The Society of Nuclear Medicine 37th Annual Meeting

SCIENTIFIC HIGHLIGHTS 1990: THE UNIVERSE WITHIN

Continuing a thirteen year tradition, in the final session of the 37th Annual Meeting of The Society of Nuclear Medicine, held in Washington, DC in June, Henry N. Wagner, Jr., MD, reviewed the scientific highlights of the Meeting, connecting current findings with past and possible future directions of nuclear medicine.

The 37th Annual Meeting of The Society of Nuclear Medicine (SNM) this year documented the evolution of a new nuclear medicine in nearly 1000 oral presentations and posters. During the Meeting, one attendee told me that he felt as if he were “trying to take a drink of water from a fire hose.” To try to turn down the flow, I have chosen those highlights that reflect the overall direction of the field.

At the opening ceremony, Secretary of Health and Human Services Louis W. Sullivan, MD, reminded us that President Bush has designated the 1990s as the “Decade of the Brain.” Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) continue to be major forces in basic and clinical neurosciences, enabling us to delve deeper into the etiology and mechanisms of disease. Thus, I have chosen as the theme for this year’s Meeting, “The Universe Within.”

Combined display of PET and magnetic resonance imaging (MRI) images is becoming commonplace, as illustrated by Watanabe et al. from Tokyo University in Japan (No. 457), who used fast low angle MRI shots (FLASH) to obtain surface MRI images of the brain that revealed cortical anatomy as accurately as direct viewing of the exposed brain. Holcomb et al. from The Johns Hopkins Medical Institutions in Baltimore, Maryland showed that when there were great anatomical variants in normal persons, the structural information was of critical importance (No. 678).

Figure 1, which is from the presentation by Matsuda et al. from Kanazawa University Hospital in Japan, exemplifies the papers that dealt with co-registration of anatomical and nuclear medicine images (No. 743).

Conventional wisdom tells us that the spatial resolution of MRI is far greater than that of PET or SPECT. But, as anatomical studies improve their spatial resolution, we approach the cellular level, then move inside the cell and enter the domain of chemistry, where the spatial resolution is molecular.

Koestler has stated: “In biological systems, what we call structure are slow processes of long duration; what we call processes are fast processes of short duration, but they are all part of the same thing.” Up to now, the practice of medicine has been dominated by anatomy and histology. Only body fluids could be studied by chemistry. Nuclear medicine involves in vivo chemistry, a new domain of medicine. Nearly four centuries ago, Locke wrote: “Anatomy is absolutely essential to a surgeon, but that anatomy is likely to afford any great improvement in the practice of physics, I have reason to doubt. All that anatomy can do is show us the gross and sensible parts of the body.” PET and SPECT reveal new images of disease, not just

*Nos. refer to abstract nos. in the Proceedings of the 37th Annual Meeting of The Society of Nuclear Medicine.
new tests for old diagnoses, as illustrated by the technetium-99m (99mTc) HMPAO study shown in Figure 2.

The patient was a homeless person diagnosed as suffering from schizophrenia. The SPECT regional cerebral blood flow study revealed decreased blood flow in the inferior prefrontal cortex, a pattern sometimes seen in depressed patients. Re-examination of the patient, who had been incarcerated, led to the diagnosis of depression rather than schizophrenia. The patient was treated with antidepressive drugs, released from jail, and showed considerable improvement. Thus, we begin to close the circle between brain chemistry and behavior.

Half of all the reports at the Meeting involved PET or SPECT, the brain being the subject of the largest number of studies (Figure 3). The number of studies concerned with neuroreceptors has tripled since 1985, indicating the current emphasis on the mechanisms of intercellular communication (Figure 4).

Of the receptor papers, 40 concerned dopamine receptors; the next largest number involved muscarinic acetylcholine receptors. Speakers presented on areas including the biochemistry of pre-synaptic neurons; synthesis, storage and secretion of neurotransmitters; post-synaptic receptors; activation of second messengers; neurotransmitter metabolism; re-uptake by pre-synaptic neurons; neurotransmission in specific diseases; and the effects of drugs.

