

jnm / ABSTRACTS OF CURRENT LITERATURE

Isotope Cisternography and Ventriculography in the Diagnosis of Hydrocephalus. M. K. Hammock, Thomas H. Milhorat, and Donald A. Davis. *Dev Med Child Neurol* 16:58, 1974.

The authors present a concise but in depth discussion of the circulation of cerebrospinal fluid (CSF). Their discussion of CSF absorption in hydrocephalus is valuable reading. They describe the cisternographic findings in several patients with communicating hydrocephalus including one with a "double-density" pattern of the lateral ventricles. They interpret this binding as indicative of radiotracer migration into the brain surrounding the ventricles. In discussing noncommunicating hydrocephalus they point out that the radiopharmaceutical may or may not migrate over the cerebral hemispheres after introduction in the lumbar intrathecal space. The basis for obstruction to flow over the hemispheres is mechanical because of ventricular system enlargement. In seven patients with obstructive hydrocephalus secondary to a block of the aqueduct, isotope ventriculography demonstrated a complete obstruction in only one but ventriculography indicated complete obstruction in all seven. The original article and list of references are excellent.

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Evaluation of a Computerized Technique for Determination of Cardiac Output and Central Circulation Times Using Gamma Camera and ^{125m}Indium. D. Falch and N. Norman. *Scand J Clin Lab Invest* 34:207-214, 1974.

The authors describe a method for quantitative radiocardiography that uses a scintillation camera, multichannel analyzer, computer, and magnetic tape recorder. Indium-113m-labeled transferrin (a pure gamma emitter with an energy of 392 keV and half-life of 99.5 min) was used as the intravascular tracer. The cardiac output was determined simultaneously by radiocardiography and by an ordinary indicator dilution technique based on continuous sampling of arterial blood. The coefficient of correlation between the results of the two methods was 0.96. The mean pulmonary circulation time was selectively determined. In 14 healthy subjects, the time was 4.90 sec (s.d., 0.84) which represented 75.8% of the interventricular circulation time. The mean pulmonary blood volume in the 14 subjects was 297 ml/m² (s.d., 38) and the mean pulmonary plasma volume 179 ml/m² (s.d., 21), or 11.1% (s.d., 1.7) of the total plasma volume. The authors state that the method is rapidly performed without stress to the patient, can be repeated at frequent intervals, and gives reliable information about cardiac function and pulmonary circulation.

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Monitoring Induction of Ovulation with Human Menopausal Gonadotropin by a Rapid Estrogen Radioimmunoassay. Donald R. Tredway, Uwe Goebelsmann, Ian H. Thorneycroft, and Daniel Mishell, Jr. *Am J Obstet Gynecol* 120:1035-1039, 1974.

Fourteen anovulatory but otherwise healthy women aged 21-34 were treated with 43 human menopausal gonadotropin (HMG) treatment cycles. These women had been unsuccessfully treated with clomiphene therapy. HMG stimulates follicular growth and in the presence of human chorionic gonadotropin (HCG) induces ovulation and pregnancy in women who have functioning ovaries. Ovarian hyperstimulation, however, can result from HMG treatment producing bilateral cystic ovarian enlargement, ascites, and hemoconcentration. For this reason it is necessary to titrate carefully the HMG dosage according to the patient's estrogen response.

HMG was administered daily and estrogen levels measured by fluorometric determination of total urinary estrogens, by radioimmunoassay (RIA) of serum estradiol, or by a rapid 4-hr RIA of immunoreactive serum estrogen. There was correlation of the results from the three methods. The RIA of immunoreactive serum estrogen was as accurate for the determination of follicular growth as the other two methods. Since it was more easily performed, it appeared to be the preferable means for adjusting HMG therapy. By means of the above quantitative procedures, ovulation was induced in 38 of the 43 treatment cycles. Seven of the 14 patients became pregnant. Ovarian hyperstimulation occurred in five treatment cycles.

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Radioreceptorassay of Human Chorionic Gonadotropin as an Aid in Miniabortion. Robert Landesman and Brig B. Saxena. *Fertil Steril* 25:1022-1029, 1974.

Miniabortion (menstrual extraction) has proven to be a successful procedure when performed in the early stages of pregnancy. Since tests for early pregnancy may not be reliable in all cases, miniabortion is often performed on women who are nongravid, which causes physical trauma and psychic stress. The authors have used an extremely sensitive radioreceptor assay of human chorionic gonadotropin (HCG) for the determination of pregnancy. The procedure entailed labeling highly purified preparations of HCG with ¹²⁵I. Plasma membranes containing a specific receptor for HCG were prepared from bovine corpora lutea in the first trimester of pregnancy.

