SNM Scientific Meeting Highlights

NUCLEAR MEDICINE IN THE 1990s: THE CHALLENGE OF CHANGE

"This meeting is evidence that nuclear medicine is beginning to turn and meet the challenge of change. Cyclotrons and positrons are becoming the new focus of nuclear medicine. . . . What we need to do now is emphasize the clinical usefulness of positron emission tomography (PET). These procedures need no longer be viewed only as research studies."

Henry N. Wagner, Jr., MD, director of nuclear medicine and radiation health sciences at the Johns Hopkins Medical Institutions in Baltimore, has made his Scientific Meeting Highlights an annual tradition as well as a felicitous closing for The Society of Nuclear Medicine's annual meetings. Last month at the Society's 32nd Annual Meeting in Houston, TX, Dr. Wagner presented his summary of the Society's scientific program for the eighth consecutive year.

In the past, I've said that it is wrong to reach a turning point and not turn. This meeting is evidence that nuclear medicine is beginning to turn and meet the challenge of change. Cyclotrons and positrons are becoming the new focus of nuclear medicine.

In the 1950s nuclear medicine was dominated by iodine-131 compounds, in the 1960s by technetium-99m, in the 1970s by thallium-201, and the 1980s by carbon-11, fluorine-18 and iodine-123.

I believe that the 1990s will be dominated by five primary radionuclides: carbon-11, fluorine-18, oxygen-15, iodine-123 and technetium-99m.

At this meeting there were 92 presentations—papers or posters—on PET, accounting for 15 percent of the 570 total presentations.

Which radionuclides were used? Number one is still fluorine-18 with 41 presentations, 27 of which were deoxyglucose. Carbon-11 was next with 26, followed by oxygen-15 with 19 (Fig. 1).

Fifty-five PET presentations were concerned with the brain. Let's stop talking about "brain scanning" and say more specifically "imaging glucose metabolism" or "dopamine receptor imaging" or "regional brain blood flow." Brain scanning has an anatomical connotation.

The greatest increase in brain papers was in neuroreceptors which are catching up to the number of papers on brain metabolism (Fig. 2). We can now characterize regional neuronal activity within the living human brain in terms of increased blood flow, glucose metabolism, oxygen metabolism, neurotransmitter activity and neuroreceptor activity.

Hippocrates said many centuries ago, "It is disgraceful in every art, and more especially in medicine, after much trouble, much display, and much talk, to do no good after all."

What we need to do now is emphasize the clinical usefulness of PET. These procedures need no longer be viewed only as research studies. They are ready to be applied clinically on a wide scale. Only support from clinical studies and from the drug industry can provide the necessary capital funds to get a PET center started.

The Brain: Metabolism Still Number One

Very prevalent diseases, such as stroke, epilepsy, and Alzheimer's disease, can be studied with PET. We're not concerned just with brain tumors, with an incidence of 4 per 100,000; we're talking about diseases with a much higher incidence, such as schizophrenia and drug addiction.

Epilepsy is the first area of clinical usefulness of PET. Focal epilepsy is associated with clearly measurable increases in glucose metabolism. During a seizure, glucose metabolism in the normal brain diminishes while it increases at the focus of the seizure. Right after the seizure, the focus becomes hypometabolic.

Dementia is the second area for PET clinically. In Alzheimer's disease, there is a very characteristic distribution of the abnormalities in the brain. Figure 3 is a deoxyglucose study performed with the ECAT III system at the University of California at Los Angeles (UCLA) (Abstract No. 105).* The resolution of the system is 4.5 mm, the best in the field to date. The pattern in Alzheimer's disease is a very strikingly reduced glucose metabolism in the temporoparietal regions. The pattern can be distinguished from other types of dementia, such as multiple infarct dementia which has a Swiss cheese appearance.

David E. Kuhl, MD, from UCLA showed us that patients with Parkinson's disease and dementia have the same characteristic distribution of the abnormality as patients with Alzheimer's disease (Abstract No. 285). In a very careful study, he found that the parietal to cerebellar ratio of glucose metabolism was the same in both the Alzheimer and

(continued on page 680)

* Abstracts are published in the May 1985 issue of *The Journal of Nuclear Medicine* and in the SNM 32nd Annual Meeting Guide.

