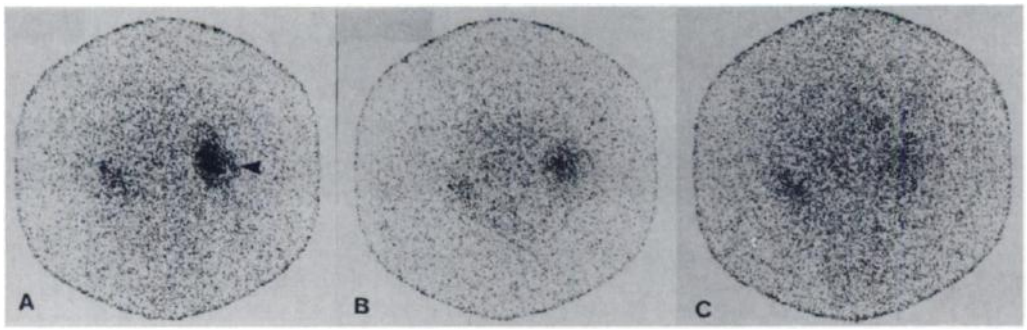

FIGURE 3. Adrenocortical images of Patient 4 with right aldosteronoma before and after the first unsuccessful and second successful TAEs. The hot nodule (arrowhead) of the right adrenal before the TAE (A) decreased in activity but still demonstrated residual activity after the first TAE (B). Disappearance after the second successful TAE (C).

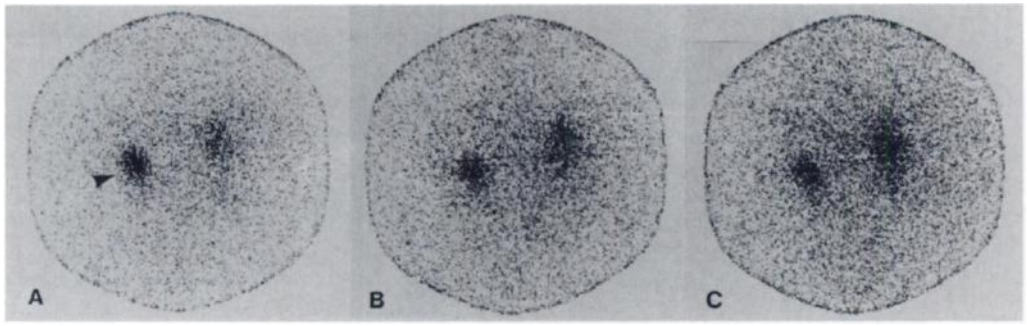

FIGURE 4. Adrenocortical images of Patient 10 with left aldosteronoma before and after the first and second unsuccessful TAEs. The hot nodule (arrowhead) of the left adrenal before the TAE (A) decreased in activity after the first TAE (B). The nodule persisted and increased in tracer uptake after the second TAE (C), suggesting unsuccessful therapeutic intervention.

successful TAE and disappearance of a hot nodule in case of completely successful TAE. This suggests that adrenocortical scintigraphy is a sensitive indicator to assess the effects of TAE with AE on aldosteronomas. The use of this scintigraphic method by injection of ^{131}I-NCL-6 within one week after TAE, in combination with measurements of plasma aldosterone levels may allow for more precise assessment of the complete or incomplete success of the TAE of aldosteronomas within 2 wk and provide earlier information on the decision for a next steps management such as no further therapy, repeated TAE or surgical operation than only the measurement of the levels of plasma aldosterone.

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EDITORIAL

The Incremental Value of Diagnostic Tests

In a recent editorial in *JNM*, Peter Valk of the Northern California PET Imaging Center (*1*) described problems in determining the specificity of [^{18}F]fluorodeoxyglucose (FDG) studies in the care of patients with cancer. As an example, Valk considered the validation of FDG imaging for detection of hepatic metastases. Even if all patients undergo subsequent surgery, lesions can only be detected if they are superficial or large enough to be palpated in the accessible portions of the liver. Small or deeper lesions will remain unconfirmed, and sensitivity of the FDG imaging will possibly be over estimated.

While measurement of sensitivity and specificity of diagnostic procedures, such as [^{18}F]FDG studies, whether performed by dedicated PET instruments or by recently developed dual-detector coincidence detections (SPECT) systems, are helpful, such parameters are not sufficient and often not knowable. Of increasing importance is the establishment of the value of the tests in meeting patients' needs reliably and consistently and in a cost-effective manner.

Assessment of the incremental value of diagnostic tests is an idea whose time has come. In modern medicine we try to be as scientific as possible. We try to make our tests as precise and as accurate as possible. Precision is a measure of the

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For correspondence or reprints contact: Johns Hopkins Medical Institution, Division of Nuclear Medicine and Radiation Health, 615 North Wolfe St., Baltimore, MD 21205-2179.

reproducibility of our tests. Accuracy is a measure of how close our observations are to the truth. We must deal constantly and effectively with uncertainty and face the possibility and costs of errors.

When I was a medical student, more years ago than I care to remember, Professor A.M. Harvey, the youngest chairman of a department of medicine in the U.S. at that time, defined diagnosis as "the identification of a disease by investigation of its signs and symptoms." Implicit in this definition is the concept that disease is an entity. This is the ontological concept of disease, as distinguished from the physiological concept of disease, in which disease is defined as undesirable deviation from the normal.