Blood samples were drawn from women who were possible candidates for miniabortion and plasma or serum was separated for radioreceptor assay. Agglutination tests were performed on morning urine samples (Pregnosticon Dri-Dot, Organon, West Orange, N.J.). The radioreceptor assay was found to be more accurate than the hemagglutination test for the detection of pregnancy in normal women, in questionable ectopic pregnancies, and in spontaneous abortions. The radioreceptor assay requires only 1 hr to perform and detects pregnancy as early as 6-8 days after ovulation. Since the most propitious time to perform miniabortion is approximately 9-13 days after the first missed menses, reliable early detection of pregnancy is essential.

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The Use of a Radioimmunoassay Specific for Human Chorionic Gonadotropin in Patients with Molar Pregnancy and Gestational Trophoblastic Disease. Gregory B. Pastoride, Donald P. Goldstein, and Thomas S. Kosasa. *Am J Obstet Gynecol* 120:1025-1028, 1974.

The clinical course of 14 women under treatment for gestational trophoblastic disease (GTD) or molar pregnancy was evaluated by means of radioimmunoassay (RIA). A solid-phase RIA and HCG-LH was compared with a RIA that was specific for the beta subunit (BSU) of HCG. The measurement of HCG levels in serum or urine is a reliable index of the amount of viable trophoblastic tissue present. When there is a complete absence of HCG activity, the patient is considered to be in remission.

The solid-phase RIA procedure was a 6-hr modification of an immunoabsorbent method that could detect 5 mU/ml HCG and 2 mU/ml of LH. The BSU RIA was sensitive to 1.25 mU/ml with occasional false-positive results, up to 8 mU/ml. In the cases studied, the BSU RIA detected HCG activity in serum from 8 to 62 days longer than did the solid-phase RIA. This difference was attributed to the lack of specificity of the solid-phase RIA, which detects LH along with HCG, thus masking the presence of the HCG secreted by viable trophoblastic cells. In treating patients with molar pregnancy and GTD, it is essential to have a dependable, sensitive, precise, and specific method to monitor HCG levels since therapy continues as long as HCG levels are detectable.

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Use of Radioimmuno-electro-Osmophoresis for the Diagnosis of Human Trichinosis. T. H. Dzbenski, W. S. Plonka, and Bozena Jedzejewska. *Experientia* 30:1269, 1974.

The authors describe a highly sensitive method for the detection of *Trichinella spiralis* infection in man by means of radioimmuno-electro-osmophoresis (RIEOP) of patients' sera. For this procedure, the antigen was derived from muscle larvae and labeled with ^{125}I . Immune sera were obtained from persons suspected of having had a recent infection with *T. spiralis* and the presence of antibodies was determined by immunofluorescent antibody (IFA) and indirect hemagglutination (IHA) tests.

RIEOP was performed on glass photographic plates covered with agarose in barbital buffer. Antigen was placed in the cathodal wells and undiluted sera in the anodal wells. After 2 hr of electrophoresis in a barbital medium, the plates were photographed, washed for 24 hr in several changes of saline and water, and then dried. The plates were placed in contact with medical x-ray film and kept in a light-tight box for 2, 4, and 7 days. After film exposure the plates were stained with amido black and again photographed.

In a study to detect anti-*T. spiralis* antibody in seven subjects, the RIEOP procedure was found to be more sensitive than IFA, IHA, double diffusion agar gel, or counterelectrophoretic methods. Unequivocal precipitation lines were visible on RIEOP plates but were lacking on the next most sensitive counterelectrophoresis plates. Unfortunately the precipitation lines in RIEOP were not clearly defined until the 7th day of film exposure. In contrast, the counterelectrophoresis method was completed within 1-2 hr. Counterelectrophoresis remains most suitable for rapid and large scale

screening and RIEOP is valuable in selected cases where sensitivity and specificity are important.

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Abnormalities in Skeletal Uptake of $^{99\text{m}}\text{Tc}$ Polyphosphate Complexes in Areas of Bone Associated with Tissues which Have Been Subjected to Radiation Therapy. P. H. Cox. *Br J Radiol* 47:851, 1974.

