Molecular Medicine: From Science To Service

Henry N. Wagner, Jr., MD presents a view of the scientific highlights of the 38th Annual Meeting of The Society of Nuclear Medicine.

The 1991 Annual Meeting of The Society of Nuclear Medicine was held in Cincinnati, Ohio in June. The following article is derived from a presentation given by Dr. Wagner, professor of medicine, radiology, and environmental health sciences at The Johns Hopkins Medical Institutions, at the final session of the meeting—a tradition now in its 14th year.

IN THE DAYS IMMEDIATELY AFTER WORLD WAR II, the use of radioactive materials in medicine was called atomic medicine. Most studies at that time involved radioactive carbon, tritium, iodine, iron and chromium. Atomic medicine became nuclear medicine. Today, the field could be called "molecular medicine," the name justified by the hundreds of radiolabeled molecules that could be used for diagnosis and treatment. More than any other medical specialty, nuclear medicine translates advances in molecular biology and biochemistry into ways of caring for sick human beings.

Diagnostic and therapeutic radiotracers can be thought of as "nanoDx" and "nanoRx" probes. The prefix nano indicates the nanomolar or picomolar sensitivity of the measurements, and the suffixes Dx and Rx indicate that these probes can be used to seek and treat abnormalities within the body. Labeled with therapeutic quantities of radioactivity, the probes can restore abnormal chemistry to normal in specific organs of the body. Injected intravenously, the hundreds of billions of molecular probes search throughout the body until they encounter recognition sites where the molecules' shape, water and fat solubility, and charge lead them to bind. The probes can then be detected and measured by their emitted photon radiation.

Figure 1 is a model of the nanoDx probe called dexetimide that has been used to map out the distribution and quantity of muscarinic acetylcholine receptors (#300). Because dexetimide can be labeled with fluorine-18 (18F) or iodine-123 (123I), muscarinic acetylcholine receptors can be imaged quantitatively by either PET or SPECT. The inactive enantiomer of dexetimide, called levetimide, has all of the properties of the dexetimide molecule except that it does not bind to acetylcholine receptors, and therefore can serve as a control in vivo measurements of acetylcholine receptors (Figure 2).

Molecular medicine can characterize many illnesses by abnormalities in the information-transfer process involving substrate transport, enzymes, and neuron-to-neuron transmission of action potentials. In the process of neurotransmission, electrical depolarization stimulates the secretion of neurotransmitter molecules, such as dopamine, from vesicles at the end of pre-synaptic neurons. These molecular messengers cross the synapse and bind to specific receptor molecules on post-synaptic neurons that recognize them by their configuration and electrical charge. Parkinson's disease and Huntington's disease involve the dopaminergic system, the subject of many presentations at the meeting.

Thirty-six presentations involved dopamine. Some were among the 112 papers or posters that employed radioiodinated compounds. Of these iodine papers, 35 dealt with the development of in vivo markers for pre- and post-synaptic neurons. The approval by the Food and Drug Administration (FDA) of 123I-labeled isopropyl amphetamine was an important factor in producing the 22 papers based on the use of this compound. FDA approval of three technetium-99m (99mTc) compounds brought about a burst of important research, much of it applicable to the development of practice parameters. Forty-eight papers involved HMPAO for the study of regional cerebral blood flow, 31 papers involved 99mTc-isonitriles for measur-
The younger generation takes for granted the use of computers in nuclear medicine—the field that more than any other paved the way to widespread use of computers in medicine. The same thing will happen with cyclotrons and PET scanners. This meeting continued to support the concept illustrated in Figure 3, that PET and SPECT have a parent and child relationship—it is far easier to label molecules with $^{13}C$ than with $^{123}I$ or $^{99m}Tc$. Nevertheless, PET successes are translated in SPECT applications on an ever-widening scale. The cyclotron and PET will continue as the core of nuclear medicine, with advances extending from the core to hospitals, which will soon be able to purchase positron-emitting radionuclides from regional radioischemies. Applications will extend still further through the development of radiopharmaceuticals labeled with the workhorses of nuclear medicine, $^{99m}Tc$ and $^{123}I$.

