

**Solitary Autonomously Functioning Thyroid Lesions—Diagnosis, Clinical Features, and Pathogenic Considerations.** Joel I. Hamburger. *Am J Med* 58: 740–748, 1975.

The author's purpose in this study was to expand the available data on autonomously functioning thyroid lesions and to clarify certain areas of confusion and controversy. Over a period of 12 years, 164 patients with autonomous thyroid lesions were studied. The lesion was nontoxic in 142 and toxic in 24 of the subjects. Women had nontoxic lesions 13 times more frequently than men and toxic lesions nearly 4 times more frequently. Larger and toxic lesions were found in older patients, suggesting that these lesions were derived from smaller nontoxic lesions. Serum  $T_3$  and  $T_4$  concentrations showed parallel deviation from the normal in most of the patients with toxic lesions. The author observed that ultrasonic procedures gave more sensitive information than radionuclide imaging in the detection of cystic degeneration of nodules. In 51 patients with a diagnosis of nontoxic lesions who were studied over a period of 1–12 years, none became hyperthyroid. However, ten of these subjects did show nodule enlargement or evidence of degeneration. Of the 24 patients with toxic autonomously functioning lesions, 20 were treated with radioactive iodine and the remaining 4 were treated surgically. Thyroid carcinoma was found in 3 of 29 patients treated surgically. One patient with a toxic functioning nodule had carcinoma in the surgical specimen.

**Evaluation of Renal and Urinary Tract Abnormalities Noted on Scintiscans. A Retrospective Study of 1,711 Radioisotope Skeletal Surveys Performed in an 18-Month Period.** F. T. Maher. *Mayo Clin Proc* 50: 370–378, 1975.

During an 18-month period 247 of 1,711 scintiscans (15%) showed peculiarities of the renal or urinary tract areas that differed sufficiently from normal to merit mention in the interpretation. In 162 patients (195 surveys), the abnormalities were classified as "minor." In the remaining 52 surveys performed on 39 patients, the abnormalities were classified as "major," i.e., confirmed by other means or considered to be of major importance in diagnosis and management. In nine of these cases scintillation defects were observed in the renal areas, and in two instances renal cell carcinoma, simple cysts, and polycystic disease were diagnosed. In three cases the nature of the mass was not determined. In the remaining 30 cases unilateral or bilateral urinary tract obstruction was indicated on the scintiscan by hydroureter and massive retention in the renal areas. These obstructive manifestations were associated with primary pelvic or prostatic malignancies or the extension of some other malignant disease. Subsequent examinations in nine of the patients showed either progression or remission of the obstruction. The author concludes that periodic repetition of the radionuclide skeletal surveys increases the value of this single procedure, both in the evaluation of skeletal uptake of activity and in the early recognition of changes that are potentially inimical to renal function. Such use of the scan may indeed improve the selection of patients for exploratory urography.

**Use of Radionuclide Imaging in the Early Diagnosis and Treatment of Renal Allograft Rejection.** Stanley R. Mandel, William D. Mattern, Edward Staab, and George Johnson, Jr. *Ann Surg* 181: 596–603, 1975.

The purpose of this study was to evaluate changes during the postsurgical period of cadaver renal transplants. By this means the authors differentiated four possible clinical courses of the transplant: (A) uncomplicated transplant, (B) polyuria established after the first 24 hr after transplantation secondary to acute tubular necrosis, (C) severe acute rejection requiring prolonged aggressive immunosuppressive therapy, and (D) early rejection crisis superimposed on an established tubular necrosis. Following intravenous injection of  $^{131}\text{I}$ -orthoiodohippuric acid, serial 5-min images of the kidney and bladder were obtained by the scintillation camera and the information was also stored in a digital computer. This information was analyzed to graph selectively the transit of IOH through the cortex and medullary portions of the kidney. The IOH transit curves were obtained from a selected area of renal parenchyma that excluded the collecting system. In oliguric patients the authors found that serial studies were valuable since acute tubular necrosis could be identified and the level of immunosuppressive treatment could be minimized during the extended period of polyuria. Thus, potentially dangerous levels of immunosuppressive drugs were avoided. Acute rejection complicating acute tubular necrosis was also identified so that high-dose steroid therapy could be administered appropriately. In those patients without polyuria the studies contributed to the early diagnosis of acute rejection. The authors also found the studies useful in monitoring the effect and duration of treatment for severe rejection crisis. The authors concluded that radionuclide imaging studies were a valuable adjunct to the management of patients with the complicated clinical manifestations that follow renal transplantation.