Castronovo, et al (*J Nucl Med* 14:604, 1973) have reported reduced uptake of $^{99\text{m}}\text{Tc}$ -polyphosphate in bone lesions following radiation therapy to these lesions. In this work reduced uptake of $^{99\text{m}}\text{Tc}$ -polyphosphate and regions of diffuse activity were found in areas of normal bone that had been exposed to radiation because of their proximity to tissues subjected to radiation therapy. In some cases regions bordering the irradiated bone showed increased uptake resulting in false-positive scans. There was no evidence of skeletal abnormalities in the irradiated regions except that observed on the scintigrams.

It is postulated that the abnormalities seen in normal bone are related to long-term radiation effects on bone physiology. Reduced skeletal uptake probably reflects a decrease in bone marrow uptake, due to reduced phagocytic activity, coupled with a decreased bone uptake, which may reflect reduced blood flow caused by degenerative changes in the blood vessels in the irradiated area. The diffuse areas of increased activity observed in some cases may result from $^{99\text{m}}\text{Tc}$ uptake in irradiated cells due to increased cell wall permeability.

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In Vivo ^{75}Se Binding to Human Plasma Proteins after Administration of $^{75}\text{SeO}_3^-$ (BBA 27535). R. F. Burk. *Biochim Biophys Acta* 372:255, 1974.

Four adult patients with a histologic diagnosis of cancer received 200-250 μCi of $^{75}\text{SeO}_3^-$ (1.25 mg selenium) as a single intravenous administration. During the first hour after injection the ^{75}Se disappeared rapidly from the plasma, but between 1 and 6 hr a large amount of the ^{75}Se returned to plasma bound to protein. Very low density and low density lipoproteins bound up to 16% of the ^{75}Se as early as 3 min after injection, and very little ^{75}Se was found bound to high density lipoproteins. Subsequently very low density lipoprotein ^{75}Se activity declined extremely rapidly, while low density lipoprotein ^{75}Se activity fell more slowly.

Denaturation of the lipoproteins with 8 M urea, treatment with 0.5 M μCi of $^{75}\text{SeO}_3^-$, or treatment with 0.5 M mercaptoethanol elicited removal of the ^{75}Se . In plasma collected 48 hr after injection, it was found that these procedures removed very little of the ^{75}Se . These results indicated that the binding of selenium to lipoproteins was different from the binding to other plasma proteins.

This study suggested that in human beings plasma selenium reacts with proteins in a manner similar to that found in the rat. Immediately following injection selenium is free or in loose association with many proteins. Selenium is then removed from plasma and is later returned bound to specific proteins.

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The Angiographic and Brain Scan Findings in Acute Non-Herpetic Encephalitis. F. H. W. Pexman, W. E. McFeely, and M. V. Salmon. *Br J Radiol* 47:862-868, 1974.

Based on brain biopsies, serology, and cerebrospinal fluid findings, 12 patients were selected for this study from a group of patients with the clinical diagnosis of encephalitis and meningoencephalitis. All 12 patients had a bilateral or a unilateral carotid angiogram and 5 were examined with ^{99m}Tc -pertechnetate brain scans. The carotid angiograms demonstrated a variety of findings including midline shift, local persistence of arterial phase, local hypervascularity or blush, early venous drainage, and multiple sites. There was no consistent pattern of the findings; they were randomly distributed among the patients. Of the five patients who received radionuclide examinations one patient demonstrated equivocal results and the other four were normal. The electroencephalograms on all of the patients were nonspecific. The importance of the findings from this study was the correlation of contrast angiograms and brain scans between acute Herpes simplex encephalitis and acute nonherpetic encephalitis. The authors felt that it was unlikely that these two types of encephalitis would be confused after a combination of carotid angiography and brain scanning had been performed.

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RISA (^{131}I) Scanning of Cerebrospinal Fluid Pathways in Children with Myelomeningocele. P. Upadhyaya, H. L. Goswamy, M. Rohatgi, A. K. Basu, and M. A. P. Rao. *Develop Med Child Neurol* 16:144, 1974.

