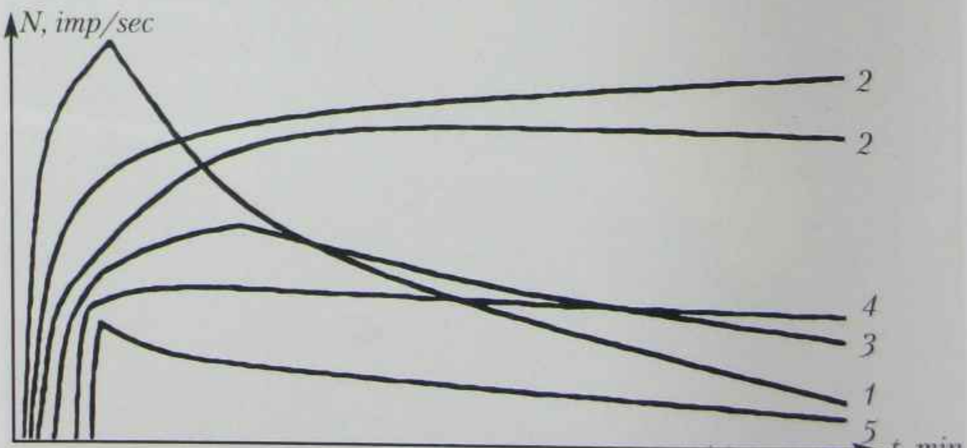


Fig. 19. Types of renographic curves: *1* — normal; *2* — obstructive; *3* — parenchymatous; *4* — isosthenuric; *5* — nonfunctioning

last two moments are the main reasons for erroneous conclusions possibility.

Quality of diagnostic information can be improved by combined usage of facilities for positive and negative scintigraphy. Thus, it is possible to differentiate malignant tumors and cysts, benign tumors, cicatricle, and sometimes inflammatory changes.

Reliability of scintigraphy in diagnostics of tumors depends mainly on the size of a tumor. At negative scintigraphy by ordinary devices it is possible to find out tumors of no less than 2 cm in diameter. Smaller tumors are revealed by the method of positive scintigraphy and with use of gamma-cameras with great resolution ability, as well as such the most modern devices as SPECT and PET. These apparatuses allow to define precisely the location and volume of pathological focus, because like X-ray CT give a layer image of the examined object with much more low radiation loading on the patient's organism. A short-lived or ultra short-lived mark is injected in an organism in a single dose with making a great number of images without additional external radiation.

Negative scintigraphy became wide-spread in diagnosis of tumors of the liver (colloid solutions, ^{99m}Tc labeled, etc., accumulating in Kupffer cells), of the kidneys (^{131}I-hyppurate, ^{99m}Tc-DMSA, etc. extracted from blood by tubular epithelium's cells), of the lungs (^{131}I-MAA — human serum albumin macroaggregates), of the thyroid (^{131}I as sodium iodide and ^{99m}Tc-pertechnetate). Spleen imaging is carried out by the red blood cells ^{99m}Tc labeled or ^{51}Cr (sodium chromate). These studies are a valuable addition to the methods of clinical X-ray and ultrasonic diagnostics.

One of the first tumorotropic agent applied for tumors diagnostics was ^{32}P. Radiophosphoric diagnostics was applied at all malignant tumors of different localization, when transducers usage, fixing beta-irradiation from the tumor, was technically possible. Radiometry of a hypothetical tumor and a symmetric healthy site of the tissue allow to determine quantitatively a degree of radionuclide accumulation.

Accumulation of over 150% of activity (in comparison with proved healthy site) is the most probably the evidence of a malignant process. As ^{32}P is a pure beta-emitter, it is possible to radiometricaly determine only superficially located tumors.

^{99m}Tc is suggested as the agent for positive scanning. The agent accumulates in the changed tumor vessels and retains in them longer than in vessels of normal surrounding tissues. The method is suitable for diagnostics only of those tumors with developed capillary net. Necessity of simultaneous positive scanning and selective angiography complicates procedure and deprives a radionuclide method of its basic advantages: simplicity and safety for the patient.

Recently diagnostic value of SPECT with ^{99m}Tc-sestamibi in visualization of a primary and recurrent cancer of the head and neck organs is proved. The results received by this method have been compared to the results received at operation and histology. Sensitivity has made up 100%. The disadvantages of SPECT are an ability of technitium to accumulate in the salivary glands, the mucous membrane of the nasal cavity and alveolar process. Nevertheless, comparison of radionuclide distribution in these anatomic structures and other healthy tissues allows to correct the diagnosis in all observations.

Diagnosis of brain tumors is based on disorders of hematoencephalic barrier and fixing in a tumor of many substances, potentially tumorotropic.

Brain metastases are the most dangerous complications and one of main causes of high death rate among oncological patients. Radionuclide methods of investigation provide high specificity in revealing tumor defeats. Technical opportunities of modern ways of radionuclide diagnostics and new radiopharmaceuticals allow to estimate condition of the brain and other organs during one investigation without additional introduction of radiodiagnostic substances. Now different technecium RPh are used as tumorotropic substances. For example ^{99m}Tc-sestamibi accumulates in tumors of the lungs, the thyroid, the parathyroid and breast glands. It is known that ^{99m}Tc (V)-DMSA is a tumor-seeking reagent, which is successfully used for detection of medullar cancer of the thyroid, soft tissue sarcomas, tumors of the head and neck, synovial giant-cell tumor, aggressive fibromatosis.

On the basis of observation of 79 children at the age from 7 to 16 years with *thyroid tumors* from the Chernobyl area, the complex of diagnostic tumor markers, which allow to estimate the efficiency of surgical and combined treatment, risk of relapse and metastasis, is developed. An optimum complex, by the authors' opinion, includes thyreoglobulin, cancer-embryonic antigen (CEA), ferritin, β-2-MG, CA-19-9 and thyrotropin. Scanning with the use of ^{99m}Tc-sestamibi at *parathyroid adenomas* in 80% of supervisions allows to localize a tumor precisely. This method helps surgeons to avoid the repeated operations.

A prognosis at *lung cancer* became substantially more accurate with appearance of new diagnostic methods. A high sensitiveness and economic substantiation of positron emission tomography with ^{18}F-fluordesoxyglucose was revealed in diagnostics of remote metastases and relapses of the disease.