POSITRONS	1982	1983	1984	1985
^{18}F	20	27	33*	41**
^{11}C	10	18	22	26
^{15}O	8	12	13	19
^{13}N	7	4	8	9
^{82}Rb	2	5	9	5
^{68}Ga	2	2	4	6
TOTAL	49	68	89	106

*FDG 24
**FDG 27

Figure 1. A breakdown of the positron-emitting radionuclides used in the studies presented at the Society's annual meetings over the past four years.

(continued from page 679)
Parkinsonian patients, who had the same degrees of dementia. Studies of this type can help us solve the puzzles of what causes these tragic diseases. Are they degenerative or environmentally-induced?

The detection of recurrent brain tumors is a third area of PET's clinical usefulness. After brain surgery, the abnormalities detected with x-ray computed tomography (CT) can represent persistent or recurrent tumor or the effects of surgery. Increased glucose metabolism provides very strong evidence that the patient still has a tumor, rather than radiation necrosis, where glucose metabolism is not increased.

At the Karolinska Institute in Stockholm, studies with carbon-11 methionine are used in conjunction with stereotactic surgery, providing the most accurate way to identify the nidus of a lesion for biopsy. Jorge R. Barrio, PhD, and his associates at UCLA use carbon-11-labeled leucine in a model to measure protein synthesis, which can be as important in studying brain development as in the study of brain tumors (Abstract No. 12). To measure protein synthesis, it is advantageous to have a nuclide with a longer half-life than 20 minutes. Gerard L. Stöcklin, PhD, and his associates at Jülich in West Germany have developed fluorine-18-labeled flurophenylalanine (Abstract No. 537). The 110-minute half-life of fluorine-18 makes it especially attractive, and they are about ready to extend these studies into human beings.

Neuroreceptors

Of the 25 neuroreceptor papers, 11 were concerned with dopamine and five with the muscarinic cholinergic system.

In 1906, Ramon y Cajal discovered that every nerve cell is connected to about 1,000 or 10,000 other nerves by means of axons and dendrites. This led to an understanding of the brain's electrical activity. Several decades later, the principle of chemical neurotransmission, which has revolutionized medicine, was discovered. Information travels along a neuron by the process of depolarization, and when the information gets to the connection between one nerve and another, chemicals are secreted that cross the synapse and combine chemically with receptors on the post-synaptic neurons.

Of the 30 to 50 neurotransmitters in the brain, the ones that are the best understood are norepinephrine, acetylcholine, dopamine, and serotonin. The process of chemical neurotransmission has made possible the tremendous advances in the pharmaceutical industry. The four leading prescription drugs in the United States act on the process of neurotransmission. Cimetidine blocks histamine receptors; propranolol blocks adrenergic receptors; diazepam (Valium) stimulates benzodiazapine receptors; and haloperidol, used to treat schizophrenic patients, blocks dopamine receptors. One tracer ligand after another is being developed to make it possible to measure the state of these receptors.

With respect to the ligand that has been available the longest, carbon-11 methylspiperone, we now have a mathematical model that should be useful for quantifying the number of receptors and the affinity of the receptors, as well as making it possible to assess endogenous neurotransmitter secretion rates by the process of competitive inhibition (Abstract No. 211). Nonspecific binding in regions such as the cerebellum is used as a standard. The caudate/cerebellar ratio gives an indication of the relative number of receptors. By means of this ratio, it was demonstrated that a relatively small dose of haloperidol, given orally four hours before the ligand, blocks the binding of carbon-11 methylspiperone to the D-2 dopamine receptor.

For the first time, we can now measure what such drugs are doing in the living human brain. It had been suspected from animal studies that neuroleptic drugs blocked D-2 receptors. Now we can see that they do and assess the degree of blockade in the brains of living human beings.

One question that was addressed was whether the drug molindone, used to treat schizophrenic patients, has a different site of action than does haloperidol (Abstract No. 214). It was thought that since the incidence of tardive dyskinesia, a complication of haloperidol treatment, does not occur with molindone, perhaps the site of action within the brain is different. The findings showed that both had the same

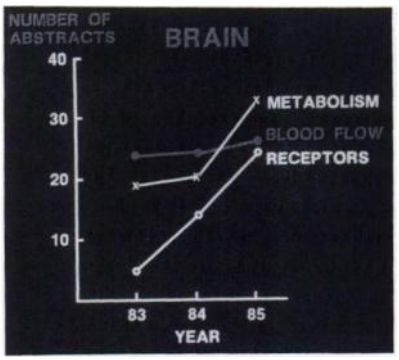

Figure 2. The number of SNM annual meeting papers on neuroreceptors is catching up to brain study presentations on metabolism and blood flow.

degree of blockade when given in clinically equivalent doses.