**Local Cerebral Blood Volume Determined by Three-Dimensional Reconstruction of Radionuclide Scan Data.** D. E. Kuhl, M. Reivich, A. Alavi, I. Nyary, and M. Staum. *Circ Res* 36: 610–619, 1975.

The absolute measurement of local cerebral blood volume (LCBV) was determined in three dimensions throughout the brain: the point-to-point concentration of radioactive blood in a transverse-section scan of the brain was obtained and compared with the concentration in the peripheral blood. Technetium-99m-labeled erythrocytes were injected into a peripheral vein and a transverse-section scan of the brain obtained. During the scan a blood sample was obtained and the activity in both the blood cells and plasma was determined. Counting data scans were reconstructed and corrected to represent the point-to-point concentration of radioactivity in the cross section of the brain. The measured concentration of blood radioactivity was used to convert the brain activity to LCBV expressed in milliliters of blood per 200 gm of blood tissue. The result was a two-dimensional map of LCBV that represented a cross section of the brain at a known level. The data processing provided radionuclide concentration analogous to an autoradiograph. Using data from five baboons, an equation was obtained for the

regression plane that relates LCBV in the center of the brain to arterial carbon dioxide tension ( $p\text{CO}_2$ ) and mean arterial blood pressure (MABP):  $\text{LCBV} = 2.88 + 0.049 p\text{CO}_2 - 0.013 \text{ MABP}$ . In human subjects LCBV values range from 2 to 4 ml/100 gm depending on location; higher values correspond to regions of cerebral cortex. Differences in blood volumes of focal brain lesions were quantified. The value of the procedure was illustrated by a patient with a clinical diagnosis of cerebral infarction. The LCBV scan indicated that the lesion had a focal blood volume three times that of normal tissue, suggesting neoplasm. Autopsy proved that the lesion was a highly vascular malignant glioma.

**Regional Cerebral Blood Flow Estimated by  $^{133}\text{Xe}$  Inhalation.** W. D. Obrist, H. K. Thompson, Jr., H. S. Wang, and W. E. Wilkinson. *Stroke* 6: 245-256, 1975.

One of the major disadvantages of the  $^{133}\text{Xe}$  inhalation method is contamination of clearance curves by radioactivity from the scalp and other extracerebral sources. Earlier, the authors proposed a three-compartmental analysis in which the first two compartments represent the faster-clearing gray and white matter while the third compartment represents the slower extracerebral tissue. Separation into three compartments, however, required an extended examination period of 40 min or more, which limited the usefulness of the procedure. This investigation described a shorter and simpler method in which  $^{133}\text{Xe}$  clearance was monitored extracranially for 10 min following a 1-min inhalation. Although limited to bloodflow estimates of the gray matter compartment, the shorter method is believed to be better suited for clinical research. Computer-simulated data were used to test the accuracy of the two different methods and to evaluate the stability of the parameters in the presence of random noise. A comparison between the two-compartment approach and the previous three-compartmental analysis indicated that, except for differences in curved length appropriate to the particular method, data for the two analyses were identical. The values for the fast-tissue compartments were in very close agreement. In this comparison a product-moment correlation of 0.91 between the two methods was obtained in the gray matter blood flow. The inhalation method tended to underestimate blood flow at very low levels but overall agreement between the two methods was quite good. The authors also reported that a direct comparison of their methods with the internal carotid injection method was currently under way. The authors conclude that application of the  $^{133}\text{Xe}$  inhalation method to clinical research appears feasible.

**Radioselenium Pancreozymin-Secretin Test as a Clinical Test for Pancreatic Exocrine Function.** M. Shichiri, N. Etani, M. Yoshida, Y. Harano, M. Hoshi, Y. Shigeta, and H. Abe. *Am J Dig Dis* 20: 460-468, 1975.

Pancreatic exocrine function was determined in 36 subjects: 17 were normal and 19 had pancreatic disease (14 with pancreatitis, 3 with pancreatic carcinoma, and 2 with pancreatic cysts). After intubation beyond the duodeno-jejunal flexure,  $^{75}\text{Se}$ -selenium was administered intravenously. The duodenal contents were aspirated at 10-min intervals for periods of up to 180 min. A continuous flow of pancreatic juices was stimulated by pancreozymin. Radioactivity was measured in the duodenal aspirates, and in separate experiments it was also measured in bile on two patients with extrapancreatic fistulas and in five patients with T-tubes in the common bile duct. A good distinction

between normal subjects and patients with pancreatic disease was obtained by measuring the radioactivity in the protein fraction of the duodenal aspirate. In normal subjects pancreozymin stimulation produced a significant increase in radioactivity from duodenal aspirate whereas the increase was approximately one-fourth of the normal in patients with pancreatic disease. The authors believe that this type of procedure might be a useful and sufficiently reliable method for detecting abnormal pancreatic exocrine function.