SPECT with ^{99m}Tc-sestamibi allows to determine correctly the stage of disease with the non small-cell lung cancer.

The sensitiveness of osteoscintigraphy in diagnosis of *bone metastases of prostate cancer* makes 100%, specificity — 77%, exactness — 82%.

It is known that conventional mammography has low specificity in some patients (at increased density of tissues, anatomic breast distortions, after surgical or radiation treatment, in young women with small breasts, in the period of menopause, at hormonal therapy). With doubtful results of mammography, breast scintigraphy with ^{99m}Tc-technetril should be included in a diagnostic scheme.

Breast scintigraphy with ^{99m}Tc-sestamibi (99mTc-MIBI) is effective addition to mammography with increased density of mammary gland tissue.

Polypositional mammoscintigraphy (MSG) is registered in front right and left lateral and lateral projections, for 4 min each, in the matrix 128 × 128 mm, in 1 hr after the injection of 420–540 mBq of ^{99m}Tc-technetril. The inspections of a patient are conducted in lying on a stomach position so that the examined mammary gland without putting over the thorax, could hung down from the table of gamma-camera.

Polypositional planar MSG provides sensitivity at detection of primary node at T1 over 88%, and at the tumors T2 and larger — 95% at specificity more than 95%. Mammoscintigraphy with ^{99m}Tc-technetril can become an effective additional method for the primary detection and estimation of tumor process spreading, at the first time lymphogenic metastasis at breast cancer (BC).

On the whole, the value of radiological nuclear medicine of diagnosis of breast tumors consists in the fact that mammography possesses a high sensitivity at BC revealing, however, specificity of the method — 50%, in 10% cases of BC the formation is "mute". Mammoscintigraphy is not a screening method, it is expedient to apply at "suspicious" mammographic findings. The MSG sensitivity — 93%, specificity — 90%.

Positron emission tomography has a limited sensitivity at detection of tumors less than 1 cm, but allows to detect tumor formations in dense glands and tumor implants in silicon prosthetic appliances.

MSG results help to define treatment management at BC: to reveal sensitivity to the pre-operative chemotherapy, to determine resectability of a tumor, to decrease the sizes of the irradiation field, to control the post-operative course.

At the distance radiation therapy planning in BC patients usually, the irradiation field includes all the internal lymph nodes on the affected side. The developed technology allows excluding of intact parasternal internal lymph nodes from such irradiation field on the basis of scintigraphy with two markers as the pointed sources of ^{57}Co, which are set in typical anatomic sites. It is shown that in more than 70% of patients the most lateral internal lymph nodes were located at a distance less than 4 cm from the middle line of the sternum, and when they are not damaged, they are easily eliminated from the field of irradiation, allowing to reduce to the minimum the radiation loading on tissue of the lungs and the heart.

Great attention is presently paid to the exposure of sentinel lymph nodes by the radionuclide methods of study. A sentinel lymph node is the first barrier detaining metastases at lymphatic tumor spreading.

Conception of sentinel lymph nodes was formulated at study of skin melanoma and breast cancer, and was later spread to other solid tumors which at of ^{99m}Tc colloid agents peritumoral introduction get to sentinel lymph nodes and are detected by special portable devices. During operation the histological study of a sentinel lymph node is possible in order to answer the question about presence of metastases in it. So, by the methods of the sentinel lymph nodes detection it is possible to diagnose the presence of subclinical metastases at the I–II stage. Last years the methods of the sentinel lymph nodes detection are used with operations concerning cancer of the large intestine, neuroblastoma, minimum invasive adenoma of the parathyroid gland.

Condition of the lymph nodes is one of the basic prognostic factors in patients suffering from tongue cancer.

Lymphoscintigraphy (LSG) at skin melanoma allows not only to improve exactness of diagnostics but also to change treatment scheme of patients with a malignant melanoma in a number of cases.

Lymphoscintigraphy in a complex with intraoperational radiometry is a reliable mean of identification of sentinel lymph nodes, which allows executing the target biopsy of the lymph nodes and selecting patients for lymphadenectomy, avoiding unnecessary extended excision of the lymph nodes, reducing the death rate of patients suffering from melanoma in 89% cases.

Sparing operations are conducted at the early stages of melanoma with correct estimation of tumor spread by lymph ways. The integrated approach to surgical treatment includes pre-operative clarification of metastases presence in the lymph nodes, determination of amount and sites of drainage lymph nodes, intraoperative biopsy of drainage lymph nodes with careful histological exam. This scheme of approach to treatment is used at tumor thickness less than 1 mm, level of invasion more than III, at presence of ulcer, pronounced regression of tumor. During the operation (in 1–4 hrs after technecium injection) for the search of sentinel drainage lymph nodes methylene dark blue and hand gamma-detector are additionally used. "Suspicious" lymph nodes are excised for histological research. Selective biopsy of a sentinel lymph node is a high-informing method of metastatic spread at breast cancer diagnosis. Appearance of sentinel lymph nodes biopsy method in BC patients allows to avoid erroneous extended lymphoadenectomy. Unfortunately, a pre-operative chemotherapy can increase the number of false-negative results at revealing sentinel lymph nodes by the lymphoscintigraphy method.

Diagnosis of abdominal tumors — both organ and extra-organ — is difficult not only at the early stage of disease. Even at presence of palpated tumor it is difficult to determine its relation to the kidneys and estimation of the functional state of the latter.

The use of dynamic scintigraphy of the kidneys is effective with this pathology. This method is intended mainly for study of renal function and urinary ways condition. It can be used also at suspicion on the disorder of development and position of the kidneys. There is literature data about possibility of the use of dynamic scintigraphy method at presence of retroperitoneal tumors.

The use of this method in oncologic patients during last five years proved its information value not only for estimation of the functional condition of kidneys but also in determination of presence of retroperitoneal tumors, their localization, prevalence of the process and its relation to the kidneys.

The retroperitoneal tumors, both primary and metastatic — are revealed as sites of atypical uptake of the agent. The degree of accumulation of the agent is significantly lower than the renal one, but higher than the background. Most pronounced imaging of the tumor is determined during the vascular phase, although sometimes its image is saved till the end of study. Distribution of the agent within the limits of the image is even. In some cases distribution was uneven with the decline of agent accumulation in the center down to the level of the background. Yet rarer the tumors visualized as "cold" with the agent uptake lower than the background level. With kidneys affection the sizes of their image change, the defects of accumulation are determined, the function of this organ changes.