The mathematical model makes it possible to measure the number of receptors, their affinity, and the effect of stimulating or blocking drugs. The initial results of PET in normal persons were comparable to those obtained in the study of human brains removed at autopsy (Abstract No. 211).

Opiate receptor activity has a different distribution from dopamine receptor activity. The thalamus, for example, which does not contain dopamine receptors, is rich in opiate receptors.

The drug naloxone blocks opiate receptors in a manner analogous to the haloperidol blocking of dopamine receptors. The initial distribution of carbon-11 carfentanil is not influenced by the administration of naloxone in nonradioactive form. At 30 to 60 minutes after injection, however, you can see that the receptors are blocked completely by the prior administration of a large dose of naloxone. If a smaller dose of naloxone is given, the receptors are only partially blocked.

It's possible now, for the first time in a living human being, to obtain a dose response curve of the effect of drugs on the brain. We can see the relationship between the dose of naloxone, which blocks the receptor, and the degree of blockade of carbon-11 carfentanil. With a large dose of naloxone, the binding is reduced to about 20 percent of the unblocked state. The use of simplified probe detector systems can be applied to the brain in a manner analogous to the early thyroid-uptake studies.

For example, we can obtain a time/activity curve from the brain of a normal subject in the unblocked and in the naloxone-blocked state, using 0.01 of the dose of carbon-11 carfentanil required for PET scanning. The cost of the probe detector instrument is 0.01 that of a PET scanner, resulting in a potential saving of factors of more than 1,000 if you want to know whether the receptors have been blocked to the desired degree by drugs such as methodone in drug addicts or haloperidol in schizophrenic patients.

Carfentanil is an agonist that stimulates the opiate receptor, and therefore, because of its extreme potency, has a pharmacologic effect, which is mild and tolerable

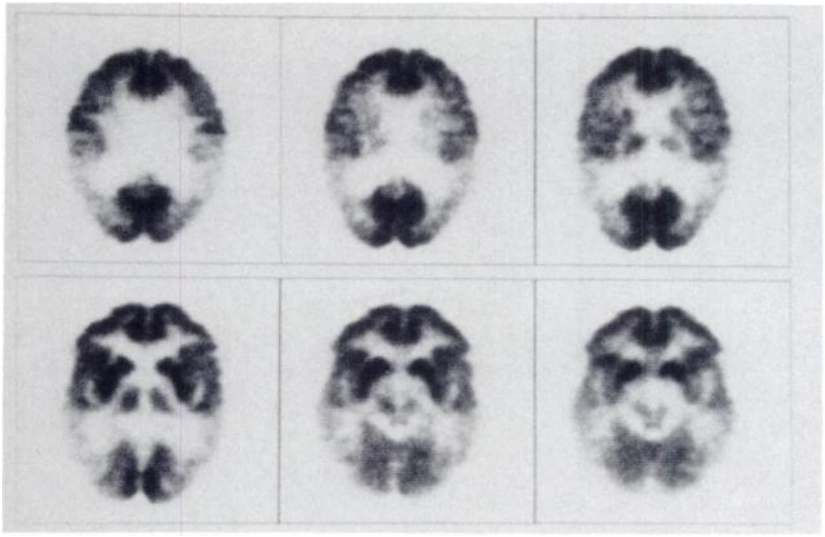

Figure 3. A deoxyglucose study of an Alzheimer's disease patient performed with the ECAT III PET system, developed at UCLA, showing the characteristic reduced glucose metabolism pattern in the temporoparietal regions.

but still detectable even with microgram doses. Antagonists, such as methylspiperone which blocks the dopamine receptor, do not have a pharmacologic effect. Steven M. Larson, MD, and his associates at the National Institutes of Health (NIH) developed fluorine-18 fluoronaltrexone, an antagonist label for μ-type opiate receptors (Abstract No. 216).