Of the 117 presentations involving positrons, $^{18}F$ was the most widely used radionuclide, and $^{18}F$-deoxyglucose was the number one radiolabeled molecule with 75 presentations. Twenty-one $^{18}F$ presentations involved pre- or post-synaptic neuronal markers. Eighty-four papers involved neuroreceptors and 36 of these dealt with the dopaminergic neurotransmission system—remarkable since the first papers on imaging neuroreceptors were presented as recently as 1984. Twenty-eight papers using $^{11}C$-labeled compounds involved the process of synaptic neurotransmission.

Among the highlights were the reports on the dopaminergic system. As shown in Figure 4, the amino acid L-dopa is converted to the neurotransmitter dopamine. When stimulated by appropriate numbers of pre-synaptic axonal action potentials, dopamine is released from vesicles, crosses the synapse, and binds to post-synaptic receptors. Any dopamine that is not bound by post-synaptic receptors is taken back into the pre-synaptic neuron via re-uptake sites where the dopamine molecules are either metabolized by enzymes or re-incorporated into vesicles. Parkinson's disease is characterized by deficiencies in the pre-synaptic dopaminergic neurons. Huntington's disease is characterized by abnormalities in the post-synaptic neurons. Brownell et al. (#304) developed a model of Huntington's disease in monkeys by injection of quinoline, the glutamate-receptor agonist, into the caudate and putamen. The post-synaptic neurons were impaired, while the pre-synaptic neurons remained metabolically intact.

In another study (#680), the neurotoxin MPTP was used to produce a model of Parkinson's disease, which destroys pre-synaptic neurons. Figures 5 and 6 illustrate the images of pre-synaptic neuronal accumulation of a cocaine analogue that can be imaged by SPECT (Figure 5) and PET (Figure 6). In a baboon where the neurotoxin MPTP was injected into an internal carotid artery, the accumulation of cocaine analogue was eliminated, while the accumulation of $^{11}C$-NMSP, a marker of post-synaptic neurons, remained intact. The baboon showed no signs of Parkinson's disease even though the basal ganglia on one side were severely impaired—supporting the concept.
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that molecular diagnosis can often precede clinical diagnosis of disease. This important concept makes possible prevention of secondary effects by early molecular diagnosis. Only a limited amount of dopamine is needed to avoid the symptoms and signs of Parkinson’s disease, and apparently it need not be distributed bilaterally.

Because of the 13-hour half-life of $^{123}$I, measurements can be carried out for over 20 hours, to a time when essentially all of the tracer is bound to the neurons with very little non-specific binding. This makes it possible to use simple, inexpensive probes to detect the abnormalities of presynaptic neurons. A 24-hour uptake can be measured in a manner analogous to the use of non-imaging probes to diagnose hyper- or hypo-thyroidism. It is predictable that in patients with movement disorders, PET imaging, SPECT imaging, and simple probe systems will be used frequently to make molecular diagnoses at an early stage of disease.

**PET and SPECT Advance Together**

Despite the many advances in the development and use of $^{123}$I tracers, the power of PET will continue, as illustrated in the study by Shiue et al from Creighton University in Omaha (#362). Taking advantage of cyclotron-produced $^{11}$C, these investigators synthesized a whole series of amphetamine analogues in studies of substance abuse. Their work illustrates that it is not necessary to divide PET centers into research or clinical facilities. The Creighton PET Center was established primarily for clinical service, but the group has made important research contributions in the study of the molecular mechanisms of abused drugs. They showed, for example, that MDMA (“ecstasy”) does not block post-synaptic dopaminergic receptors. The best thing that could happen for PET research is that the results be applicable to patient care. The public is vitally interested in studies that help people. If cyclotrons and PET continue their rapid growth, the public can benefit from a continual stream of important, new labeled molecules that will be translated into more widespread application by the use of $^{123}$I and SPECT. If one looks back at the annual SNM meetings since 1986, PET studies were followed in steady progression by SPECT studies. Both now account for half of all the nearly 900 papers presented at the 1991 meeting. Stated briefly, if SPECT can do it, do it with SPECT. PET will always be able to do things that SPECT can’t do. If SPECT can do tomorrow what PET is doing today, PET will go on to do other things.