The purpose of this investigation was to provide a complete profile of the pathways in case of altered cerebrospinal fluid flow by means of composite ^{131}I -RISA scans that included the head and neck and trunk. Twenty-five children born with myelomeningocele were examined; all were under 10 years of age and 21 were 6 mo or younger. Of the 20 children studied by intrathecal injection 15 had a lumbosacral defect and 12 presented clinically detectable hydrocephalus. The remaining five children were studied by intraventricular injection and all had evidence of hydrocephalus. After the injection of ^{131}I -RISA into the lumbar thecal space or one of the lateral ventricles, images of the head and neck were obtained at varying intervals and in five patients composite images were obtained that included the head, neck, and trunk. Based on the results, the group receiving the lumbar intrathecal injections were divided into three groups. In seven cases radioactivity had gained access to the basal cisterns within 1-3 hr after thecal injection, cerebral subarachnoid spaces were visualized subsequently, and significant clearance had occurred in 24 hr. None had clinical hydrocephalus. In ten cases the tracer followed the same sequence as in the first group but there was insignificant clearance by 24 hr. All of these children had clinically evident hydrocephalus. In two children of this group the myelomeningocele sac was defined. In three cases the RISA was injected directly into the myelomeningocele sac where the tracer remained and after 24 hr there had been no cranial dispersal of the tracer. In five patients who were injected directly into the dilated lateral ventricles there was no significant clearance of the tracer and composite scans demonstrated that the isotope migrated into the myelomeningocele sac and the concentration in the sac progressively increased. In none of the 24-hr scans had the isotope moved into the

basal cistern. They concluded that possible three sets of abnormal mechanical factors were responsible for the stasis of the cerebrospinal fluid: Caudal migration of the hind brain, mechanical blockage at the site of the myelomeningocele sac, and subarachnoid blockage at the level of the tentorium cerebellum. They suggested that there was a need for the development of primary reconstructive surgical procedures to restore the normal cerebrospinal fluid pathway.

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Radionuclides and Bone—from ^{226}Ra to ^{90}Sr . Silvanus Thompson Memorial Lecture. F. W. Spears. *Br J Radiol* 47:833, 1974.

The dosimetry of bone-seeking radionuclides is approached in such a way as to give information relevant to the induction of tumors and of bone marrow diseases, e.g., leukemia. Detailed calculations are presented for ^{226}Ra and ^{90}Sr , two elements that can replace calcium on the hydroxy apatite lattice. These long-lived radionuclides give quite different absorbed dose distributions on a microscopic scale since ^{226}Ra emits short-range, high LET alpha particles while ^{90}Sr emits long-range, low LET beta particles.

The calculations of energy deposition are based on measured distributions of path lengths through trabeculae and marrow spaces and are thus linked directly to the structure of individual bones. This method avoids the artificiality of describing irregular structures by simple geometric shapes and reduces a three-dimensional problem to a linear calculation. The mean absorbed dose factors for red marrow and for endosteal tissues in a 10- μ zone covering the trabecular surfaces is calculated. Results are also given for the beta emitters ^{14}C , ^{45}Ca , ^{22}Na , ^{18}F , ^{32}P , and ^{90}Y . Experimental TLD studies with bones from dogs raised on a diet containing ^{90}Sr gives agreement within approximately 20% of the values calculated by this method.

The implications of these results for radiobiology and radiation protection are discussed, as is the dose to infant bone from ^{90}Sr fall-out. Translation of the results of radionuclide toxicity studies from animals to man must take into account the differences in microscopic bone structure and the resultant differences in dose rates due to the incorporation of any given radionuclide.

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^{99m}Tc Complexes for Skeletal Scintigraphy. Physico-Chemical Factors Affecting Bone and Bone-Marrow Uptake. P. H. Cox. *Br J Radiol* 47:845, 1974.

This study investigated the mechanism of bone uptake of a number of ^{99m}Tc complexes for skeletal scintigraphy. The phosphate in bone is predominantly present as a double salt of calcium phosphate and calcium carbonate (apatite) or as hydrated tricalcium phosphate. The reason why the more complex pyrophosphate or the high molecular weight polyphosphate is more effective as a bone-scanning agent is difficult to explain on the basis of exchange processes. This work investigated the possibility that other factors that related to the technetium complex might influence bone uptake.

Experimental evidence suggested that the technetium is

not bound to the phosphates and that the phosphates are not essential for bone localization. The degree of bone uptake appears to be related to the reducing capacity of the reducing agent used and to the chelating capacity of the polyphosphate or other complexing agents. The ^{99m}Tc becomes incorporated into bones due to either an inherent bone-seeking capacity when reduced to the Tc(IV) state or to complex formation with bone-seeking reducing agents such as tin or titanium. The role of the polyphosphates and other complexing agents is primarily that of chelating agents that prevent colloid formation. This effect is reflected by the bone marrow uptake ratios.

From this study a ^{99m}Tc -titanium citrate complex and a ^{99m}Tc -titanium hexametaphosphate complex emerged as potentially interesting skeletal scanning agents.