No field of medicine is better suited to apply the physiological approach to diagnosis than the field of nuclear medicine, and no test exemplifies it better than FDG studies of patients with cancer. To illustrate this point, I will describe two patients who were recently referred to me.

Patient LM is a 57-yr-old business man who in February 1996 was found to have moderately to poorly differentiated invasive prostatic adenocarcinoma. He had a resection of the prostate and removal of two lymph nodes that did not reveal evidence of cancer. A total-body ^{99m}Tc-phosphonate bone scan performed to search for skeletal metastases from the prostatic cancer was negative, but it did detect a "defect involving the upper pole of the right kidney." Further assessment was suggested and an ultrasound study of the kidneys was interpreted as revealing what were thought to be multiple cysts in both kidneys. The largest was in the right kidney, measuring 8 cm in diameter, and the report stated: "Even though this probably represents a benign mass, the possibility of a malignancy within this mass cannot be entirely excluded. Computed tomography is suggested for further evaluation."

The subsequent CT scan was interpreted as: "The mass does not meet the criteria for a benign simple cyst. It may be benign but cannot be definitely defined as a benign lesion on the basis of CT criteria." Accordingly, the patient came to Johns Hopkins to have the lesion removed. The patient was reluctant to be operated on again because he had had massive pulmonary embolism following the prostate surgery and nearly died. He was scheduled for surgery of the right kidney as soon as the effects of his anticoagulant therapy had worn off.

Because he was a personal friend, he came to see me and I asked him to ask his urologist what he, the urologist, thought was the probability of cancer, and he replied "60%". I recommended an FDG study, which revealed a large hypoactive area surrounded by FDG accumulation that was interpreted as displaced normal kidney tissue. The FDG report was: "There is less than a 5% probability that the large lesion in the kidney is malignant. There is a high probability of polycystic kidney disease.

On the basis of the FDG study, the surgery was cancelled, and now—6 mo later—the patient is still sailing in his yacht on the Chesapeake Bay and will have subsequent evaluation at 6-mo intervals.

Patient DB is a 38-yr-old accountant who had headaches, intermittent hypertension, mild episodes of sweating, but no panic attacks. She had biochemical evidence of a pheochromocytoma (norepinephrine level 1065 mcg/24 hr and a dopamine level of 1090 mcg/24 hr). Laparoscopy revealed a bladder lesion, and the patient underwent surgery in 1990. An ectopic pheochromocytoma was removed from the dome of her bladder.

On a routine follow-up examination 6 yr later, she was found to have biochemical evidence of a probable recurrence of the pheochromocytoma. An MRI scan revealed a lesion on the right side of the uterus. A radioiodinated MIBG study failed to reveal any lesions. An FDG study revealed markedly avid accumulation of the [^{18}F]FDG in one large and one small lesion just above and behind the bladder. Another lesion was seen on the anterior surface of the bladder. On the basis of the FDG study, the patient was operated on, and all the lesions were resected. The patient tolerated the surgery well and went home within 4 days.

The questions addressed by the FDG studies in these two patients was whether the lesions avidly accumulated [^{18}F]deoxyglucose, which would greatly increase the probability of malignancy and lead to surgery. In the first case, the danger, discomfort and expense of surgery was avoided. In the second case, the patient's life expectancy was greatly increased.

The concepts of specificity and sensitivity were introduced into medical diagnosis in 1959 by Ledley (a dentist) and Lusted (a radiologist) who proposed that Bayes' theorem was a useful model for describing and quantifying the diagnostic process. In the ontological approach, Bayes' theorem quantitatively tells us the probability that the "patient has a disease." In the physiological approach, it tells us quantitatively the probability that the patient's test values fall outside the statistically defined range of normal persons. How far the test results are from the desired values in normal persons gives an indication of the severity of the disease. It is not enough to interpret test results as normal or abnormal. I prefer to use decades of probability, while others use the categories: definitely abnormal, probably abnormal, probably normal and definitely normal.

It is convenient to express results as "likelihood ratios," rather than probabilities because their use facilitates combining the results of multiple independent tests. One simply multiplies the likelihood ratios from each test. In the physiological/biochemical approach, such as FDG tests, the results are expressed quantitatively. To cite a simple example of the increased information of quantitative results, is it better to say a patient is "hypertensive," or to state that his blood pressure is 220/130, which is of far greater significance than if it were 160/90?

Implicit in the anatomical, ontological approach to disease, which was all that was available before regional biochemical tests, such as FDG accumulation, is the concept of a "gold standard," most often assumed to be the histopathological evidence. We must remind ourselves of the subjective nature of the interpretation of histopathology and the fact that it too must validate its accuracy. Unfortunately, human beings, including physicians, become anxious when faced with uncertainty and assume certainty when not justified. The best test is assumed to be perfect. In fact, many of us are old enough to have encountered the statement that "last year's test was perfect, and this year's test is even better."

Histopathology is no longer the only quality control force in medicine today, now that the entire course of the patient's illness, and in fact, the rest of the patient's life, is being monitored. No longer is it enough to try to "identify the disease" from which the patient suffers. We need to address all the questions that describe the practice of medicine: What is wrong? How did it happen? What is going to happen? What can be done about it? Is the treatment cost-effective?

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

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