Another new receptor ligand is carbon-11 suriclone, an agonist of benzodiazapine receptors (Abstract No. 213). Dr. O. Inoue and his associates at the National Institute of Radiological Sciences in Japan have used another ligand, carbon-11 RO-15-1788, to image benzodiazapine receptors in a human being (Abstract No. 454). The distribution of the benzodiazapine receptors is significantly different from that of either dopamine or opiate receptors.

The cerebellum, for example, is rich in benzodiazapine receptors. The benzodiazapine system is an inhibitory system, presumably moderating the stimulatory systems. Dr. Inoue's poster documented the relationship between the benzodiazapine system, as studied with carbon-11 RO-15-1788, and the dopaminergic system.

Another tracer, reported first at this meeting, was carbon-11 dexetimide, useful for studying acetylcholine receptors, with the added advantage of being able to be iodinated (Abstract No. 215).

Dexetimide can be labeled with iodine-125 and iodine-123 as well as carbon-11. An isomer is available (a levo form, levetimide) that can be used to measure nonspecific binding, an important advantage. Even though dexetimide is an antagonist, it has a strong pharmacologic effect, so that large blocking doses cannot be given. Fortunately, nonspecific binding can be assessed with levetimide. Results with iodine-123 dexetimide in human beings proved its specificity. In contrast to the case with dopamine and opiate receptors, the visual cortex is rich in acetylcholine receptors.

Another approach to the synapse is via monoamine oxidase inhibitors. The Brookhaven National Laboratory investigators described carbon-11 deprenyl and carbon-11 clorgyline, which inhibit monoamine oxidase activity (Abstract No. 148). Further studies will have to be done to prove that the binding of this ligand to the monoamine oxidase enzyme is specific. Monoamine oxidase is the enzyme that metabolizes amine neurotransmitters, such as dopamine, serotonin and norepinephrine.

Other carbon-11-, iodine-123-, and iodine-125-labeled ligands are iodolysergic acid diethylamide (LSD), known to bind to serotonin receptors. Iodine-123-labeled LSD was found to be even more specific for serotonin receptors than LSD, and methyl-iodo-LSD was found to

(continued on page 682)

Figure 4. The "image of the year," a SPECT scan of technetium-99m PAO uptake (right), comparable to a brain-blood flow image with iodine-123 IMP (center). The image at left is from x-ray CT.

(continued from page 681)

be even better. The specificity of carbon-11 methyl-bromo-LSD for S2 serotonin receptors was indicated by the blocking effect of the drug ketanserin.

Brain Growth and Development

A major area in which nuclear medicine can make important contributions is the study of the growth and development of the brain. Michael E. Phelps, PhD, and his associates at UCLA are beginning to study glucose metabolism during brain development (Abstract No. 187). They reported deoxyglucose studies in five-day-old infants, as well as in children 11 weeks, 7.6 months, and two years of age. These patients had focal epilepsy, and this approach of using one group of patients as a control for another group will probably be used more and more in nuclear medicine.

In five-day-old infants, glucose metabolism is limited to regions such as the motor cortex, but at 11 weeks, and 7.6 months, the pattern gradually approaches the distribution pattern of metabolic activity in adults. In mentally retarded two-year-old babies, Dr. Phelps's group observed the same pattern, chiefly in the motor cortex and thalamus, seen in five-day-old infants.

Another approach to the study of birth defects may be the use of misonidazole, reported by the group of Kenneth A. Krohn, PhD, and his associates at the University of Washington in Seattle (Abstract No. 93). This tracer binds to living brain cells only when the oxygen concentration is 15 percent below normal. It may be useful as a probe for oxygen concentrations in mental retardation, as well as in cerebrovascular disease.

Advances in Cyclotron Chemistry

To simplify PET studies, Robert F. Dannals, PhD, of Johns Hopkins, and B. Långström of the University of Uppsala in Sweden, developed a $1,000 system to produce carbon-11 alkyliodide and carbon-11 methyliodide, used in labeling many tracers such as dexetimide (Abstract No. 539). Gerald L. Stöcklin, PhD, and his group have simplified nucleophilic fluorination (Abstract No. 146). Nucleophilic fluorination involves the fluoride ion rather than the use of F2. Crown ethers are used as reagents to permit labeling of fatty acids, glucose, neuroleptic analogs, and proteins, etc.

