Test for depression called unreliable

A blood test that is routinely used by psychiatrists in the diagnosis and management of serious depression is inappropriate for clinical use and should be used only as a research tool, according to a growing number of scientists who have been studying the utility of the laboratory test. The test, called the dexamethasone suppression test (or DST), is worse than useless in accurately diagnosing melancholia, or biological depression, some researchers say: it raises false expectations among patients seeking an exact diagnosis and targeted treatment, and if not interpreted with caution it can lead to misdiagnosis and mistreatment. A major advocate of the test contends, however, that it is the sloppiness of psychiatric diagnosis and laboratory procedures that has produced the conflicting data on the DST.

Significantly, the warnings about the DST come not from those who view depression as a psychological reaction to life events, but rather from the mainstream of biological psychiatry: psychiatrist and endocrinologist Peter E. Stokes of Cornell University Medical Center in New York, one of the originators of the test during the 1960s, claims that the DST is both insensitive (that is, it misses too many seriously depressed people) and nonspecific (it picks up too many who are not depressed). As a result the test cannot be used with confidence as either a general screening test or as a test to confirm a preliminary diagnosis of depression. Stokes's conclusions, presented at the recent meeting of the American Psychiatric Association in New York, are supported by the still unpublished recommendations of a government panel of scientists, which (based on a conference held last summer) will also discourage routine use of the DST.

What the DST measures is the activity of a neuroendocrine system called the hypothalamic-pituitary-adrenal axis (HPA), which for years has been known to be abnormal (usually hyperactive) in many depressed patients. The theory goes back 50 years to the work of Harvey Cushing, a surgeon who found that people with an overactive adrenal gland (now known as Cushing's disease) often suffer from depression as well. A subsequent finding, that doses of cortisol (the adrenal hormone) can cause mood disturbance in normal subjects, led to an intensive investigation of adrenal malfunction in depression—and ultimately to the DST. In normal people a dose of dexamethasone acts through the HPA axis to suppress the body's own release of cortisol. In many depressed people, the feedback loop of the HPA axis seems to malfunction; they are said to "escape" suppression as their adrenal gland continues to pump out high levels of the hormone.

Today, few doubt that there is an HPA dysfunction underlying some depression. What is in dispute is whether or not the DST is useful in identifying patients with such a biological dysfunction — a condition most psychiatrists would treat with anti-depressant drugs or electroconvulsive therapy rather than psychotherapy.

The DST was introduced independently in the 1960s by Stokes and by psychiatrist Bernard Carroll (now at Duke University), who has become the major advocate of the DST as a clinical tool. Carroll says that the DST will accurately identify 68 percent of inpatients who are carefully diagnosed as melancholic, and that only 6 percent of non-depressed subjects will have an abnormal DST. Stokes's data, which come from the major depression research project sponsored by the National Institute of Mental Health, indicate that "nonsuppression" is not at all specific to depression: 50 percent of manic patients escaped suppression, as did 20 percent of schizophrenics and 10 percent of normal, healthy subjects. Stokes's report was only one of dozens at APA that indicated diminished confidence in the DST: a study by University of Iowa psychiatrist Bernard I. Grosser, for example, put DST sensitivity (more typically) as low as 15 percent.

One explanation for the discrepancy, Grosser says, is that while most researchers use the DSM III (APA's standard diagnostic manual) in the clinic, Carroll uses his own more exclusive criteria—including a family history of depression—to diagnose biological depression. Carroll agrees, but he says that it is not the DST that is on trial; instead, he says, it is clinical psychiatric diagnosis that is notoriously unreliable and needs validation. He says that he is skeptical about any data from the NIMH depression study, which he believes has been skewed by sloppy patient selection. In addition, he says, laboratories use a variety of methods to analyze DST data, but many psychiatrists are too unsophisticated to appreciate the differences when they interpret the results. Test results can be contaminated by alcohol abuse, over-the-counter drugs, and even by weight loss and aging, Carroll notes; critics reply that depressed people are very rarely purists.

What all this means to the consumer is unclear. The test itself presents no significant physical risk, but according to its critics, there is the risk that a patient with abnormal DST will wrongly end up being treated with drugs or ECT or, on the other hand, that a truly depressed patient with negative results will decline such treatment. By all accounts, the test is in great demand by patients and in widespread use by psychiatrists. Carroll says the DST can be useful in predicting treatment response, relapse and even suicide, but others insist that the data are inconclusive: as much as every psychiatrist yearns for a simple acid test for depression, they say, the DST is not it. *—W. Herbert*

A molecular sunlight 'funnel'

Developing a system that can easily and efficiently use sunlight to split water into its component parts oxygen and hydrogen (a fuel source), long has been a goal of photochemists. Now a fortuitous laboratory finding has led to improvement in the ability of a previously reported water-splitting system to capture light energy and convert it into hydrogen. While the amount of hydrogen produced by the system still is trivial in terms of commercial application, says one of its developers, Michael Grätzel of the Ecole Polytechnique Federale de Lausanne in Switzerland, the recent finding does represent a step forward, at the basic research level, in the field of solar energy conversion.

One of the many significant hurdles that still must be cleared in solar energy research concerns the limited ability of certain semiconductor materials to "harvest" sunlight. It is generally accepted that the water-splitting systems that include the more cheap and chemically stable semiconductors are those with more potential for commercial application. Unfortunately, the semiconductor materials that meet those requirements usually are able to absorb (and therefore utilize) only a limited portion of the solar spectrum. Consequently, one active area of solar energy work is the search for "sensitizers"—substances that act to "funnel" more sunlight energy into the water-splitting system than could be captured by the semiconductor alone. At the Electrochemical Society meeting last week in San Francisco, Grätzel reported that he and colleagues found a cheap, simple and effective way to sensitize their water-splitting system.

The system consists of titanium dioxide (TiO_2) semiconductor particles in solution. Without a sensitizer, water is split by TiO_2 electrons that hop from a "ground" to an "excited" state (the conduction band, or CB) when the TiO_2 particles absorb light. When a sensitizer is added, it can utilize more light to produce excited electrons that presumably are injected into the semiconductor particles to split water.

Previously investigated approaches to sensitizing water-splitters include addition to the solution of expensive metal-containing structures or complex molecules that resemble chlorophyll, the light-absorbing pigment in plants (which conduct the light-induced water-splitting process called photosynthesis). And initially, Grätzel set out along these same lines to sensitize his TiO_2 particles. At the suggestion of Franco Scandola of the University of Ferrara in Italy, he began to investigate the sensitizing ability of a metal-containing 8-hydroxyquinoline (an industrial chemical) structure.

During this study, team member Virginia