At defeat of lymphatic system the combined application of indirect radionuclide lymphography with small-disperse colloidal RPh is especially useful.

Diagnosis of primary and metastatic tumors of bones is realized with labeled osteotropic agents (^{99m}Tc labeled phosphates). ^{99m}Tc-MIBI is used for diagnosis of osteogenal sarcomas.

For diagnosis of pheochromocytomas it is used ^{131}I-methaiodobenzilisanidin, which appeared to be informative also at other tumors — for diagnosis of neuroblastoma, medullar thyroid cancer, retinoblastoma, melanoma, bronchocarcinoma.

One of perspective methods of diagnosis of tumors and metastases is radionuclide immunoscintigraphy with use of monoclonal antibodies.

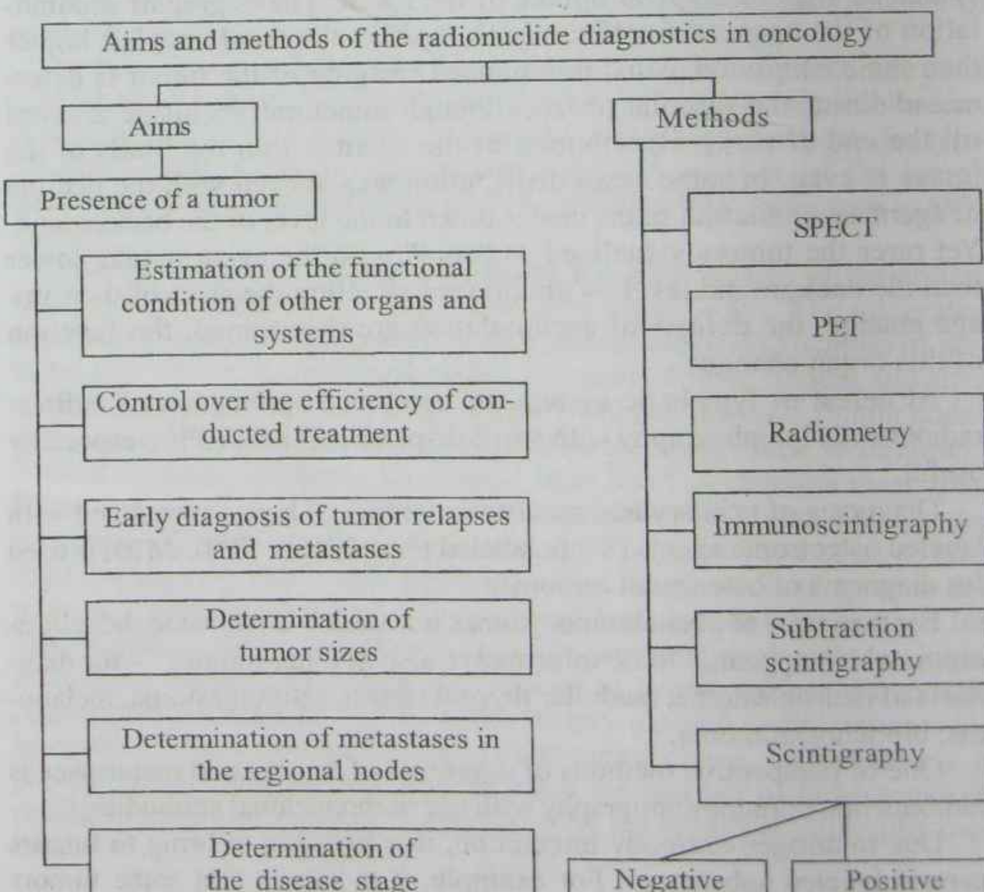
Due to antigen-antibody interaction, it is possible to bring to tumors certain labeled substances. For example, it is known that some tumors have increased contents of fibrinogen, therefore ^{131}I labeled antibodies to human fibrinogen can be used as an agent for scintigraphy. With the purpose to increase specificity of investigation, monoclonal antibodies are used as a label. This direction of radionuclide diagnostics in nuclear medicine has received the name radioimmune detection.

Use of standard radioimmunological sets enables to determine presence of CEA, alpha-fetoprotein and other tumor markers.

Key Concepts of the Theme

Tumorotropic radiopharmaceuticals, "hot foci", "cold foci", specific and non-specific tumorotropic agents; positive and negative scanning, SPECT, PET, radionuclide diagnostics of tumor diseases of various bodies and systems.

The Formalized Structure of the Theme Contents



Questions for Independent Work

1. What problems on the way of successful treatment of oncological patients can be solved by means of radionuclide methods of diagnostics?
2. Semiology of the diseases revealed by means of radionuclide diagnostics methods.
3. What radiopharmaceuticals are used for diagnosis of tumors of different organs and systems?
4. What tumorotropic radiopharmaceuticals can be referred to specific and nonspecific?
5. Positive and negative features of SPECT.
6. The essence of the method of diagnosis of space-occupying lesions of the brain.
7. The tumorotropic substances used for diagnosis of brain metastases.
8. What clinical cases need usage of radionuclide methods for addition to mammography?
9. What is the sentinel lymph node?
10. What method is the most sensitive among methods of radionuclide diagnostics?

Alternative-test Problems for Self-checking

1. Is it possible to use methods of radionuclide diagnostics for early detection of a tumor?
2. Is use of citrate-gallium effective for the control of conducted treatment?
3. Is the method of negative scanning absolutely reliable?
4. Is it possible to correct the diagnosis with SPECT application?
5. Is it possible by means of new radiopharmaceuticals to estimate the condition of the brain within a single study?
6. Is it possible to estimate efficiency of the surgical and combined treatment, risk of relapse and metastatic spread of thyroid tumors by means of a complex of diagnostic tumor markers?

Tasks and Problem Situations

1. Note the positive and negative features of investigation with gallium citrate-67.
2. Explain what determines RPh tumorotropism.
3. Determine the factors defining reliability of scanning in diagnosis of tumors.
4. What RPh is a tumor seeking reagent?