An example of the transition from PET to SPECT can be found in Alzheimer's disease studies. Xenon-133, used by investigators from the University of Iowa (Abstract No. 445), iodine-123 isopropyl iodoamphetamine, used at Harvard University (Abstract No. 96), and iodine-123 HIPDM, used at Indiana University (Abstract No. 450), showed the characteristic temporo-parietal distribution in patients with Alzheimer's disease.

Yoshiharu Yonekura, MD, from Kyoto University in Japan, reported that in stroke patients, iodine-123 isopropyl iodoamphetamine will not accumulate if the brain tissue is dead, indicated by lack of oxygen uptake, even when the region is hyperfused (Abstract No. 94).

"Image of the Year"

The "image of the year" is a technetium-99m-labeled propylene amine oxime derivative (Fig. 4), a brain-blood flow agent developed at the University of Missouri (Abstract No. 62). The images are comparable to those made with iodine-123 isopropyl iodoamphetamine, but you can administer ten times as much radioactivity with technetium-99m as with iodine-123. A competing compound has been developed in which an amino group was added to the multipurpose diaminodithiol core to increase its retention in the brain (Abstract No. 63). This designed radiopharmaceutical stays in the baboon and monkey brain long enough to be imaged by SPECT. Time will tell which of the several technetium-99m-labeled brain-blood flow agents is going to be the best.

Alan R. Fritzberg, PhD, and his colleagues at the University of Utah have produced technetium-99m mercaptoacetyltriglycine, which seems to have the adequate properties to replace iodine-131 hippurate (Abstract No. 233). Investigators at the Massachusetts Institute of Technology and Harvard have developed multipurpose neutral complexes that can enter cells or cross the blood-brain barrier, and are trying to develop suitable technetium-99m-labeled fatty acids (Abstract No. 2).

Mark M. Goodman, PhD, and Furn F. Knapp, Jr., at Oak Ridge National Laboratory are trying to develop a glucose analog that can be used to measure regional glucose metabolism in the brain and heart using SPECT. The group reported a model compound, iodovinyl-D-allose, that can be labeled with iodine-125 (Abstract No. 517).

Better Instruments

In addition to chemical advances, important advances in instrumentation were presented at this meeting. Efforts are being made to decrease the number of photomultiplier tubes with the goal of decreasing the cost while maintaining (or even improving) the sensitivity and resolution of PET scanners. One of the systems couples 32 detectors to four photomultiplier tubes. J.S. Karp and Gerd Muehllehner, PhD, of the University of Pennsylvania, reported the first clinical studies with their hexagonal bar positron camera, which shows a resolution of 7.5 mm (Abstract No. 1). Perhaps we can hope that PET scanners may be available

(continued on page 684)

"Fortunately, nuclear medicine is moving beyond diagnosis into prognosis and monitoring treatment."

(continued from page 682)
in the $500,000 range. Gordon L. Brownell, PhD, with his group at Massachusetts General Hospital, has developed a system also designed to reduce cost by decreasing the number of photomultiplier tubes (Abstract No. 104).

Several investigators have used maximum likelihood algorithms in reconstruction of PET data. One example, described by an NIH group, makes it possible to accurately measure concentrations of radioactivity in small structures of the brain, such as the caudate nucleus (Abstract No. 71). The method uses the physical characteristics of the scanner, the statistics of the data, and anatomical information, derived from either CT or nuclear magnetic resonance (NMR) images, to carry out the reconstruction. In structures such as the caudate nucleus, there is an error introduced by underestimation of the amount of activity in the region. Using Carson's algorithm, we can obtain an accurate representation of the concentration of tracer.

Advances in SPECT instrumentation include the system, produced by Lim and colleagues of Technicare, consisting of three rotating cameras (Abstract No. 418). As sensitivity increases, resolution increases and 8-mm lesions can be detected by this device.

A question that remains open is whether the multi-camera or ring design will be the eventual configuration of SPECT imaging. A Shimazu instrument at Kyoto University uses a ring configuration with fan beam columnation to increase sensitivity. Only time will tell whether a ring configuration will justify its expense relative to a rotating camera system.

The Heart

There has been a steady decrease over the last five years in the number of heart papers (Fig. 5). One factor may be the increasing attraction that echocardiography has for cardiologists.

Fortunately, nuclear medicine is moving beyond diagnosis into prognosis and monitoring treatment.