**Molecules of the Mind**

Studies of the brain fall into three major categories: blood flow, metabolism, and neuronal markers. The rapid rise in studies of receptors (84 papers) has been possible because many drugs have been developed that act by binding to receptors. These drugs can usually be labeled with $^{11}$C or $^{18}$F. The number of studies of brain tumors with PET radiotracers began in 1988, and has increased since then. Over the next 5-10 years, both PET and SPECT are likely to increase in the study of patients with cancer, as in the studies of the heart and brain. Dementia, epilepsy, and stroke were extensively investigated, and drug abuse has become an area of increasing interest. A whole session was devoted to depression. Several studies reported reduced glucose metabolism or blood flow in the frontal cortex of depressed patients. Mayberg et al (#717) observed increased binding of $^{11}$C carfentanil to opiate receptors in the anterior temporal and inferior frontal lobes of depressed patients. They observed a 31% increase in binding of carfentanil to opiate receptors, suggesting that, as in the case of temporal lobe epilepsy, there may be a relationship between the opiate system and neuronal activity reflected in glucose utilization.

In the study of regional cerebral blood flow, there were 41 papers using HMPAO, with 21 involving $^{123}$I-isopropyl amphetamine. Progress was reported by Devous and his colleagues from the University of Texas Southwestern Medical Center (#266), describing the simultaneous measurement of $^{123}$I and $^{99m}$Tc radiotracers in studies of the effects of mental stimulation on regional cerebral blood flow. The patient was injected under controlled conditions with $^{123}$I-IMP and then with $^{99m}$Tc-HMPAO after sensory stimulation or administra-
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tion of a drug such as Diamox. Both radionuclides are then imaged simultaneously, which not only halves the examining time, but also eliminates problems of positioning or movement. This dual-isotope method was also validated by Juni et al. from William Beaumont Hospital in Royal Oak, Michigan (#202), who compared the number of vascular defects seen with IMP with those seen with HMPAO. In a few patients, more defects were seen with IMP.

Nakagawara et al. from Sapporo, Japan (#697), compared 99mTc-ECD and 123I-IMP in patients with cerebrovascular disease. Because the extraction efficiency of ECD is lower, this agent was less able to show reactive hyperemia, the so-called "luxury perfusion," in patients with stroke. Regions of increased regional cerebral blood flow were seen with IMP and HMPAO that were not seen with ECD. Podrecka et al. (#348) showed that, with care, one can get very good reproducibility in serial measurements of HMPAO brain uptake. Several presentations described how stimulating cerebral blood flow with Diamox improves the detection and delineation of lesions (#695, 698, 700, 701).

Activation of the brain by performance tasks was carried out in studies with FDG, oxygen-15 (15O) and, increasingly, with SPECT measurements of regional cerebral blood flow. For example, in a study by Fazio et al. from Milan and Rome (#479), memory circuits of the brain were mapped out in patients with amnesia using FDG (Figure 7). In comparison with normal persons, the patients had a significant reduction of metabolism in interconnected cerebral regions, including the hippocampal gyr, thalamus, and cingulate cortex, and other cortical structures.

Momose et al. from Tokyo University (#185) used 15O-water to assess the response of normal and schizophrenic subjects to saccadic and anti-saccadic eye movements stimulated by watching parallel bar lights. The saccade inhibiting system of schizophrenic subjects was impaired, and PET objectively measured the degree of impairment (Figure 8). The same group also showed that activation of the visual cortex by visual stimulation persists for 15 minutes after the eyes have shut.

This persistent cerebral activity was not seen in the case of hearing or somatosensory stimulation (#693).

Modeling of SPECT studies of regional cerebral blood flow was illustrated by Tanada and associates from Ehime, Japan (#10). Advantages not only in subjective interpretation, but also in quantification result from the use of high resolution or ultra-high resolution SPECT systems as illustrated in the report of Matsuda et al. from Kanasawa University Hospital (#724, Figure 9). This paper exemplifies the increasing use of co-registration of anatomical information from MRI with molecular information from PET, and regional blood flow measurements with SPECT. With the ultra-high resolution system one can detect very small changes and by proper co-registration assign them to specific brain structures. Quantification is improved with better spatial resolution because "partial volume" effects are reduced.

An advance in instrumentation was presented by Barrett et al. from the University of Arizona (#875). Their three-dimensional SPECT imaging system, with the spatial resolution of 5-6 mm, under advanced stages of development, is well suited to dynamic SPECT because the system has no moving parts. The designers have paid particular attention to correcting for attenuation and scatter. Barrett stated that "SPECT quantification has acquired a bad name." That, he says, no longer need be the case.