**Towards the Assessment of the Limitations on Computerized Axial Tomography.** P. R. Smith, T. M. Peters, H. R. Muller, and M. Elke. *Neuroradiology* 9: 1-8, 1975.

The purpose of this study was to establish objective criteria for comparing different algorithms and instruments for computerized axial tomography. Reconstruction of brain sections was applied to the same scan patterns by different methods, and in addition the effects of varying the amount of data available to the reconstruction program were evaluated. The instrument utilized in this study was an EMI scanner with a  $160 \times 160$  reconstruction matrix. They found that no reasonable distinction could be made between the various algorithms used to reconstruct the tomograms as far as their clinical relevance to the investigation of intracerebral structure was concerned. They did observe, however, a significant difference between the pictures obtained from the EMI scanner and those obtained using the FOURIER methods because the latter do not show the "overshoot" artifacts between the skull and brain. These appear in most EMI images that are produced with the original programs and can be mistaken for subarachnoid space. The second part of the experiment involved the number of measurements needed to reconstruct the image. They found that reduction in samples (from 180 to 90 scans and from 158 to 100 points per scan) did not significantly affect clinically interpretable detail in the reconstructed tomogram. Geometrical considerations were used to show that sufficient information to reconstruct could be extracted from only about 90 scans, because high-resolution information cannot be represented adequately on this sampling grid. Such contributions would apparently be interpreted as noise in the reconstructed image. The authors' final point concerns the photographic presentation of data; they compared the linearly interpolated EMI image and the EMI image as displayed on the cathode-ray tube. The difference between the two was essentially the difference between the two display systems. The authors emphasize the importance of a picture whose density varies smoothly. The authors felt that an EMI picture that is as close as possible in appearance to a conventional radiograph, even though its resolution is lower, helps the eye to avoid being distracted from information that the picture may contain.

**Comparison of Radio-Iodinated Serum Albumin and Blue Dextran as Indicators to Measure Rate of Formation of Cerebrospinal Fluid.** A. N. Martins, A. Ramirez, and T. F. Doyle. *Exp Neurol* 47: 249-256, 1975.

The purpose of this study was to compare the characteristics of two nondiffusible indicators ( $^{125}\text{I}$ -human serum albumin and blue dextran) in the measurement of the rate of formation of cerebrospinal fluid by means of in vitro experiments and a series of ventriculocisternal perfusion experiments on rhesus monkeys. One perfusion needle was passed into the left lateral ventricle, and another needle was connected to a polyethylene tube that was passed into the cisterna magna and the free (outflow) end of the tube was

positioned at the level of the cisterna magna. The perfusion fluid, a balanced salt solution containing trace amounts of  $^{125}\text{I}$ -human serum albumin and blue dextran, was administered at the rate of 0.181–0.240 ml/min. The effluent from the cisterna magna was collected for 3.5 hr after the fluid collected during the first 2.5 hr had been discarded. The mean rate of cerebrospinal fluid formation calculated from the dilution of  $^{125}\text{I}$ -IHSA was 37.6  $\mu\text{l}/\text{min}$ ; the cerebrospinal fluid formation calculated from the blue dextran was 37.1  $\mu\text{l}/\text{min}$ . Data based on the dilution of blue dextran had one-tenth the coefficient of variation of that calculated from  $^{125}\text{I}$ -IHSA. This difference was attributed to the counting variability because of the low energy of  $^{125}\text{I}$ . The authors concluded that blue dextran was preferable to  $^{125}\text{I}$ -IHSA for the measurement of cerebrospinal fluid formation.