5. Is the following list of breast conditions exhaustive for ambiguous mammography results: increased density of tissue, anatomic distortion of the mammary gland?

6. Designate sphere of application of the sentinel lymph nodes concept?

Chapter 11
RADIONUCLIDE DIAGNOSTICS IN STOMATOLOGY

Radionuclide studies in stomatology are used for estimation of morphology and function of the salivary glands, their ducts at inflammatory, dystrophic, and tumor defeats. The main methods of radionuclide diagnostics of salivary gland diseases are scanning, radionuclide salivary gland imaging, salivary radiometry, scintigraphy of the salivary glands.

The basic function of the salivary glands — production and secretion of saliva to the oral cavity. Iodide analogue is usually used as RPh.

Reduction in ability of the salivary gland to concentrate radionuclide is characteristic for reduction of salivary glands function. The obstruction of the great salivary duct is reflected on the scan of the salivary glands in the form of a delay of radio-activity more proximal from obstruction. Scans of the salivary gland can show assimetry of the salivary gland caused by radiation damages. The most part of salivary gland tumors accumulate less pertechnetate than the surrounding normal tissue.

There is the following observation.

A woman (58 years old) 3 months ago has found a mass under the lower jaw on the right. The mass quickly enlarged and was painful. Edema of the face, loss of the body weight and cancer were absent in anamnesis. On scan of right parotid gland with ^{99m}Tc there was revealed focal reduction of absorption of tracks by the gland tissue. Function of the right parotid gland was normal. Presence of malignant tumor or local inflammation was suggested. After right-hand thyreoidectomy, mucoepidermal carcinoma was diagnosed.

Radionuclide salivary gland imaging is a method of radioisotope study of the salivary glands function which reflects concentration and secretory function of the salivary gland. The method consists in registration and measurement of radiation intensity above the parotid glands. ^{99m}Tc-pertechnetate is usually used as a RPh.

The curve obtained during radionuclide salivary gland imaging contains 3 segments: 1) the vascular segment — during 1 min fast lifting of the curve is observed, which reflects radionuclide delivery from blood to the gland; 2) absorptive segment — during 20–30 min strengthening of gland radioactivity is observed down to balance between delivery and excretion of the indicator; 3) a secretory segment — in 25–30 min after the beginning of investigation, excretion of radionuclide with saliva prevails over outflow from blood.

Increase in radionuclide accumulation in glands and a prolong period of its maximal accumulation is observed at the initial stage of chronic parotitis, and also xerostomia of I degree. Reduction of agent accumulation down to full gland dysfunction is observed at late stages of chronic defeat, as well as at xerostomia of II–III degree.

Scintigraphy of the salivary gland is carried out in 20 min after ^{99m}Tc-pertechnetate intravenous injection at the direct and both lateral projections. For a normal gland even radionuclide distribution in it and precise outlines of scintigraphic images are typical.

The enlargement of the salivary gland and irregular tracks distribution in it is observed at the initial stage of parotitis. However, in late stages of parotitis and xerostomy of the III degree the scintigram is impossible to be obtained because of low radionuclide accumulation in it.

The tumor of the salivary gland can be shown by focal defect in its image.

Change of topography of the salivary gland can be caused by a tumor originating from the next tissue.

Both pertechnetate and iodide concentrates in interlobular duct cells. Radionuclide tracks provide the functional information about the salivary glands which can be useful at such system diseases as sarcoidosis, rheumatoid arthritis, erythromatous system lupus and other collagen vascular diseases, which may lead to manifestation of the gland tissue infiltration syndrome.

Pertechnetate absorption decreases at focal bulging of the gland, usually caused by inflammation, cysts, abscesses or primary neoplasms. Lymphomatous cystoadenoma which concentrates the pertechnetate is benign and it is usually bilateral.

Visualization of the salivary gland can be successful at differentiation of diffuse inflammations caused by viral or bacterial infection, toxic substances, such as alcohol, or physical agents, such as radiation; in all these cases absorption of pertechnetate decreases, and gallium absorption increases, like in case with infiltration with system diseases, if plasmatic cells and lymphocytes infiltrate segments. 75% of patients with sarcoidosis are characterized by increase in gallium absorption, which decreases at treatment.

The diffuse swelling takes place at functional or mechanical obstruction of the main or numerous peripheral excretorial ducts.

At a syndrome of lymphocytes infiltration, arthritises (usual rheumatoid ones) dryness of the oral cavities and eyes as a result of salivary and lacrimal glands disease is often observed. Erythematous lupus, sclerodermia, nodular periarthritis, polymyositis, sarcoidosis, lymphoma or tuberculosis can cause also lymphoid infiltration.

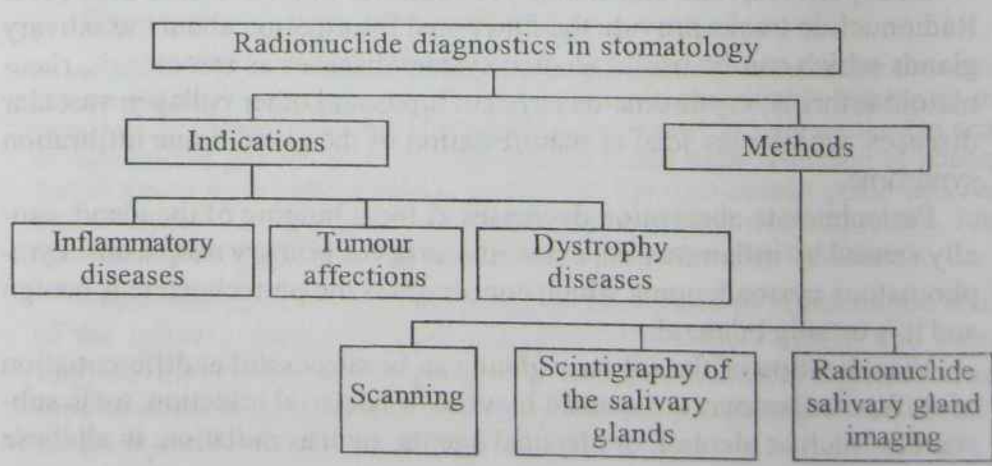
At the initial stage of inflammatory disease increased delivery of agent can cause hyperemia, but damage of channels decreased absorption. Contrast cialography and CT are more exact methods than nuclear investigations conducted for determination of anatomic abnormalities.