Cholinergic Neurotransmission

The molecular dissection of a mental disease was illustrated by the studies of the cholinergic system by the group at the University of Michigan under the leadership of David Kuhl, who this year presented an outstanding nuclear pioneer lecture. Lee et al. (#143) presented parametric images of the brain indicating regional cerebral transport of the radioligand TRB that binds to muscarinic cholinergic post-synaptic receptors. Other images portrayed the distribution volume, which reflects the regional availability of acetylcholine receptors. In patients with Alzheimer's disease, the transport of the tracer to the receptors was reduced in the temporoparietal and other re-
gions, but the acetylcholine receptors were normal. The same group showed that increases in regional cerebral blood flow associated with visual stimulation in normal persons did not interfere with the measurement of the regional availability of benzodiazepine receptors, which were not affected (#301). These two papers illustrate the robustness of the mathematical modeling used in kinetic analysis of receptors. It was possible to clearly separate the delivery of the tracer to various regions from the receptor density within the regions, even in the presence of great increases or decreases in the delivery of the tracer to the receptors. Separate parametric images showed regional transfer rate constants or receptor availability. Extending the pioneering work of Reba and Eckelman, they found that the post-synaptic receptors are intact in Alzheimer's disease. Perhaps the defects in Alzheimer's disease are in pre-synaptic neurons. This question is likely to be answered at next year's meeting now that pre-synaptic neuronal markers are available and their use validated.

**Other Neuroreceptors**

Advances in the development of better ligands for examining serotonin receptors were illustrated by Sadzot et al from Liege, Belgium, using 18F-altanserine, which was more selective than previously described tracers. Miletich et al from the National Institutes of Health and Georgetown University used 18F-fluorothienylcycloexylpiperidine (FTCP) to assess the excitatory amino acid neurotransmission process (#420). Delforge et al from Orsay, France presented a model for in vivo quantification of D2 dopamine receptors, the most widely studied receptor system to date. This group also found increased striatal dopaminergic D2 receptor density in Rett syndrome measured with 123I-lisuride (#448). Whether D2 dopamine receptors are increased in some patients with schizophrenia remains unclear, but improved modeling and increasing numbers of studies over the next few years are likely soon to provide the answer.

In Parkinson's disease, Tatsch et al from the University of Munich (#445) were able to use 123I-iodobenzamide to distinguish the density of dopamine receptors in patients with Parkinson's disease from those patients with variants of the illness, such as progressive supranuclear palsy. In the latter, receptors were impaired, but not in idiopathic Parkinson's disease. These findings are important for treatment. Patients with normal post-synaptic receptors are likely to benefit from treatment with receptor agonists such as bromocryptine, or the administration of the dopamine precursor L-dopa. Those patients with impaired receptors are not.

A study by Bartenstein et al from Hammersmith Hospital in Queen Square, London (#215) represents the first example of being able to assess endogenous secretion of a neurotransmitter by competitive inhibition of the binding of a radiotracer. In patients with petit mal epilepsy, induced by hyperventilation, there seemed to be release of endogenous enkaphalin resulting in a more rapid washout of 11C-diprenorphine from the brainstem and lateral parietal cortex. These studies need to be extended by mathematical modeling to be certain that increased blood flow is not a factor in the observations. Price et al (#648) used such modeling and 11C-flumazenil to examine benzodiazepine receptors.

**Focus on the Heart**

Presentations concerned with the heart have increased steadily since 1985 as a result of the introduction of thallium, SPECT, and more recently, the new technetium blood flow agents. As in the case of studies of the brain, both PET and SPECT papers have increased in parallel, reflecting the synergistic relationship of the two modalities. There were 77 papers on thallium, 30 on isonitriles, 22 on teboroxime, and relatively few on ventricular function.

Nuclear cardiology illustrates how PET and SPECT can make important contributions to the development of practice guidelines, which are now under development as part of programs of "managed care" that are increasing in number in...
Many reports indicated how nuclear cardiology can help predict and assess the effects of revascularization procedures, help avoid needless coronary angiography, and improve the diagnosis of coronary artery disease. With both thallium-201 (201TI) and 99mTc-teboroxime, Taillefer et al of Montreal (1146) were able to reveal normal regional myocardial blood flow despite the presence of angiographic evidence of coronary stenosis. Presumably, collateral vessels compensated for the stenotic lesions, or the lesions were subcritical. Such findings have the potential for greatly reducing needless revascularization procedures.