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Tumor and Skeletal Imaging in Bone Carcinoma: An Experimental Demonstration. O. S. Okuyama, Y. Ito, T. Sato, K. Takahashi, and T. Matsuzawa. *Radiology* 113:681-685, 1974.

Experimental carcinoma cells were implanted within the medullary cavity of the left ishium in 24 laboratory rabbits. Within 2 weeks after inoculation palpable masses developed subcutaneously and radiographs demonstrated osteolytic lesions of the pelvis at the site of implantation. Bone-seeking radiopharmaceuticals, ^{87}Sr -chloride, ^{99m}Tc -pyrophosphate, ^{67}Ga -citrate, and ^{99m}Tc -bleomycin (separately and in combinations), were administered to the animals. After injection of the various radiopharmaceuticals radionuclide images were obtained and the animals were sacrificed at different intervals for organ radioassay. Within 1 hr after injection of ^{67}Ga -citrate the radionuclide was deposited in viable tumor tissue and bone. When ^{67}Ga -citrate and ^{87}Sr were administered together their distribution in osteolytic areas and nonaffected bone were relatively similar but in tumor the concentration of ^{67}Ga was approximately six times that of ^{87}Sr . The distribution of ^{99m}Tc -pyrophosphate in bone was similar to that of ^{87}Sr and similarly did not concentrate in tumor. Gallium-67-citrate and ^{99m}Tc -bleomycin were administered simultaneously and their distributions in bone and neoplasm were similar. The relative concentration of ^{67}Ga -citrate and ^{99m}Tc -bleomycin in the tumors compared to their concentration in bone was not sufficiently different to consider either radionuclide as a preferable agent for the detection of bony metastasis.

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Impaired Ventilation in a Patient with Angiographically Demonstrated Pulmonary Emboli. R. M. Kessler and B. J. McNeil. *Radiology* 114:111-112, 1975.

About 5 hr after the onset of pleuritic chest pain, dyspnea, and cough, a 22-year-old man had a pulmonary perfusion

study with ^{99m}Tc -iron hydroxide particles and a ventilation study with xenon. The particles study revealed obstruction to perfusion of the entire right lower lobe and superior segment of the left lower lobe. An immediately subsequent ventilation study demonstrated poor ventilation in the superior segments of both lower lobes. Angiography revealed central clots that nearly occluded both main pulmonary arteries and clots filled the inferior vena cava. The authors point out that although matches (perfusion ventilation) are more common in ventilatory disorders, they may also occur after pulmonary embolization. The decrease in ventilation to a region of obstructed blood flow appears to be secondary to bronchospasm, which has been well documented by animal investigations. Since bronchospasm following pulmonary arterial embolization may occur, a decrease in ventilation in the same site as a decrease in perfusion does not necessarily rule out pulmonary embolism.

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Statistical Consideration in Lung Imaging with ^{99m}Tc Albumin Particles. L. L. Heck and J. W. Duley, Jr. *Radiology* 113:675-679, 1974.

The purpose of this investigation was to determine the number of particles of albumin microspheres labeled with ^{99m}Tc required to provide satisfactory lung images. In two normal patients particles were injected daily for 5 days with the total number of microspheres increasing daily: 1500, 5000, 15,000, 30,000, and 135,000. The amount of radioactivity for the varying concentration of microspheres was kept relatively constant, from 0.5 to 1.0 mCi/dose. Images were obtained by both scintillation cameras and rectilinear scanners. Computer-generated displays also were obtained from simulated scans with varying concentrations of particle counts and varying collection times. The computer analysis demonstrated that increasing the number of counts, i.e., collection time, does not improve image uniformity unless an adequate number of labeled particles are present. However, an increased number of labeled particles within a specified area did improve spatial distribution and the images demonstrated less variability from one area to another. Spurious scan abnormalities were found in pulmonary studies when less than 15,000 particles were administered. If less than 30,000 particles were injected the authors felt that spurious scan irregularities could be observed near the periphery of the lungs. The loss of particles in the syringe must be considered when determining the concentration of particles and the volume of solution to be injected. The authors' final recommendations were that a minimum of 60,000 microspheres was needed for adequate lung images and that greater than 150,000 microspheres was unnecessary. Since ^{99m}Tc -pertechnetate is available in such high specific activity they cautioned that a routine imaging dose might easily be tagged to fewer than 10,000 microspheres or macroaggregated particles.

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