Iodine-123 Receptor Ligands

A major highlight of the Meeting was the large number of iodine-123 (123I) radiopharmaceuticals that have been used in human studies. Their broad application in the study of human disease and the care of patients will induce industry to make them broadly available and hasten their review by regulatory agencies. This plethora of agents has resulted from decades of advance in the knowledge of structure/activity relationships with respect to permeability of the blood/brain barrier and cells, affinity of binding to receptors, and better understanding of factors affecting non-specific binding. The development of 123I-labeled spiperone, which binds to D2 dopamine receptors, revealed the road to progress. First, the drug industry identified spiperone as a drug that binds to D2 dopamine receptors. After its successful labeling with carbon-11 (11C) and fluorine-18 (18F), spiperone was then labeled with 123I at the 4-prime position; but non-specific binding was too high for the agent to be useful. The spiperone molecule was then labeled in the 2-prime position, which made it possible for Yonekura et al. from Kyoto University in Japan to carry out the first successful images in human beings (No. 767).

Another class of dopamine receptor ligands—the benzamides—has also been used successfully to study human dopamine receptors in vivo, as described in a paper published by Costa et al. and in presentations at the SNM Meeting by Innis et al. from Yale University in New Haven, Connecticut in collaboration with Kung of the University of Pennsylvania in Philadelphia (No. 757) (Figure 5).
Other human studies of D2 dopamine receptors with $^{123}$I iodolisuride were presented by Mazière et al. from the Service Frédéric Joliot in Orsay, France (No. 263). Ido et al. from Tohoku University in Sendai, Japan described a D2 receptor ligand available in the $^{11}$C and $^{123}$I form (No. 300). Kessler et al. from Vanderbilt University in Nashville, Tennessee showed the important advantages of using $^{123}$I epidepride (No. 301) to facilitate mathematical modeling and reduce radiation dose. The longer half-life of $^{123}$I allows for longer studies than are possible with $^{11}$C or $^{18}$F. By the end of 12 hours there was essentially no non-specific binding of the $^{123}$I tracer. Not only dopamine receptors, but other receptors, including sigma receptors, which are abnormal in autopsy studies of patients with schizophrenia, can be examined (No. 376).

Radiopharmaceuticals for assessing muscarinic cholinergic receptors are available labeled with $^{18}$F, $^{11}$C, or $^{123}$I (No. 772). In Figure 6, a baboon study is shown in which both the active detro-and inactive levo-enantiomer were administered, greatly facilitating the correction for non-specific binding. Frey and colleagues from the University of Michigan in Ann Arbor reported several major advances with $^{11}$C tropanyl benzilate (No. 10). With this agent, they showed “parametric” images portraying the regional distribution of the rate constants describing delivery of the tracer to the receptor sites, as well as images of the regional “distribution volumes,” which reflect the number and affinity of available receptors (Figure 7).

The Michigan group also presented results of studies with a marker for presynaptic cholinergic neurons, iodobenzovesamical (No. 374). Thus, we now have markers for pre- and post-synaptic neurons of the dopaminergic (No. 823) and muscarinic cholinergic systems. Markers will eventually be available for many specific types of neurons, marking a breakthrough in clinical and basic neurobiology.

**Neuronal Bioenergetics**

Receptor imaging provides a way to assess specific neuronal populations. The exact roles that the receptors play in the process of neurotransmission remains to be determined. We need to know what affects their synthesis and metabolism. On the other hand, measurement of neuronal energy supply and the synthesis of neurotransmitters, such as dopamine, are now possible in human beings as well as animals. This enables researchers to identify regional hypo- or hyper-function states, which, in turn, reveal regions of unusual neuronal activity. An example was the study of identical twins by Resnick et al. from the University of Pennsylvania (No. 184). Twins offer a unique opportunity to investigate cause and effect relationships in diseases such as schizophrenia because an identical twin...
of a schizophrenic patient has a 50% chance of eventually developing the disease. Resnick observed that a twin at high risk of developing schizophrenia did not have any abnormal regions of glucose utilization. The schizophrenic twins had higher than normal glucose utilization in the caudate/putamen, but one could not be sure that the findings were not the result of prior neuroleptic drug treatment.