Differences among the various myocardial perfusion agents were illustrated by DiRocco et al of Bristol-Myers Squibb (#163), who showed that the agents differ in the so-called "roll-off" of tracer activity in regions of high blood flow, as in an exercise study. The extraction rolls off at high blood flow because the extraction efficiency falls. Teboroxime had the least roll off because of its higher extraction. The degree of liver accumulation of the tracer is another difference among myocardial perfusion tracers, as illustrated in the Montreal study (#46). Rapid development of new technetium-labeled myocardial perfusion tracers continues. An important advance in 99mTc chemistry was described by Duatti et al from Italy and France (#69), based on the use of a new class of compounds, the nitritodithiocarbamates. In their studies of different species, the pig was the only animal where this tracer was not extracted by the heart, a finding different from that of Deutsch and his colleagues, who found that the pig was the best model with other technetium compounds. Another interesting myocardial perfusion agent was described by Marmion et al (#70) from Italy and Cincinnati. The agent had a rapid clearance from the blood, prolonged retention in the heart, and little kidney uptake. Thus, while the presently available 99mTc tracers represent important advances, there is still room for thallium studies, with improved myocardial perfusion agents just around the corner.

Another advance in nuclear cardiology was simultaneous, double-isotope imaging with 201TI and 99mTc. Shimada et al from Jikei University, Tokyo, and Shimadzu Corp., Kyoto (#638) used multiple regression analysis to separate 201TI photon energy from that of 99mTc. They obtain a complete energy spectrum for each voxel, so that they can record activity voxel by voxel at 64 different photon energies, and then correct for the technetium scatter in the thallium window. They applied the method to the study of the thyroid.

A group from Siemens, working with investigators at Cedars-Sinai Medical Center in California (#388) applied the same principle to the heart. We may soon see studies where thallium is injected at rest and then the patient is exercised and injected with a technetium blood flow agent. Both radionuclides can then be imaged simultaneously. Comparisons with serial studies using only 99mTc tracers are needed.

Beanlands et al from the University of Michigan (#506) evaluated copper-62 (62Cu) PTSM as a myocardial perfusion agent, before and after the administration of adenosine. The goal is to make PET studies possible without a cyclotron by using tracers obtained from a generator. Unfortunately, the 62Cu parent has a 9-hour half-life, and thus would require regional centers for efficient preparation and distribution. Gallium-68 tracers are also under development—the parent, germanium-68, has a long half-life, and would be a more feasible source for PET tracers.

Of the metabolic studies of the heart, there were 25 papers employing FDG, and 5 involving acetate metabolism. Myocardial viability was a major topic. It is quite possible that a segment of the myocardium may be viable, but not improvable by revascularization. Illustrating the importance of...
radiotracer technology in prognosis as well as diagnosis. Tamaki et al from Kyoto (#549) looked at the prognostic significance of increased accumulation of FDG in a hypoperfused myocardial region (Figure 10). It has been suggested that glucose utilization indicates that revascularization may be needed. Yet, as seen in Figure 11, the percentage of the patients free from major untoward events, such as sudden death, myocardial infarction, or intractable angina, was far less in patients who had FDG accumulation in hypoperfused areas than in those who didn’t, presumably because these patients had milder disease than the others.

Neurocardiology

There were 8 papers on adrenergic receptors. The Michigan group continues to lead in the development of tracers for the study of both the sympathetic and parasympathetic nervous systems of the heart (#556). The innervation of the ischemic heart shows a greater degree of impairment than does the reduction in blood flow, again supporting the concept that has been suggested in the past that the nerves to the heart may be the most sensitive indicator of ischemic damage. Wakasugi et al (#509) addressed the question of whether reduced uptake of MIBG by pre-synaptic neurons in cardiomyopathy was an indication that the neurons are damaged, or whether endogenous catechols occupying the receptor compete with the uptake of the radioligand. They examined the accumulation of 123I-labeled MIBG by pre-synaptic neurons after administration of adriamycin for 7 weeks. They showed that there was a great reduction in the accumulation of the MIBG, which was the result of both neuronal damage and adrenal secretion of catechols. This study was an excellent example of dissection of the abnormalities of neurochemistry resulting from toxins.