A group from Massachusetts General Hospital investigated the prognostic significance of negative thallium scans, and reported that the incidence of deleterious events (such as myocardial infarction) in such patients was equal to that in the general population (Abstract No. 112). The same group also used antimyosin antibodies, which accumulate in areas of myocardial infarction, to image infarct size (Abstract No. 109).

Investigators at Hahnemann University in Philadelphia were able to identify, using exercise thallium-201 scintigraphy, a subgroup of hypertensive patients who were at a high risk for developing myocardial infarction or other complications (Abstract No. 110). They also reported that some asymptomatic patients who had coronary artery bypass grafts could be shown, with exercise radionuclide ventriculography, to have abnormalities associated with subsequent complications (Abstract No. 114). They identified patients at high risk, who should have more aggressive follow-up and possibly be considered for recatheterization and regrafting.

A group in Melbourne, Australia, presented a very straight-forward study showing that in patients with all types of heart disease, survival decreased as left ventricular ejection fraction decreased (Abstract No. 354).

Myocardial Metabolism

Thirteen papers were concerned with fatty acid metabolism, and 11 with other myocardial agents. A group at UCLA continues to use the principle that when the heart muscle is alive but impaired, it prefers to metabolize glucose instead of fatty acid, presumably because it is the most efficient source of energy. They correlated glucose and blood flow measurements with the effects of revascularization (Abstract No. 364). When blood flow was down but glucose metabolism was up, 85 percent of the abnormal segments in the patients improved. When both glucose metabolism and blood flow were down, however, only 2 of 27 segments improved and 24 had no change. Such measurements could help select those patients with coronary disease who will benefit from surgery.

A West German group compared iodine-123 heptadecanoic acid with carbon-11 palmitic acid (Abstract No. 370). Results showed that mentally stressed patients have a decreased rate of washout for both iodine-123 heptadecanoic acid and carbon-11 palmitic acid from the mycardium, indicating decreased beta-oxidation of fatty acids and a shifting to glucose metabolism.

A study from the University of Texas showed a decreased fatty acid uptake in patients with myocardial infarcts, but a paradoxical increase in fatty acid accumulation and delayed washout in regions served by stenotic arteries (Abstract No. 203).

SPECT studies of the heart included 9 thallium-201 studies. The potential benefits of SPECT in cardiology, such as improved accuracy over planar imaging, are becoming a reality, particularly in single vessel disease (Abstract No. 200).

Improved quantification of SPECT provides for the next step—automatic interpretation. Dr. R. Itti, of Trousseau University in France, reported that computer use can be extended from image creation and processing to image interpretation (Abstract No. 247). From the experience of 207 cases, Itti's computer stored data so that a test group of 87 subsequent patients could be interpreted by discriminant analysis. The computer was found to be at least as good, if not better, than subjective interpretation. With a 5 percent false positive rate, the computer was 85 percent sensitive compared with a 75 percent sensitivity for visual interpretation. The computer handles six features by means of discriminant analy-

sis; most people cannot effectively handle more than three variables.

Nuclear Pharmacology

Jean-Louis M. Barat, MD, of Hôpital Universitaire in France, studied the effect of propranolol on rest and exercise ejection fraction to see if ventricular function impairment in hyperthyroid patients resulted from excessive beta-adrenergic activity (Abstract No. 115). Propranolol, which blocks the beta-adrenergic system, decreased the rest ejection fraction and prevented its rise during exercise, indicating that excessive beta-adrenergic activity (at least at the neurotransmitter or neuroreceptor level) is not the cause of ventricular dysfunction. The abnormality may be located at the level of the calcium channels, since verapamil did not have the same effect.

In a study from the University of Bonn, Germany, nuclear techniques were used for studying another drug, captopril. They could demonstrate the pharmacologic action of captopril on ejection and regurgitation fraction in patients with valvular heart disease (Abstract No. 307). Captopril was also used by Eva V. Dubovsky, MD, and her colleagues from the University of Alabama to determine whether hypertension in patients with kidney transplants is caused by renin secretion from the native or the transplanted kidney (Abstract No. 303).

More and more, nuclear techniques are being used in monitoring treatment. A group at the Harbor-UCLA Medical Center used washout of labeled aerosols from the lung to monitor patients being treated for *Pneumocystis carinii* pneumonia, a disease that can frequently complicate AIDS (Abstract No. 243). The clearance rate was faster during active infection than during the recovery state, and could be quantified to compare one type of therapy with another.