An example of how one combines studies of bioenergetics and neurotransmission was the study by Otsuka et al. of Kyushu University in Fukuoka, Japan (No. 745). As illustrated in Figure 8, in Parkinson's disease, accumulation of 18F L-DOPA was impaired, but regional glucose utilization patterns were normal; in parkinsonism resulting from other causes, such as tumors, there were abnormalities of both dopamine synthesis and cortical glucose utilization.

Barrio et al. (No. 57) from the University of California, Los Angeles (UCLA); Gjedde et al. (No. 58) from the Montréal Neurological Institute in Canada; and Pate et al. from the University of British Columbia in Vancouver, Canada (No. 769) increased our understanding of the modeling of 18F L-DOPA accumulation in the basal ganglia. Pate et al. showed that re-uptake into pre-synaptic vesicles does not play an important role in the time-activity curves, while amino acid transport processes at the blood/brain barrier do. Blocking the enzyme that converts L-DOPA to dopamine has a major effect on tracer accumulation, supporting the concept that the tracer is a useful index of dopamine synthesis.

The use of regional blood flow tracers, such as 99mTc HMPAO or 123I iodoamphetamine, is analogous to the use of thallium-201 (201Tl) to study the heart. They all help answer these questions: Is the brain abnormal, and, if so, how extensive is the abnormality? Is the pattern of distribution of the abnormality characteristic of a specific disease? In which regions should one examine the process of neurotransmission or the state of neuroreceptors? What is likely to happen to the patient? What is the course of the disease or the response to treatment? For example, in depressed Parkinson's disease patients, we focus on serotonin metabolism in the inferior pre-frontal cortex. For this purpose, 18F ethyl ketanserin, as presented by Moerlein and Perlmuter from Washington University in St. Louis, Missouri (No. 303), and 18F alterserin seem promising. Other tracers under development include 18F fluorobenzylpiperone (Mach et al., University of Pennsylvania; No. 835), 18F NCQ (Hallidin et al., Karolinska Institute, Stockholm, Sweden; No. 839), 11C methylenperidol (Suehiro et al., The Johns Hopkins Medical Institutions, Baltimore, Maryland; No. 754), and iodine-125 iodoethylpiperone (Guillevaux et al. INSERM, Tours, France; No. 372) for D2 dopamine receptors and 11C RO 15-788 (Price et al., Johns Hopkins; No. 8) and 18F flumazenil for benzodiazapine receptors (Loc'H et al., Service Frédéric Joliot; No. 818).

Moerlein, Washington University; No. 840).

Marking pre-synaptic neurons with tracers that are transported back into pre-synaptic vesicles helps identify disease but also is helpful because these receptors are the site of action of anti-depressive drugs as well as illicit drugs. For example, the dopamine transporter, or pre-synaptic re-uptake site, is believed to be related to the addictive effects of cocaine. Several new radiopharmaceuticals make it possible to examine the re-uptake process; 11C citalopram for serotonin (Scheffel et al., Johns Hopkins; No. 759); iodobenzovesamicol for acetylcholine (Jung et al., University of Michigan; No. 374); and two new compounds that bind to the dopamine transporter (Scheffel et al., Johns Hopkins and the National Institute of Drug Abuse; No. 54).

Figure 9 shows the results of administering a tracer that binds to the cocaine re-uptake site in pre-synaptic neurons in baboons (No.54). The sites of pre-synaptic uptake of acetylcholine have been examined with iodobenzovesamicol (No. 374) and a phenyl piperidino cyclohexanol tracer (Shureiki et al., State University of New York at Buffalo; No. 766).

Image of the Year

Researchers presented 127 99mTc papers, 33 concerned with HMPAO, 28 with isonitriles, and 27 with antibodies. These agents stimulated many major advances in SPECT scanners, including the use of fan beam collimation, dual tracers, and magnification to improve SPECT resolution. A major highlight, complementing the advances in both SPECT and PET radiopharmaceuticals, was improved SPECT instrumentation.