In the area of preventive medicine, a study by Moerlein et al from Washington University (#71) examined the process by which LDL (low-density lipoproteins) or VLDL (very-low-density lipoproteins) are removed by receptors, many of which are in the liver. If the receptors are saturated, the LDL or VLDL continues to circulate and may end up in scavenger cells to form the basis of atheromata. The investigators labeled the very-low-density and low-density lipoproteins with 99mTc and found that when rabbits were fed with diets high in cholesterol, tracer accumulation in the liver was greatly reduced. The cholesterol impaired the accumulation of LDL by the liver, making it available for accumulation in atheromata. Although they used a scintillation camera, the study could be carried out with probes that could be more widely applied to populations at risk. The study indicates how it is possible to move back into the early stages of a disease when preventive measures can be applied.

Nuclear Oncology

Antibodies continue to dominate nuclear oncology, although many exciting papers involved PET studies of cancer. The use of monoclonal antibodies is becoming routine in studies of patients with colorectal cancer (#133). SPECT is what makes the difference. In a study by Chatal in France (#137) of carcinoma of the ovary, the negative predictive value of immunoscintigraphy was 92 %, that is, the studies were 92 % accurate in saying that these patients did not have metastatic cancer of the ovaries. Such patients require second-look operations, but if one can be 92 % sure that a patient does not have metastatic carcinoma of the ovary, surgery would not be necessary.

With the large number of companies who have applied to the Food and Drug Administration to obtain approval of monoclonal antibodies or fragments, it is only a matter of time before one of these is approved. When that happens, it is likely that many more of these agents will be available. Exemplifying the value of antibody studies, Berna et al from Barcelona (#491) observed striking bone marrow regeneration after hormonal therapy of carcinoma of the prostate using an anti-granulocyte antibody labeled with 99mTc. Munz et al (#608) studied patients with prostatic or renal carcinoma. The detection of skeletal metastases with the monoclonal antibody directed against granulocytes was more effective than the use of phosphonates in patients with prostatic or renal cancer. Many more lesions were detected with the antibody.

The use phosphonates for monitoring treatment for carcinoma of the prostate hasn’t worked well because of the difficulty in distinguishing residual tumor from the healing process. With the anti-granulocyte antibody, the lesions reveal themselves as “cold,” while a favorable response to treatment of the lesion is “hot,” representing a return of granulocyte precursors. Therefore, the antibodies were more effective in monitoring treatment.

Wahl et al (#306, 308) used PET to detect axillary metastases in cancer of the breast and evaluate the response of the patients to chemotherapy. They observed a decrease in metabolism before the tumor shrank. Many tumors have receptors such as steroid receptors in carcinoma of the breast and somastatin receptors in other cancers, including carcinoma, glomus tumors, and medullary thyroid carcinoma. Kwekke-
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In the study of 3911 patients, the most frequent adverse reactions were: chest pain (9.4%) including angina pectoris (7.2%), electrocardiographic changes (2.8%), palpitations (2.7%), and dizziness (1.8%).

Adverse reactions occurring in greater than 1% of the patients in the study were chest pain (17.7%), headache (12.7%), dizziness (11.8%), electrocardiographic abnormalities (ST changes - 15.8%, T changes - 14.8%), pruritus (10.5%), rash (7.4%), flushing (3.4%), coughing (0.5%), nausea (0.2%), vomiting (0.6%), and flushing (0.4%).

Less common adverse reactions occurring in 1% or less of the patients within the study included: Central and Peripheral Nervous System: Dizziness (0.5%), headache (0.2%), vertigo (0.1%), photophobia (0.1%), tremor (0.1%), epigastric discomfort (0.1%), syncope (0.1%), and convulsions (0.1%).

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boom et al (#305) from Rotterdam and Berne used indium-III (111) octeotide, an analogue of somatostatin, to image tumors containing somatostatin receptors. They proposed that such agents have therapeutic as well as diagnostic potential.