Several studies indicated that technetium-99m DTPA aerosols give comparable information to xenon-133 and krypton-81m in studies of patients with pulmonary embolism. A study from Hôpital Henri Mondorin in France showed the effect of patient position on the clearance of technetium-99m DTPA (Abstract No. 241).

Oncology

Oncology accounted for about 12 percent of the papers. Of the 65 papers on monoclonal antibodies, 20 were concerned with labeling and chemistry, and 15 human studies were reported. Melanoma, lymphoma, and colon cancer are the diseases most commonly assessed with monoclonal antibodies.

In a study from Yale, Ronald D. Neumann, MD, and his colleagues compared gallium-67 and indium-111-DTPA-anti-p-97 monoclonal antibody in patients with metastatic melanoma (Abstract No. 49). The sensitivity was comparable for each agent alone, but improved when the two agents were combined. Those tumors that accumulated gallium frequently would not accumulate the p-97 antibody and vice versa.

A study from M.D. Anderson Hospital in Houston showed that the sensitivity of monoclonal antibodies in melanoma depends on their site, being 100 percent sensitive in lymph nodes with decreasing sensitivity in other regions (Abstract No. 480). They showed the importance of using a 5 mCi dose in carrying out these detection studies.

Another study from the same group indicated that one of the problems is the nontumor distribution of the antibodies. Only a small concentration goes to the tumor, with large amounts going to other regions (Abstract No. 477). One antibody, the ZME-018 anti-melanoma antibody, has a preferential accumulation in the spleen, whereas the p-97 antibody has a preference for the liver.

A whole series of papers support the concept that SPECT defines the extent of tumors better than planar imaging.

Labeled Cells

There has been a great interest in labeled platelets. Monoclonal antibody labeling of leukocytes results in less damage to the cell than indium-111-labeled oxine. A group at Thomas Jefferson University used the B79.7 monoclonal antibody to study the kinetics of platelets and to compare one label to another (Abstract No. 100). A study at Yale showed significant differentiation of acute rejection from acute tubular necrosis using indium-111-labeled platelets in patients with renal transplants (Abstract No. 84).

Imaging Thrombi

Several groups reported techniques for detecting clots using iodine-131-anti fibrin monoclonal antibodies. A group at the Mount Sinai Medical Center in New York is investigating the use of technetium-99m-labeled low-density lipoprotein to identify atheroma (Abstract No. 561).

MIBG

Keigo Endo, MD, of Kyoto University, described the use of radioiodinated meta-iodobenzylguanidine (MIBG) to diagnose medullary thyroid cancer and neural tumors (Abstract No. 385).

The University of Michigan group continues to relate the uptake of this agent to the autonomic nervous system. It showed that over the counter sympathomimetic drugs have a very striking effect on the uptake of MIBG in the salivary

(continued on page 686)

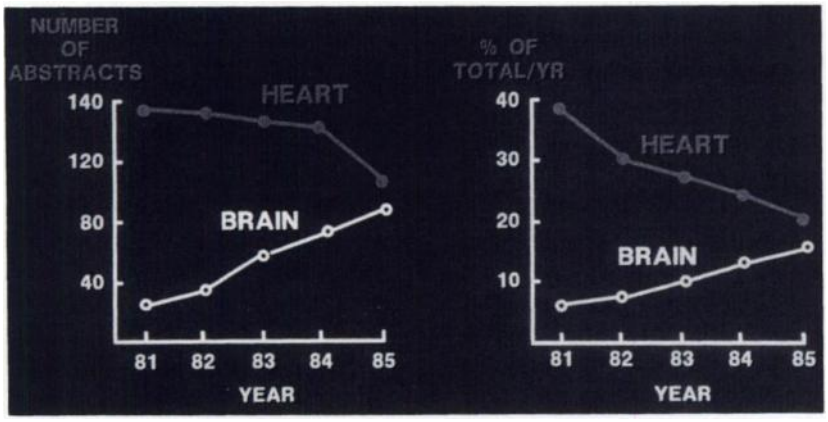

Figure 5. A comparison of heart and brain study abstracts presented at the SNM annual meeting since 1981.