As Image of the Year, I have selected the images in Figure 10 from Ichihara, Matsuda et al. (No. 697) because of their exquisite spatial resolution and high quality. Many presentations were concerned with improvements in data acquisition and data processing of SPECT imaging, which are
essential if SPECT is to remain SPECTacular and not become suSPECT. SPECT requires the same rigor, modeling, quality control, and critical analysis that has been applied to PET. It behooves all persons now employing SPECT to pay careful attention to previous PET problems and solutions, so that they will not have to re-invent the wheel. Fortunately, many problems associated with rotating SPECT cameras in the past have been eliminated by the development of multi-detector ring SPECT scanners. Goddard et al. from Yale University provided an example of how the failure to adequately take into account variability in the arterial partial pressure of $^{13}$C dioxide, which has a profound effect on cerebral blood flow, can create pitfalls in both SPECT and PET measurement of regional cerebral blood flow; hyperventilation produces changes in the order of 30% (No. 343).

Clinical Research

SPECT has facilitated studies of specific clinical entities. For example, $^{123}$I isopropyl amphetamine (IMP) made it possible to examine patients with spinocerebellar degeneration by revealing gross abnormalities in blood flow to the cerebellum when structural changes were slight, as shown by Nagase et al. from Jikei University in Tokyo (No. 747). Similarly, Chen et al. from the University of Southern California in Los Angeles (No. 727) observed that while 40% of patients with central nervous system lupus erythematosis had MRI abnormalities, a far greater number had striking abnormalities in SPECT. Tatsch et al. from the University of Munich in the Federal Republic of Germany (FRG) (No. 499) examined patients with human immunodeficiency virus (HIV) infections and concluded that in HIV infections: (1) there were measurable alterations in cerebral perfusion even in the absence of superimposed opportunistic bacterial or other infections; (2) changes were observed frequently even in the early stages of disease; and (3) abnormalities were usually shown by SPECT before structural lesions could be detected by computed tomography (CT) or MRI.

In amyotrophic lateral sclerosis, Waldemar et al. from Rigshospitalet in Copenhagen, Denmark (No. 462) found that when a thalamic abnormality involved the posterolateral thalamus, there were usually no associated cortical effects; but when the lesion was in the medial thalamus, there was a striking decrease in cortical blood flow and abnormalities of cognition.

Functional Localization

The degree of specialization of regions of the brain has been a major question in neuroscience for centuries. Measurement of regional blood flow and glucose utilization provides important information. Techniques can disclose functional as well as structural abnormalities. A decrease in glucose utilization resulted from deafferentation of the primary and secondary visual cortex in the patients studied by Wong et al. from the Wadsworth VA Medical Center in West Los Angeles (No. 750). In sharp contrast, studies by Kanno, Uemura et al. from the Research Institute of Brain and Blood Vessels in Akita, Japan (No. 221) showed that glucose utilization (and presumably neuronal activity) in the primary and secondary visual cortex was abnormally increased in persons who had been blind for years but who continued to live active lives. Thus, it seems that the visual cortex is concerned with representation of information about external space, rather than just vision.

Mental Function and Brain Chemistry

Berman and her colleagues at the National Institute of Mental Health in Washington, DC (No. 179) showed the importance of controlling the focus of the subject's mental
functioning as much as possible during the examination of brain chemistry. The concept that the brain can be put at "rest" is a misconception. The performance task should reflect the particular mental function of concern. Various tasks, including a "delayed alternation task," which involved recent active memory and short-term decision making, activate frontal lobe neuronal activity.

Clinical PET/SPECT

Immediate clinical applications of PET/SPECT to the brain fell into three major areas: brain tumors, dementia, and epilepsy. The principle that PET successes are translated into SPECT applications was seen again. For example, Carvalho et al. from Harvard Medical School in Boston, Massachusetts used $^{201}$Tl and $^{99m}$Tc HMPAO studies to determine whether a patient's symptoms were due to recurrent tumor or the effects of radiation therapy (No. 496). An avid accumulation of both agents greatly increased the probability that the lesions were tumorous.

