

Simple breath test may lead to reduced hospital stay for many transplant patients

While most patients bounce back from transplant surgery within a week or two, they can't go home from the hospital until their doctor has fine-tuned their dosage of drugs to prevent organ rejection. This dosage adjustment process, which is guided by daily blood tests, can take weeks—even months—of trial-and-error tinkering. As such, about half of all transplant patients must spend two or three extra weeks in the hospital after they've recovered from the operation itself.

This time-consuming, delicate drug-balancing act is crucial because too little of an immunosuppressant drug such as cyclosporine can cause organ rejection while too much can lead to irreversible kidney damage or seizure.

This costly and potentially dangerous dosage guessing game may soon be obsolete, thanks to a patented breath test developed by a U-M Medical Center researcher. By simply breathing through a straw into a vial of liquid, a patient's cyclosporine metabolism rate can be measured in minutes instead of weeks. To date the technique has been tested, with excellent results, on approximately 70 kidney transplant patients at the U-M Hospitals.

"With the breath test, we can consistently predict the true correct dose of cyclosporine that an experienced physician would perhaps arrive at through two months of tinkering," says inventor Paul B. Watkins, M.D., associate professor of internal medicine and director of the General Clinical Research Center at University Hospital." The breath test may one day replace blood monitoring of cyclosporine

levels and at the very least should provide a very convenient guide to physicians dosing the drug."

Immunosuppressants are difficult to dose because they are metabolized differently by each patient: Someone whose body processes cyclosporine very quickly may require a dose that's 10 times higher than a patient of similar proportions with a sluggish metabolism. Cyclosporine metabolism rate is determined by the body's level of enzymes called cytochromes P450.

The test is simple: First, Patients are injected with a tiny radiolabeled dose of the commonly prescribed antibiotic erythromycin. The drug is used instead of cyclosporine because it is metabolized by the same P450 enzyme as the immunosuppressant—but with little or no risk of side effects. "Erythromycin is one of the safest drugs known; during the test we give less than one-one-thousandth of the normal dose", Watkins says. About 20 minutes later, the patient blows through a straw into a vial of colored liquid for about 20 seconds until it turns clear. The amount of radiolabeled carbon dioxide—a metabolic product of the erythromycin—that's trapped in the solution is then measured in the laboratory, and this amount correlates to the patient's P450 enzyme level.

Watkins hopes to develop similar breath tests to help physicians more accurately dose estrogen replacement therapy, birth control pills and Taxol, the ovarian cancer drug.

For more information about the breath test, please call (313) 936-8080.

From : Grand Rounds, The University of Michigan Advance, Winter/Spring 1994.