The search continues for a 99mTc receptor-binding ligand for tumors. DiZio et al from Missouri (#68) used rhenium as an analog for technetium in the development of a labeled progesterone tracer for detecting carcinoma of the breast. Rhenium-188 (188Re) reported by the Oak Ridge group (#155) can be used for both diagnosis and therapy. It emits a 155 KeV gamma 15% of the time, and can be obtained from a parent with a 69-day half-life, so it would be readily available both as an antibody label and as a therapeutic agent. Pappata et al (#716) from Orsay, France looked for peripheral benzodiazepine receptors on gliomas and found that the tracer PK 11195 labelled with 11C accumulated in some but not all glial tumors. The tracer was displaceable, indicating that it was binding to the receptors when these were present.

Many studies showed how both PET and SPECT can help distinguish radiation necrosis from persistent or recurrent tumor (#38). Tonami et al from Kanasawa, Japan (#222) showed that preoperative assessment of mediastinal involvement of the lung, using 201Tl, was 84% accurate. Peter Bent of Brigham Hospital indicated that SPECT can distinguish radiation therapy effects from recurrent gliomas, based on the use of combined 201Tl and HMPAO imaging (#101). The researchers found there was a good separation of patients with recurrent tumor from patients with radiation changes. Another study, however, by McKusick and colleagues concluded that thallium is not a reliable predictor of recurrent brain tumor (#194). In my opinion, no single type of study should be expected to be perfect. Glucose utilization by brain tumors is at times confounded by the fact that the normal brain consumes glucose. Thallium may not be taken up by some tumors. Both studies should be available and used in the light of the patient’s specific problem.

Infections

Thirty-one papers concerned infection, illustrating an area where nuclear medicine is making strides. A study from the Mayo Clinic (#397) showed the value of indium-labeled leukocytes in detecting osteomyelitis in diabetic patients, a difficult problem. The investigators found that indium-labeled white blood cells were more accurate than technetium-labeled phosphonates. A large series of patients with infections studied with antigranulocyte antibody indicated the value of this approach (#393, 394, 395). One could get a more accurate picture of the extent of infection than with phosphate bone scans. The sensitivity and specificity in the detection of suspected osteomyelitis was improved by kinetic analysis. In a series of patients with bacterial endocarditis, the combination of ECHO with antigranulocyte antibody-imaging was very effective. Another common disease effectively studied with monoclonal antigranulocyte antibodies was acute appendicitis (#595).

Practice Parameters and Managed Care

The costs of diagnostic and therapeutic medicine are under going close scrutiny, rather than the costs of one diagnostic test compared to another. In December, 1989, an act was passed by the U.S. Congress that created the Agency for Health Care Policy and Research. With a first-year budget of $160,000,000, the agency’s goal is to enhance the quality and establish the effectiveness of health care services by considering diseases, such as myocardial infarction, or cataract, or diabetes, and assessing how patients should be cared for, and how decisions should be made. The agency will try to determine what works, how treatment should be planned and monitored, and how we can determine whether the patients have improved, by how much, and at what cost.

Naomi Alazraki, MD, has taken a step forward in establishing a group within The Society of Nuclear Medicine that will examine how nuclear medicine technology can increase the cost-effectiveness of medical practice parameters. This meeting demonstrates the important contributions that nuclear medicine can make. Cost effectiveness will be assessed in terms of whether we can exchange imaging costs with surgery costs, as well as by our ability to reduce operative complications through better selection of patients.

A study from the University of Pittsburg (#383) showed how complications after liver transplantation could be detected by mebrofenin hepatobiliary imaging. At this meeting 11% of all the papers presented had to do with monitoring treatment. No other field has the techniques that can monitor treatment the way that nuclear medicine can. Some 25 papers were concerned with the monitoring of cancer treatment, 19 with neuropsychiatry treatment. In a complicated and expensive operation such as a liver transplant, where the costs are in the hundreds of thousands of dollars per patient, simple measurements can detect complications at the earliest stages. A study from Guys Hospital (#18) in patients with a very common disease, chronic low back pain, indicated a lesion in 60% of the 70 patients. Such studies may help separate patients who have muscle spasms from patients to have lesions that should be further investigated. Another example of how nuclear medicine can improve medical practice was a study from Germany that took a quantitative look at patients with bone fractures (#21, 22). What better way to monitor the response of the patient to treatment than to study various physiological processes such as hyperemia, new bone growth, and disuse osteoporosis.

In summary, the meeting documented the spectacular growth in the science and clinical applications of nuclear medicine. It truly has become molecular medicine.

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