In partial complex epilepsy, an important characteristic of SPECT studies of regional cerebral blood flow is that the patient can be injected at the start of a seizure and at various times thereafter, although this requires that the patient be monitored continuously in a special unit. The studies by Newton et al. from Austin Hospital in Heidelberg, Australia (No. 18) showed that within 30 seconds of the end of a seizure, the site from which the seizure originated in the lateral temporal lobe (hyperperfused during the seizure) became hypoperfused, while the medial temporal lobe continued to have high blood flow.

Biersack, Grunwald et al. from the University of Bonn, FRG (Nos. 17, 749) studied patients with temporal lobe epilepsy and found that in certain patients SPECT indicated a greater abnormality in the temporal lobe on the side opposite the site from which other data indicated that the seizures arose. When the left temporal lobe was resected, in five of the six patients, memory was impaired after surgery due to involvement of the right temporal lobe as revealed in the SPECT studies.

The amobarbital (WADA) test, used to assess possible speech or memory complications of temporal lobe resection in patients with epilepsy, was improved by adding $^{99m}$Tc HMPAO to the amytal at the time of injection into the internal carotid artery (Jeffery et al., Johns Hopkins; No. 461), which supplies the anterior and middle cerebral arteries in all cases, but the posterior temporal lobe only about 20% of the time.

In Figure 11, the upper figure is from a normal person. The lower left is from a patient whose medial temporal lobe is not perfused by an internal carotid injection. The lower right is from a patient whose medial temporal lobe is well perfused, and the WADA test would be valid. The purpose of injecting the anesthetic amytal into the carotid artery is to predict whether speech or memory abnormalities are likely to occur if a large part of the temporal lobe is resected. Using a high resolution SPECT scanner, Jeffery et al. were able to image the distribution of the amytal after injection and, thus, determine whether the medial temporal lobe was in fact being perfused with the anesthetic. If the region was not perfused, the test was not valid in predicting whether memory loss would be likely to occur after temporal lobe resection. In such cases, the posterior cerebral artery must be injected, although this is at times a complex procedure, often with untoward consequences.

The value of improved spatial resolution of both PET and SPECT can be seen in studies of epilepsy, such as those done by Derenzo et al. from the University of California at Berkeley (No. 176) and in the studies by Jones et al. from the NIMH, during which a 4 mm resolution was achieved by the use of special collimation (No. 699). With the improved resolution, the NIMH group showed that iodinated quinuclidinyl benzilate bromate (QNB) reflects the state of muscarinic cholinergic receptors and not just regional cerebral blood flow. The use of a rotating multi-slit aperture system made it possible for Rogers et al. from the University of Michigan (No. 257) to build a high resolution SPECT system that uses magnification to yield a 1 mm resolution in mice, 2 mm in rats, and 5 mm in dogs. Thus, in small animals, SPECT spatial resolution has exceeded that of PET, which is is limited by the 1-2 mm range of positrons in tissue.

Another example of a clinical SPECT procedure requiring both a high resolution scanner and quantification was the study by Van Heerden et al. from Johns Hopkins (No. 736). Figure 12 shows that Van Heerden used $^{99m}$Tc HMPAO to determine the effects of balloon occlusion of
the internal carotid artery on blood flow in the pre-operative assessment of patients with intra-cranial aneurysm not amenable to surgery, who were, thus, candidates for ligation of the internal carotid artery. A second injection was made after trial occlusion of the internal carotid artery with an inflatable balloon to reveal quantitatively the degree of reduction in regional cerebral blood flow. Quantification is necessary because there is an absolute threshold below which complications of the ligation are likely to occur.