Duct obstruction is characterized by delay of radioactive pertechnetate after stimulation by citric acid.

Key Concepts of the Theme

Indications to radionuclide diagnostics in stomatology; methods of radionuclide diagnostics applied in stomatology; radionuclide semiotics of stomatologic diseases; radiopharmaceuticals used in stomatology.

The Formalized Structure of the Theme Contents



Questions for Independent Work

1. How does great glandular obstruction look like at the scan of the salivary glands?

2. How are initial and late stages of parotitis displayed on scan?

3. How does a tumor of the salivary glands look like at the scintigram?

4. At which diseases and by what means with the help of radionuclide diagnostics can one obtain information about the glandular tissue infiltration syndrome?

5. What can cause the gland topography change?

6. What reduces pertechnetate absorption?

7. What methods are preferable for stomatologic abnormalities determination?

Alternative-test Problems for Self-checking

1. Do you agree with the statement that reduction of salivary gland ability to concentrate radionuclide is characteristic for salivary gland function reduction?

2. Is the statement that the curve received at radionuclide salivary gland imaging has 2 segments true?

3. Is the list of diseases which can be found out by means of radionuclide methods complete: sarcoidosis, reumatoid arthritis?

Tasks and Problem Situations

1. Make the list of RPh necessary for needs of stomatologic patients.

2. Explain to the patient how long radiocialography will take?

3. Choose a method for determination anatomic anomality of salivary gland.

Chapter 12

PEDIATRIC PROBLEMS OF RADIONUCLIDE DIAGNOSTICS

Use of methods of radionuclide diagnostics in a pediatric practice has some distinctions caused by anatomic and physiological features of children's age. To guarantee proper results of radionuclide study in pediatrics, it is necessary to know variants of methods for adults.

Though main principles of gamma-scintigraphy concern both children and adults, but methods of study differ. So, the time necessary for each image is rather short and consequently the child can relax only for a short while between the periods of the image. It is important that the patient is as closer to the collimator surface as it possible. Small patients can be placed directly on the collimator closed by a thin plywood or a plastic sheet.

To receive a satisfactory γ-image, the child should be motionless during the study. For the child's immobilization they use hands, capacities with sand, etc. Sedatives are frequently used: oral introduction of chloralhydrate with slow beginning but long-term action: intravenous introduction of phenobarbital has quick start, but shorter duration.

The portion of radionuclide injected to the child should be individually determined and is reduced up to a practical minimum on the basis of calculation of a proportion: body weight of the child / body weight of the adult.

^{99m}Tc phosphate (diphosphate) is used for the bone image. The peculiar feature of a growing skeleton radionuclide image is increased concentration of radionuclide in zones of growth. To establish details of bones in small children, it is necessary to add the image with the high resolution. Computer processing and SPECT also help to make details precise.

Bone scintigraphy can not differentiate septic, rheumatic and traumatic arthritis since any process causing hyperemia has similar manifistation.

The sign of osteomyelitis is intensive central absorption of radionuclide on the site of the affected bone.

It is difficult enough to differentiate on scintigrams chronic osteomyelitis and osteomyelitis of traumatic origin. For this problem solution, application of the gallium-67 is recommended, intensive deposit of which is evidence of infection.

Necrosis of the bone in children at Perthes' disease is possible to diagnose before the radiographic signs appear.

Bone infarcts in children are most often associated with sickle-cell hemoglobinopathies, steroid therapy. It is impossible to distinguish bone infarct osteomyelitis basing only on the radionuclide study since inflammation can develop at the site of bone infarct existed before. Bone infarct is identified by the use of ^{99m}Tc-colloid sulfur, gallium-67 or leukocytes labeled by gallium-67.

Bones scintigraphy reveals the radiographically invisible fractures in children. Any scintigraphical study of the trauma is recommended to include lower extremities entirely since fractures often involve some sites. The scintigraphical image of the bone can be used also for estimation of trauma complications, orthopedic procedures, identification of pseudoarthrosis, artificial limbs, at comparison of the femoral epiphyses' heads which slid off.

Osteosarcoma and Ewing's sarcoma usually increase concentration of radionuclide like in osteomyelitis, osteoid osteomas and traumatic cysts of bones.

The raised or normal activity can testify to malignant process, for example, metastatic neuroblastoma and hysteocytosis.

Lytic damages of bones are not practically diagnosed by the help of radionuclide methods. Osteoid osteomas, osteoblastomas, chondroblastomas are revealed by locally increased activity of radionuclide.

Radionuclide investigation is extremely important in children suffering from pain in bones or lameness if the damage cannot be revealed radiographically.

The increased intensity in growth plate activity is revealed in children suffering from rickets.

In pediatric practice the methods of radionuclide diagnostics are now wide spread in urological and nephrological clinic. Non-traumatic studies for children, a relative simplicity of execution in a combination with high informative value of received results were the reasons for inclusion of these methods in an obligatory complex of modern inspection in uronephrology of children's age.

At healthy children of elder age the renographical curve is characterized by the following time parameters: the vascular site lasts for 10–40 sec, secretory — 1–3 min and excretory — from 4 to 20 min. The difference within the limits of no more than 1 min of the left and right kidneys parameters is quite possible for the conclusion about a normal condition of filtration-excretion process in a given patient. The degree of radiation dose on the child at this investigation as much as 10–100 times lower than at urography and even more — at roentgenoangiography. Negative results of radionuclide study are more authentic and allow to exclude renal diseases and to prevent application of roentgenological studies which have greater radiation loading. Some authors consider that X-ray study of the child with suspicion on uronephrological disease should start with radionuclide study. Radionuclide study can be used for the control over the quality of conducted treatment. The estimation of efficiency of medical measures first of all depends on the affected system functions restoration which is more reliably confirmed by the method of radionuclide study.

The majority of renal agents are selected according to their physiological properties. Renal function and the collecting system status can be estimated by agents which are filtered by glomerules, such as radiographic contrast media (^{99m}Tc-DTPA) or secreted by renal glomerules iodide-131 (^{131}I), ^{99m}Tc mercaptoacetyltriglycine (MAG3). The agent which binds in the cortex is used to estimate functioning renal parenchyma — ^{99m}Tc-DMSA.