**Radioimmunoassay for Motilin.** J. R. Dryburgh and J. C. Brown. *Gastroenterology* 68: 1169–1178, 1975.

Motilin is a compound from pancreatic juice that stimulates motor activity in denervated or transplanted stomachs in dogs. Pure motilin injected intravenously into dogs produced increased motor activity in the body of the stomach similar to that observed after alkalinization of the duodenum. The authors undertook a radioimmunoassay for motilin to determine if that agent was the one released into the circulation during perfusion of the duodenum with alkaline solutions. Highly purified  $^{125}\text{I}$ -motilin was used as the tracer and it had a sensitivity range from 10 to 320 pg. No cross-reactivity was demonstrated with gastric inhibitory polypeptide, secretin, glucagon, gastrin, cheolecystonin, pancreozymin, or vasoactive intestinal peptide. In dogs with denervated pouches of the stomach and a Mann–Bollman fistula, duodenal alkalinization increased gastric motor activity in the fundic pouches with a corresponding increase in serum motilin. The authors' results strongly support the hypothesis that motilin is the peptide released upon the alkalinization of the duodenum.

**Carcinoembryonic Antigen (CEA): Ten Years' Perspective.** D. P. Stevens. *Aust NZ J Med* 5: 169–170, 1975.

The author succinctly summarizes the status of several radioimmunoassays for carcinoembryonic antigen (CEA) and comments on the sensitivity and specificity of the procedure. He points out that CEA values found in noncancerous conditions are generally in the lower "positive" range, levels that, when found in patients with cancer, often are associated with a localized surgically curable tumor. While a higher level of CEA makes a diagnosis of cancer more likely, the author observes that the higher level also suggests the presence of metastasis. Although helpful prognostically, the findings are generally irrelevant to therapy. The author proceeds to summarize current clinical applications for testing for CEA in peripheral blood: (A) corroboration of clinical suspicion of cancer (a negative test does not exclude the possibility of the presence of cancer); (B) screening for cancer in selected populations (the "false-

positive" rate attributable to heavy smoking, benign gastrointestinal disorders, and perhaps advancing age itself dictates that simple screening for cancer by means of CEA alone does not justify the effort); (C) postresection followup (a return of CEA levels to normal within 2 weeks of tumor surgery suggests successful resection but continued elevated CEA levels indicate widespread cancer); and (D) chemotherapy and radiation (there is little evidence that determination of CEA levels reflects the success of chemotherapy). The initial enthusiasm for CEA has given way to skepticism but perhaps wider experience may lead to a clearer perspective of the role of CEA in tumor diagnosis, therapy, and prognosis.

**Carcinoembryonic Antigen in Patients Suffering from Ulcerative Proctocolitis.** A. B. S. Mitchell, A. Morton Gill, R. T. Orchard, and R. A. Parkins. *Am J Dig Dis* 20: 407–417, 1975.

The authors measured carcinoembryonic antigen (CEA) levels by means of radioimmunoassay serum samples in 59 patients who had ulcerative proctocolitis. Their group of patients was compared with reported epidemiologic studies for this disease; they were found to have a similar sex ratio and age of onset but were also found to have a more limited extent of involvement. Elevated CEA concentrations were found in 11 of the 59 patients (18.3%). Of the 11 patients with an elevated titer of CEA, one had colonic carcinoma and another was pregnant. In the remaining nine the overall prevalence of elevated CEA levels was 17.5%. In ulcerative colitis the incidence of elevated CEA was 19.9% and in ulcerative proctitis, 7.1%. Patients with elevated plasma CEA values and those with normal values were compared in relation to factors associated with an increased propensity for the development of carcinoma complicating ulcerative colitis. The only difference between these two groups was found to be the severity of the initial attack. In a followup study that extended for at least 18 months no carcinoma has been manifested. The authors conclude that elevated CEA levels can be only regarded as genuine false positive in the detection of colorectal carcinoma.

**Alpha-Fetoprotein in Lung Cancer Metastatic to the Liver.** S. H. Tsung. *Arch Pathol* 99: 267–269, 1975.

A 42-year-old man with bronchogenic carcinoma who had metastases to the liver was found to have positive serum  $\alpha$ -fetoprotein by counter electrophoresis. Immunofluorescence showed that the site of this protein synthesis was in the liver parenchyma adjacent to the tumor. Alpha-fetoprotein antiserum was found to be monospecific for  $\alpha$ -fetoprotein in the tissue evaluated by the immunofluorescence method since tumor cells in the lung and the liver were negative for fluorescence. These findings raise the possibility that hepatic cells around metastatic foci undergo regeneration and produce  $\alpha$ -fetoprotein. This has been found in regenerating livers of mice after partial hepatectomy. This study poses interesting questions on the use and implications of the radioimmunoassay tests for  $\alpha$ -fetoprotein.

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