Dual Isotope SPECT

DeVous et al. from the University of Texas Southwestern Medical Center in Dallas reported a major advance using $^{131}$IMP and $^{99m}$Tc (No. 730). Figure 13 shows DeVous’ images of regional cerebral blood flow measured first with $^{131}$ IMP and then with $^{99m}$Tc HMPAO after the administration of a carbonic anhydrase inhibitor to increase cerebral blood flow. The researchers imaged the distribution of both tracers simultaneously, which greatly facilitated co-registration of identical regions. The use of both tracers makes it possible to carry out perturbation studies under any circumstances, or in any place outside the nuclear medicine department, and subsequently bring the patient to the SPECT scanner for the simultaneous imaging of regional blood flow during both states at the time the patient is injected. This dual isotope capability is a unique advantage of SPECT.

Obsessive Compulsive Disorder

Goodman et al. from Yale University (No. 183) found increased metabolic activity in the anterior and posterior cingulate gyrus of the prefrontal cortex in patients with obsessive compulsive disorder compared to normal controls, but the differences were not great and the overlap was large. Another group examined the effect of drug treatment on similar patients (No. 182).

Fujibayashi et al. of Kyoto University (No. 810) demonstrated a striking decrease in brain glucose utilization, which correlated with a decrease in the accuracy of learned avoidance behavior in mice with a genetic abnormality that caused accelerated aging. The deficiency was not reflected in overall neuronal mass because regional blood flow and extraction efficiency of IMP failed to decrease. Sgouros et al. from New York Hospital-Cornell Medical Center in New York City (No. 585) reported that irradiation of the brain of rats with 1000 rad increased the pentose pathway from 2% to 30% of total glucose metabolism, which might prove to be a general indicator of damage.

The Chemistry of the Unconscious

Sensory or motor activation of the brain results in regional increases in glucose utilization, but the effects are small, amounting to only a few percent of total brain glucose utilization. Last year, Ackerman and Lear showed that these small transient increases are chiefly the result of anaerobic glucose metabolism. As in the case of muscles, it takes time before oxygenation can keep up with the neuronal demands for energy. What then are the factors influencing global cerebral glucose metabolism? Many studies indicate that the coefficient of variation of glucose utilization among normal persons is about 15% to 20% and that it is as high as 10% within the same persons studied at different times. Most people have assumed that the variance is chiefly technical, but Camargo et al. from Johns Hopkins explored whether biological factors were involved (No. 267). Technical factors including errors in measuring the plasma activity curves introduced large errors reported Chen from UCLA (No. 662), but there are biological factors as well. For example, 70% of the variance in glucose utilization was attributable to regions of the brain that included the limbic system, while only 10% involved the sensory/motor and visual cortices and the cerebellum.

An important clue to explain what causes global glucose utilization was provided by the study by Beradi et al. from the National Institutes of Health in Bethesda (No. 738), which indicated that memory performance in healthy, elderly subjects correlated with resting glucose utilization. Presumably, basal glucose utilization of the brain reflects unconscious neuronal activity, involving memory and autonomic control of the cardiovascular, gastrointestinal, and other organ systems. Only a small amount of neuronal activity seems to be involved in conscious mental activity. Thus, a major advantage of PET/SPECT studies of the brain is that we can study regional blood flow and biochemical changes associated with unconscious as well as conscious mental function.
Will Rubidium-82 PET Replace Thallium-201?

This was an important topic at the SNM Meeting. Maclntyre et al. from the Cleveland Clinic Foundation in Ohio compared the two agents (No. 395) and found that the accuracy of rubidium-82 PET studies was significantly better. Ohtani et al. of Kyoto University (No. 151) advocated a double injection method, rather than the delayed “re-distribution” procedure. When compared to normal wall motion, hypokinesis, and akinesis as standards, these investigators found that the double injection method was better, and should be the standard of comparison with FDG or rubidium-82 studies.

Will Technetium-99m Isonitriles Replace Thallium-201?

The relative merits of $^{99m}$Tc isonitriles and $^{201}$TI studies were widely debated at the Meeting. A basic study of cultured myocytes by Piwnica-Worms et al. of Harvard Medical School helps answer this question (No. 120). These investigators provided evidence that isonitrile retention in myocytes is related to mitochondrial function. Since $^{201}$TI reflects the plasma membrane transport of sodium and potassium ions, the two agents reveal two different aspects of myocyte function that may have different sensitivities for the detection of myocardial disease.