The estimation of renal condition consists of two parts: renal morphology is estimated by ultrasound and renal function — during the radionuclide study. Both congenital and acquired conditions are characterized by reduction of renal function; radionuclide investigation surpasses excretory urography by informative value. During a newborn period this combined technique of display is excellent in an estimation of cysts dysplastic conditions, obstructive nephropathy and renovasal infringements.

The enlarged kidney filled with liquid looks like an area free of photon on scintigraphical at the images received soon after an injection. The next image can be obtained after an injection within 24 o'clock. At obstructive conditions there is a gradual accumulation of an isotope, usually, within two hours.

Multicystic kidneys do not reveal early dysfunctions. However, weak accumulation of radionuclide within the limits of the kidney can be observed in 24 hours. The renal venous thrombosis (unilateral or bilateral), most often comes to an end by reduced perfusion and filtration without derangement of activity in the collective tubules system. The perfusion and the mentioned function are absent or noticeably reduced in the patients with renal arterial obstruction and renal cortical necrosis. Peripheral defects can lead to embolism again.

Greater intrarenal masses are found out with sonography, but small masses can be found out as a nonfunctioning tissue with radionuclide deposition defect. The nature of the defect (a tumor, cyst, abscess) is not determined by the radionuclide method.

Scintigraphy with the cortical agent of ^{99m}Tc DMSA is a sensitive method for detection of renal parenchyma condition abnormalities. Cortical agents can be useful also in detection of congenital morphological abnormalities (horseshoe kidney).

Cortical agents provide sensitive and specific damage of renal parenchyma with acute pyelonephritis. A typical defect is found out in acute stage of infection: a sphenoidal reduction of absorption spreading usually from the central area up to periphery. The defects, detected at the acute stage of infection, are partially or completely removed after antibiotic treatment. SPECT can make scintigraphy more precise with detection and analysis of parenchymatous defects. Scarring is the reason for defects which preserve for a long time. At the height of infection or when the mentioned defects are unproved to be present before, acute pyelonephritis can be confirmed by the image with labeled leukocytes or ^{67}Ga.

In estimation of vesicoureter reflux and quantitative determination of urinary bladder function the radionuclide cystography is rather sensitive. For the first time cystogram of the boy is carried out radiographically to determine urethral anatomy. Both initial, and subsequent studies are carried out with radionuclides in girls.

The vesicouretral reflux can cause damage of renal parenchyma. The reflux of infected urine gives risk of scarring.

Radioisotopes play an important role in postsurgical estimation of transplanted kidneys. Frequency and type of radionuclide investigation depend on a clinical situation. Investigations are carried out more often in the post-operational period to be convinced that blood supply and drainage are not damaged.

Radionuclide study of the liver and the spleen in children began to develop with low-radiotoxic RPh introduction into the pediatric practice. Congenital anomalies of the liver and the spleen (alongside with defects in other organs and systems) are mostly met in the pediatric practice. Hepatic cirrhosis can be found in children caused by hepatitis, cystic fibrosis.

The severe form of jaundice takes place in newborns. Congenital biliary atresia and severe hepatocellular disease of different origin are differentiated usually. In these cases the slow hepatic transit of labeled Tc-compounds (with a half-life period of 6 hrs) at severe hepatic diseases with transit time about 168 hrs takes place. Absence of visualization of the gall bladder and large intestine find even after 24 hrs at patients with biliary atresia. At newborn hepatitis absorption can turn out to be normal or accelerated.

At newborns it is difficult to differentiate jaundice because of hepatocellular disease and congenital anatomic anomaly of a bile tree. Numerous disorders in infant age can cause severe cholestasis which it is impossible to differentiate from biliary atresia by clinical methods or ultrasonography. IDA ^{99m}Tc-agents provide the most exact method of estimation of biliary tracts condition in newborns. These agents are also used after operation. Hepatobiliary drugs are excreted by the liver to the bile-excreting system, with a subsequent output to the gestrointestinal tract. With hepatocellular disease, intrahepatic cholestasis and/or biliary obstruction urinaty tract provides an additional way of excretion. In a usual clinical situation an icteric newborn has significant hepatocellular dysfunction, renal excretion of radionuclide is increased. Serial images in patients with sever intrahepatic cholestasis show activity in the gastrointestinal tract sometimes in 20–24 hrs while at biliary atresia there is no visualization of the gall bladder or intestine. At serious cholestasis even in at presence of anatomically intact biliary system, the gall bladder and/or gastrointestinal activity cannot be identified.

Use of IDA ^{99m}Tc derivatives in infants is high sensitive but lower specific (85–95% accuracy).

^{99m}Tc-pertechnetate allows finding out the displaced gastric mucous membrane in children (for example, Meckel's diverticulum and Barrett's esophagus.

The gastrooesophageal reflux in children is connected with a set of clinical problems (allergy, asthma, dyspnoea). At first a patient is given a drink of barium with the next X-ray exam. However, the scintigraphic method is more sensitive. Interpretation of reflux studies includes identification of frequency and degree of the reflux and detection of pulmonary aspiration. False-positive diagnosis of pulmonary aspiration is sometimes caused by dirty skin or clothes.

In children's pulmonology the radionuclide diagnostics is expedient and concurrent with X-ray method only with two diseases: at congenital vascular hypoplasia of lungs and thromboembolism.

At radionuclide investigation of lungs in children in the gamma-cameras by means of ^{133}Xe it is not always possible to receive the image of lungs in the deep inhalation and exhalation phase with visualization of decreased ventilation departments since the children can not execute respiratory acts properly.

The scan of a perfused lung in patients with congenital heart diseases show nonsegmental irregular defects spread along both lungs. Redistribution of perfusion leads to rather increased activity in the upper lobes, and pleural exudate can be a reason of a "crack" — a site of reduced activity between two lobes of the lung. Corresponding radiographic findings usually concern determination of vessels, lines of partitions and other signs of interstitial pulmonary hypostasis. In some patients the congenital heart disease is accompanied by emphysema or chronic bronchitis that is the reason of ventilating abnormalities. At congenital heart diseases perfusion defects can preserve some days long after disappearance of radiographic abnormalities.

