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New Horizons in Medicine

New technologies continue to bombard biomedical research and the practice of medicine. This was evident in a recent symposium in which progress in the use of nuclear magnetic resonance (NMR) was emphasized.* Applications of NMR that were discussed included structural determinations of proteins and use of NMR in clinical diagnosis, including localization of pathology and detection of aberrant metabolic patterns.

In studies of protein structure, NMR is a useful supplement to x-ray determinations and can provide information not obtainable with x-rays. With NMR one can investigate the behavior of proteins and other macromolecules in an aqueous medium. Thus one can observe effects of *p*H and determine binding of water both in the interior of a protein and also at its surface. NMR has a particular advantage in dealing with proteins and peptides that cannot be crystallized. X-ray crystallography is not applicable to such substances.

Structures of about 50 proteins have been determined. Their molecular weights are in the range of about 5,000 to 15,000. Larger molecules present difficulties since the NMR ^{1}H spectra are exceedingly complex. At the symposium, the use of three-dimensional Fourier transform NMR and of ^{15}N-labeled amino acids was mentioned, along with advanced computer programs. However, speakers suggested that a molecular weight of 40,000 might be an upper limit for determination of structures by NMR.

The application of NMR to clinical medicine has expanded rapidly. In 1981, only two magnetic resonance imaging (MRI) devices were in use in the United States. In 1987, 600 were being used here and another 100 in Europe. MRI is particularly helpful for imaging soft tissue, including skeletal musculature, and especially the pelvic region in both females and males. In tissues with tumor involvement, delineation of the pathology by MRI is often superior. Accurate knowledge of the extent of tumors is crucial to choice of appropriate surgery or other therapy. Determination of the existence and location of tumors in the brain can often best be done by MRI. One can follow the evolution of hematomas with time, and one speaker reported that MRI techniques had facilitated detection of an earlier contusion in a battered child. The usefulness of MRI in clinical diagnosis has been such that equipment is reportedly occupied two shifts a day, 7 days a week, in some places.

In development of improved instruments for clinical use, there are some limitations. To obtain higher resolution and better performance one would wish to operate at higher magnetic fields than those currently employed (1.5 to 2 teslas, that is, 15,000 to 20,000 gauss). However, obstacles to higher fields include large, expensive magnets, costly site preparation, and reported feelings of discomfort when volunteers exposed to 4 teslas move their heads.

A promising area for further investigation is in vivo studies of the distribution and metabolism of ^{13}C and ^{31}P compounds. George K. Radda at Oxford has studied 2000 patients in whom he has made observations on distribution of phosphate compounds in normal and diseased states. He can detect and monitor about eight different entities including adenosine triphosphate (ATP), phosphocreatine, and inorganic phosphate. If circulation of blood is limited, oxygen needed for the production of ATP is not available in sufficient quantity, and pain, heart failure, and stroke ensue. Examination of phosphorus constituents of muscle has been particularly useful. Radda has also noted that phosphocreatine increases in liver tumors. Brain was more difficult to study, but again patterns of phosphorus were changed in tumors. He also found that epileptics had abnormal phosphocreatine compared with ATP.

R. G. Shulman of Yale reported use of glucose tagged with ^{13}C in the one carbon position. He was able to follow the conversion of glucose to glycogen in skeletal muscle and note differences between normal and diabetic patients. He also showed that the path of conversion in the brain of glucose to γ-aminobutyric acid proceeds via glutamic acid.

During the past few years applications of NMR in biomedical research have expanded rapidly. Prospects are excellent for continued expansion as techniques evolve and there is a further increase in the use of computers and computer graphics.—PHILIP H. ABELSON

*Third International Conference on New Horizons in Medicine, held at the Scripps Clinic and Research Foundation, La Jolla, CA, 30 October to 1 November 1988. Honorary chairman, Cecil H. Green, and co-chairmen, Richard A. Lerner and Peter E. Wright.