Will Adenosine Replace Dipyridamole?

A potential advantage of adenosine over dipyridamole in increasing myocardial blood flow is that the agent is very short-acting, so that if toxic effects occur, they are of short duration (Nos. 108, 110). Adenosine is particularly useful in patients unable to adequately exercise, but it should not be used if it is believed that the patients would be unable to tolerate the exercise.

Innervation of the Heart

Metaiodobenzylguanidine (MIBG) was the first agent used to measure the state of pre-synaptic neurons in the heart, and it continues to be a sensitive indicator of disease. Wakasugi et al. from the Center for Adult Diseases in Osaka, Japan (No. 533) showed that abnormalities of beta adrenergic innervation, which become abnormal while blood flow remains normal, are the most sensitive indicators of myocardial damage from adriamycin.

Carbon-Ill meta-hydroxyephedrine, developed by the University of Michigan group is a more specific agent for measuring beta adrenergic innervation (No. 532). Carbon-Il1 hydroxyephedrine was useful for imaging of pheochromocytoma (No. 158). The advantage of the new beta adrenergic compounds is that mathematical modeling has been developed for quantification. Beta adrenergic innervation was impaired in patients with dilated cardiomyopathy as...
tracers for the study of cancer patients continue development at University Hospital, Groningen, The Netherlands (No. 163) and at Washington University (No. 164). The group under Strauss at the German Cancer Research Center in Heidelberg, FRG continues to use PET to monitor patients with bronchogenic carcinoma (Nos. 247, 269), colorectal cancer (Nos. 400, 444, 779), melanoma (No. 403), and liver metastases (No. 780). Vander Borght et al. from the University of Louvain Medical School in Brussels, Belgium used $^{11}$C thymidine to monitor liver regeneration as well as to assess tumors (No. 602).

An example of progress that continues to be made in the use of monoclonal antibodies in cancer is the study of Yeh from Memorial Sloan-Kettering Cancer Center in New York City (No. 145), who used an $^{125}$I antibody to gangliosides to detect lesions in patients with neuroblastoma. Results were better than with MIBG or phosphonates.

A new radiopharmaceutical likely to achieve widespread use is $^{99m}$Tc-labeled antigranulocyte antibodies. A study by Duncker et al. from the Hospital de Sant Pau in Barcelona, Spain found that phosphonates detected only 53% of bone metastases, while the antibody studies of bone marrow detected 78% (No. 185). Combined bone marrow and bone scanning provided more complete detection of osteolytic and osteoblastic metastases. Striking bone imaging was shown by Hawkins and the group from UCLA (No. 402), as shown in Figure 14.

Neither time nor space permits description of many other excellent papers, including studies of the effects of drugs in diseases such as diabetic neuropathy (No. 601), the detection of thrombi with $^{99m}$Tc tracer (No. 287), the combined use of HMPAO and DTPA administered by aerosol to detect pulmonary fibrosis (No. 271), and many others. All document the broad spectrum of applications of the tracer principle to the diagnosis, prognosis, treatment, and study of the pathogenesis of human disease.

Over three decades ago, the cartoon in Figure 15 was shown at the meeting of the International Atomic Energy Agency in Vienna, Austria. It reveals the mind set of the pioneers in the field at that time, who never dreamed that nuclear medicine would develop to the advanced degree seen at this year’s SNM Meeting. Advances have been evolutionary, at times revolutionary, in radiopharmaceutical and instrument development, in basic science and clinical research, and in applications to patient care. The major message of the 1990 Meeting can be expressed in the words of the late Dag Hammarskold: “Only he who keeps his eye fixed on the far horizon will find the right road.” It is now abundantly clear that the road of nuclear medicine has two lanes: PET and SPECT.

Henry N. Wagner, Jr., MD
The Johns Hopkins Medical Institutions
Baltimore, Maryland