The accent in pediatric nuclear cardiology is put on diagnostics of congenital heart anomalies and efficacy of operation. Ischemic heart disease is met in children seldom and is connected with congenital anomalies of coronary arteries and acquired conditions like Kawasaki's syndrome and cardiomyopathy.

Application of radionuclide study of the brain in children allows identifying vascular pathology, inflammatory changes, attacks. Brain radionuclide angiogram with the use of ^{99m}Tc-pertechnetate (DTPA) is used for determination of brain death. Vascular deviations at children can be secondary after hypoxia, asphyxia and vascular thrombosis. During some viral inflammatory processes, such as herpes, meningoencephalitis, etc. the radionuclide image can reveal defects before CT or MRI.

A sensitive method for detection of brain vascular infringements was created on the basis of new brain RPh, which get through the hematoencephalic barrier.

The cysternography with ^{99m}Tc, DTPA or with ^{111}In-DTPA can be executed in children.

Radionuclide studies at thyroid diseases are the most-effective in comparison with other techniques and provide a full and authentic diagnosis.

Children suffer often from congenital hypothyrosis. Clinical picture of this disease is diverse; therefore its diagnostics is not always timely. Rather early diagnostics takes place no more than in 50% of cases. At congenital hypothyrosis the diagnosis is established quite often at the age of 1–2 years and later. Often the patients go to the pediatrist with other diseases: rickets, Down's disease, anemia, etc.

There are distinguished 4 forms of hypothyrosis: primary, secondary, tertiary and iodide-deficient. At *primary* hypothyrosis disorders of hormone formation takes place in the thyroid gland itself. At *secondary* hypothyrosis — synthesis of thyrotropic hormone of the hypophysis is broken. *Tertiary* hypothyrosis is caused by hypothalamus dysfunction and TTH secretion decreasing. *Hypothyrosis caused by iodide deficiency* takes place at Hashimoto's disease or thyroid damage.

The diffuse toxic goiter in children arises in pre- and pubertal period. Duly diagnostics is usually late. Quite often children suffering from thyrotoxicosis because of the wrong diagnosis are followed up for several months and even years by the rheumatologists, the neuropsychiatrist, but not by the endocrinologist.

At present diagnosis of thyroid diseases is carried out by radionuclide methods *in vitro,* which have a number of great advantages over other known diagnostic tests, as they exclude X-ray influence on an investigated organism; reflect homeostasis of the internal medium of an organism with high sensitivity; can be used without any restrictions with the diagnostic purpose repeatedly and during dynamic supervision; execution is technically simple. TTH/TRH-test is used for diagnosis of functional condition of the thyroid gland in children with suspected hypothyrosis. Synthetic TRH agent which is injected on an empty stomach intravenously in amount 100–200 µg is used in this test. The blood sampling from the vein is conducted directly before and 30 min after TRH introduction. Serum concentration of thyrotropic hormone of hypophysis is measured in two tests. TTG determination is based on the radioimmune test. Division of free and bound with antibodies hormones occurs with the use of the double antibodies principle (replacement of radioactive one by a non-radioactive one.

Radionuclide visualization of the thyroid gland at children is carried out in 20 min – 1 hr after intravenous introduction of ^{99m}Tc-pertechnetate. The technique of scintigraphy in the gamma-camera is simple; However, it demands immobility of the child's body during 20–30 min, which is difficult for little children.

Scintigraphy at children is indicated only in case of suspected remote metastases of the thyroid cancer. Radioactive iodine in amount of 37–111 mBq is injected. Investigation of the entire body is carried out in 2 days. At presence of distant metastases of the thyroid cancer, metastatic tumors of the lungs and bones as a result of intensive accumulation of iodine are well visualized on scintigrams.

Congenital hypothyrosis. Insufficiency of the thyroid function in a newborn leads to disorders of the subsequent hormonal development of a person. Clinical signs depend on extent of thyroid damage. Now it is known that even subclinical forms of hypothyrosis cause multiglandular and metabolic disorders, influence psychomotor development and formation of reproductive function of a person. Low intellect, emotional slackness, decrease in working capacity, infertility quite often are consequences of congenital dysfunction of the thyroid gland which has not been diagnosed in time and in this connection children were not cured. If treatment of hypothyrosis begins in due time since the neonatal period, severe psychoneurological and somatic infringements of child's development can be prevented. At the same time, as statistical analysis proved, hypothyrosis can be revealed on the basis of clinical symptoms probably not earlier than the 3rd month of life, i.e. at terms when irreversible changes in the central nervous system, leading to intellectual growth and development disorders down to the profound mental retardation take place.

Clinical signs of hypothyrosis within first 3 months of life are low-specific.

Two forms of hypothyrosis by etiologic sign are distinguished now:

1. Primary hypothyrosis — intra-uterine underdevelopment of the thyroid gland. This form is the most widespread (is observed at the rate of 1:3000, 1:4000). Hypoplasia or aplasia, or its ectopic location of the thyroid, more often hypoglossal are diagnosed. Congenital hypothyrosis can be observed with normal anatomic location of the thyroid gland, but with deranged synthesis of thyroid hormones as a result of genetic defect of the enzyme system. In these cases quite often there is a congenital goiter.

2. Secondary hypothyrosis develops as consequence of congenital insufficiency of hypothalamic-hypophysial system and is met much less often than primary hypothyrosis 1 : 20,000.

Hormonal diagnosis of hypothyrosis includes complex determination of contents in blood of thyroxin (T_4), triiodthyronine (T_3), thyrotropic hormone (TTH) thyroxin-binding globulin (TBG).

Leading diagnostic parameters of thyroid function are T_4 and TTH levels. Optimum terms for diagnosis of hypothyrosis are the 3rd–5th day of life as contents of hormones in the umbilical blood within first days of life does not reflect true condition of thyroid functions in the newborn. At primary hypothyrosis T_4 level is lowered, and TTH — is considerably raised, i. e. there is an inversely proportional dependence between TTH secretion and degree of T_4 decrease.

The secondary hypothyrosis is characterized by decrease in T_4 at absence of TTH raised secretion.