(continued from page 685)

glands and in the heart (Abstract No. 138). If you get a false negative result when using this test to detect pherochromocytoma, you should consider whether the patient is taking over-the-counter sympathomimetic drugs. Their studies also indicate that sympathomimetic drugs have an effect on the systemic adrenergic nervous system.

This group also treated seven neuroblastoma patients with iodine-131 MIBG (Abstract No. 314). Three patients had subjective improvement, but none had objective improvement.

Gastroenterology

Dr. Tai Heng Yeh of Taiwan studied esophageal motility in patients with diabetes (Abstract No. 159). He found that 91 percent of his diabetic subjects had esophageal dysfunction, presumably on the basis of neuropathy. Rex Berlyn, MD, and colleagues from the University of Minnesota, studied the inhibitory effects of the dietary sugar substitute xylitol on gastric emptying, and correlated them with the decrease in caloric intake (Abstract No. 296).

Bone Density

Absorptiometry is an economically controversial issue in terms of third-party payment, but is unequivocally helpful in osteoporosis patients. Several studies were reported, including one from Heinz W. Wahner, MD, of the Mayo Clinic, who generated a probability estimate of vertebral fractures occurring in women depending on the measurement of bone density (Abstract No. 89).

Nuclear Magnetic Resonance

Thirteen papers and five posters were presented on the clinical use of NMR (Fig. 6). Nuclear medicine techniques can also play a role in developing the physiochemical basis of T-1 and T-2 measurements by NMR. We can take a lesion, such as a tumor, quantify T-1s and T-2s and relate them to physicochemical processes defined by nuclear medicine methods. We know that the NMR signals are related to cell size and water content, but we need to relate them to in vivo biochemistry measured with radioactive tracer techniques.

With NMR, we can now perform studies in young infants with no potential radiation risk. David H.I. Feiglin, MD, and his colleagues from the Cleveland Clinic reported the use of NMR in newborn infants to detect and monitor treatment for congenital heart disease (Abstract No. 5).

> "Chemistry relates the structure of the brain to the function of the mind. The discoveries concerning the chemical basis of physiology, particularly in mental functions, are as revolutionary as the discoveries in atomic physics at the turn of the century and the revelations in molecular biology and genetics in the 1950s."

Revolutionary Discoveries

In the classic book, *Principles of Psychology*, published in 1890, William James made this statement: "Chemical action must, of course, accompany mental activity, but little is known of its exact nature."

Nuclear medicine is the only technique that is able to study the chemical basis of mental function. The three different viewpoints for the study of the human brain are structural, functional and, now, chemical. Chemistry is what relates structure and function, and chemistry relates the structure of the brain to the function of the mind.

In my view, the discoveries concerning the chemical basis of physiology, particularly in mental functions, are as revolutionary as the discoveries in atomic physics at the turn of the century and the revelations in molecular biology and genetics in the 1950s.

Henry N. Wagner, Jr., MD

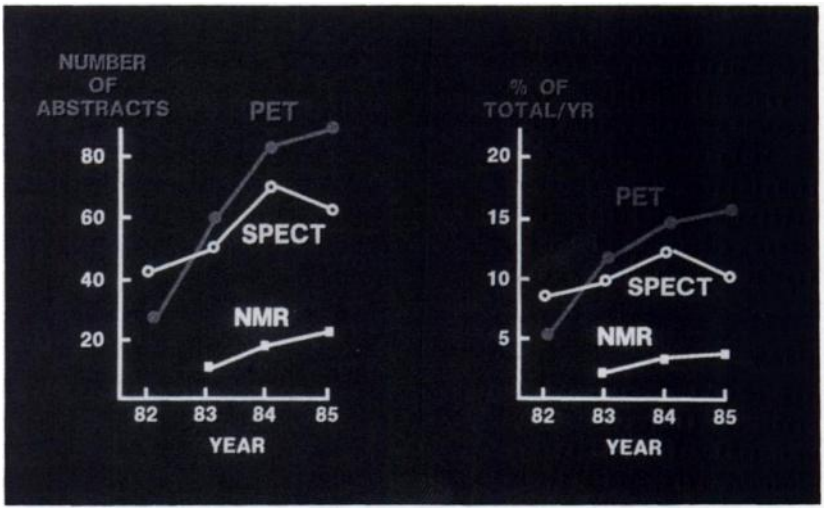

Figure 6. The number of NMR abstracts presented at the SNM annual meeting has doubled since 1983.