On the basis of conducted hormonal studies the prognosis and pathogenetic therapy are determined. In future during treatment dynamic supervision over the level of thyroid hormones takes place, which allows estimating efficiency of conducted therapy. The conducted studies by the RIA method in prematurely born children revealed significant decrease in thyroid hormones level not only at birth but also within the next 3–4 weeks of life especially responsible for formation of the central nervous system.

In pathogenesis of this condition it is possible to determine 4 leading reasons:

1) primary decrease in the thyroid gland function;

2) decrease in functional activity of the hypophysial-thyroid system as a whole;

3) dyshormonogenesis;

4) low level of TTH.

Such transitory character of changes of hormonal levels in premature newborns, nevertheless, is necessary for estimating as a pathological condition influencing adaptable mechanisms of postnatal development, metabolism decrease and leading to retardation of CNS development, which may cause developmental lagging in subsequent periods of life.

Considering great social importance of early treatment of congenital hypothyrosis to prevent mental retardation, radioimmunological tests are developed for determination of thyroid function in newborns as a part of the social program of mass examination of all newborns. For investigation, a blood drop is taken from a newborn's heel and is put on a filtering paper.

The radioimmune method is used to determine the contents of general and free T_4, general and free T_3, TBH in blood, thyrotropin and thyreoliberin level is established. Thyrotropin is the hormone of the anterior lobe of the hypophysis which at emission in blood strengthens function of the thyroid gland and is accompanied by increased T_4 and T_3 concentration. These hormones stimulate thyroliberin secretion, which, in turn, strengthens thyrotropic function of the hypophysis.

Thyroglobulin is the basic component of follicles colloid of the thyroid gland (in the norm 7–60 μg). Concentration of thyroglobulin increases at thyroiditis, toxic adenoma, diffuse toxic goiter and especially at thyroid cancer and at its metastases in other organs.

In the norm T_4 70–150 nmol/l, T_3 — 1.3–9.5 nmol/l. Rise of T_4 and T_3 is typical for hyperthyrosis, fall — for hypothyrosis. Important value has calculation of the rate of general thyroxin to TBH. Decrease in the latter is observed at renal diseases. Parameter T_4 (TBH) allows to differentiate precisely eu-, hypo- and hyperthyroid conditions.

Key Concepts of the Theme

Peculiarities of performance of radionuclide diagnostics methods at children; the field of radionuclide diagnostics use at diseases of different organs in children; radiopharmaceuticals used in pediatric practice.

The Formalized Structure of the Theme Contents

The field of radionuclide diagnostics use in pediatric practice

The bone system	Osteomyelitis Arthrites Osteonecrosis at the Pertes' disease Infarct of the bone at sickle-cell hemoglobinopathies Fractures Rachitis Tumors
The urinonephrologic system	Obstructive nephropathies Renovasal disturbances Polycystic disease Renal venous thrombosis Vesicourethral reflux Renal transplantation
The liver, the spleen, the gastrointestinal tract	Hepatic cirrhosis Jaundice of newborns Congenital hepatitis Cytomegalovirus infection Splenomegaly Functional aspleny Meckel's diverticulum Gastrointestinal bleeding Gastroesophageal reflux
The lungs	Congenital hyperplasia of pulmonary vessels Thomboembolism
The cardiovascular system	Congenital heart defects Kawasaki's syndrome Cardiomyopathy
The thyroid gland	Hypothyrosis
The central nervous system	Vascular pathology Inflammatory changes Brain death

Questions for Independent Work

1. Under what conditions can one obtain a satisfactory gamma-image in children?

2. Peculiarities of radionuclide image of bones in children.

3. Radionuclide semiotics of bone diseases in children.

4. What diseases of bones cannot be differentiated by means of radionuclide methods?

5. Time parameters of renographic curve in elder children.

6. Radiopharmaceuticals used in renal transplantology.

7. At what diseases can functional splenomegaly be observed?

Alternative-test Tasks for Self-checking

1. Is the method of radionuclide diagnostics is competitive with the X-ray method at congenital hypoplasia of pulmonary vessels in children?

2. Is the method of radionuclide diagnostics of thromboembolism in children competitive with the X-ray method?

3. Are there advantages *in vitro* diagnostics at revealing diseases of the thyroid gland?

4. Can bone scintigraphy differentiate septic, rheumatic and traumatic arthritides?

5. Whether it is possible to distinguish bone infarcts and osteomyelitis by means of radionuclide methods?

6. Is it possible to find out typical damages of bones by means of radionuclide methods?

Tasks and Problem Situations

1. Choose RPh which will help you to differentiate chronic osteomyelitis from osteomyelitis caused by a trauma.

2. Are all the bone tumors revealing local increased activity of radionuclide listed below: osteoid osteomas, osteoblastomas?

3. Which method of the listed below should be chosen, taking into account the radiation dose: radionuclide study, urography, roentgenography?

4. Which of the following methods — CT, MRI, radionuclide diagnostics — is more preferable at diagnosis of viral diseases like herpes?

5. Which RPh are necessary for performance of cisternography in children?

6. Can ^{131}I be applied in a children's practice? If yes, name the clinical cases of its usage.

ABBREVIATIONS

AFP — α-fetoprotein
BSA — biological substances analyses
CEA — cancer embrionic antigen
ChGTH — chorionic gonadotropic hormone
CS — cerebral scintigraphy
CT — computer tomography
ECG — electrocardiography
EEG — electroencephalography
FDG — fluorodeoxyglucose
HSA — human serum antibodies
HVL — half-value layer
LSG — lymphoscintigraphy
LTE — linear transfer of energy
MRI — magnetic resonance imaging
MSG — mammoscintigraphy
PEP — pulmonary epithelium penetrance
PET — positron emission tomography
PSA — prostatic specific antigen
RCA — radionuclide cerebral angiography
RCMG — radionuclide cysternomyelography
RIA — radiommunologic analysis
RPh — radiopharmaceutical drug
RRA — radioreceptor analysis
SPECT — single photon emission tomography
TBH — thyroxinbinding hormone
TG — thyroid gland
TGA — thyreoglobulin antibodies
TPET — two-proton emission tomography
TTH — thyrotropic hormone
US — ultrasonography

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The manual gives a short sketch of history of radionuclide diagnostics and the contribution of the Ukrainian scientists to its development. The main principles and methods of radionuclide study are described. The most important question of radioactive safety and private questions of radionuclide diagnostics are provided in the book.

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