2005 v1

General Clinical Research Center

University of Tennessee Health Science Center

Of Special Interest:

- **New GCRC facility at Methodist University Hospital**
- **Bicycle ergometer gets a workout in the GCRC**
- **Notes from the Director**

Ongoing Studies Are Actively Recruiting Volunteer Subjects For Research in:

- **Diabetes**
- **Diet Comparisons**
- **Pharmacokinetics**
- **Scleroderma**

In continuous operation for 40 years, the UTHSC GCRC was located at the William F. Bowld Hospital until January of this year when it opened a state-of-art facility at Methodist University Hospital. Present at the ribbon cutting ceremony, July 12, were from left: Robert J. Wyatt, M.D., GCRC Assistant Director ; Gary Shorb, Methodist LeBonheur Healthcare CEO; Michael Dockter, Ph.D., College of Medicine Associate Dean for Research and Administration; Lawrence Hak, Pharm. D., GCRC Scientific Advisory Committee Chair; Samuel Dagogo-Jack, M.D., GCRC Associate Director; Bruce S. Alpert, M.D., GCRC Program Director; Henry G. Herrod, M.D., College of Medicine Dean and GCRC PI; Cam Welton, Methodist LeBonheur Healthcare COO; Cecelia Sawyer, Methodist University Hospital Administrator, and Chaplain Elvernice "Sonny" Davis.

Photo by G. Songe

In 1959, in support of research into the cause and treatment of human disease, Congress directed the National Institutes of Health to establish clinical research centers throughout the United States.

The University of Tennessee Health Science Center was one of the first universities to be awarded an NIH grant to establish a General Clinical Research Center.

With the help of volunteer participants, academic researchers strive to find answers to complex health questions taking basic science into the realm of human subjects' research. The UTHSC provides research support to established academic researchers as well as new investigators.

In the last year, the GCRC has provided support to clinical investigators conducting research into the causes and treatment of cardiovascular disease, diabetes, Hepatitis C, periodontal disease, obesity, and rheumatoid arthritis, as well as studying the genetic basis of these diseases and other conditions.

Studying the pharmacokinetics of metoprolol

Robert B. Parker, Pharm.D., demonstrates the state-of-the-art bicycle ergometer purchased for use in his study of the effects of Paxil® on metoprolol.
Photo by G. Songe

Dr. Robert Parker, UT Associate Professor of Pharmacy, decided to study the effects of the anti-depressant Paxil® on the anti-hypertensive agent metoprolol because both are frequently concomitantly prescribed for patients who are experiencing depression following a heart attack or who have heart failure. There is a dearth of information on the interaction of these drugs.

"Many patients with cardiovascular disease also suffer from depresssion," explained Dr. Parker. Medications such as Paxil® and other SSRIs are frequently prescribed for them.

Continuing he said, "We know that medications like Paxil® can inhibit the liver's ability to break down many drugs."

While there is a small amount of data on Paxil®'s effect on immediate release metoprolol (brand name Lopressor®), he said there is an absence of data on Paxil®'s interaction with the extended release formulation, (brand name Toprol-XL®).

Metoprolol is primarily metabolized by the hepatic CYP2D6 isozyme and therefore susceptible to drug-to-drug interactions by the inhibition of this enzyme. Dr. Parker notes that Paxil® is a potent CYP2D6 inhibitor.

Given the differences in the properties of the two metoprolol formulations—immediate release and extended release—there may be important differences between these agents in their response to Paxil®-mediated CYP2D6 inhibition.

Thus, Dr. Parker and his co-investigator, board-certified cardiologist Judith Soberman, M.D., designed their study to first investigate Paxil®'s effects on Toprol-XL®; and then to compare its interactions with Toprol-XL® versus Lopressor®.

A total of 15 consented healthy volunteers, whose CYP2D6 gene indicates they more quickly metabolize the metoprolol and who meet the inclusion criteria, are being admitted to the GCRC after an overnight fast.

Prior to administration of the study drug, a GCRC nurse inserts an IV catheter for blood collection. A 5 ml. venous blood sample is collected prior to administration of the study drug.

There are blood collections at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 24 hours after the drug is given. These blood samples are analyzed to determine the metoprolol plasma concentration.

Seven standardized three-minute upright exercise tests are administered by the GCRC nurses using a programmable bicycle ergometer and a protocol designed by Dr. Soberman.

The workload is standardized for each subject to produce a heart rate of 85% of the predicted maximum. GCRC nurses record the heart rate and systolic blood pressure at intervals.

Dr. Parker explained that the heart rate goes up with exercise and metoprolol blunts that increase. With the administration of Paxil® the investigators expect the plasma concentration of metoprolol to increase.

Since the load on the bike is always set at the same individualized standard for all subsequent exercise tests for that subject, Dr. Parker said the presumption is that any differences in heart rate are due to changes in the medication.

To date nine subjects have completed the nine week protocol, two are in the process and four have yet to join the study.

GCRC nurse Kathy Pitts said, "It has been interesting to me to see the effects—blood pressure, pulse and the exercise tests—of the Paxil® on the metoprolol for all the subjects who have completed the study so far."

General Clinical Research Center

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Serving clinical physicians from VAMC, Methodist Hospitals, Le Bonheur Children's Medical Center, St. Jude Children's Research Hospital and The Regional Medical Center.

Notes from the director

We have all settled into the new GCRC facility on the 8th floor of the East Wing of Methodist University Hospital, the "flagship" of the Methodist Healthcare system. (Methodist Healthcare is the third largest hospital in the country based on 2003 admissions.)

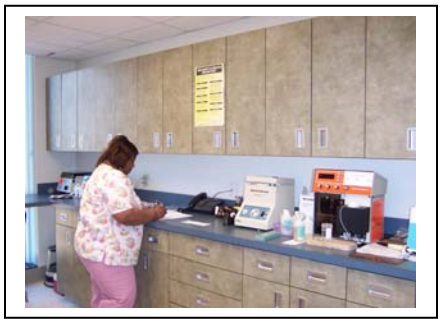
The whole atmosphere is bright and upbeat compared to our aged facility at the Bowld Hospital.

All of the administrative offices are in proximity to each other, facilitating communications between departments. The conference room has enough space to fit all of the members of the Administrative Committee for our monthly meetings.

The design of the GCRC is conducive to providing efficient patient flow and optimal aid for our research nurses.

There are both individual private exam rooms and a small "ward" area for studies with more than one participant at a time.

The laboratory area contains state-of-the-art equipment with ample counter space for processing specimens and overhead storage cabinets for medical supplies.



Bruce S. Alpert, M.D.
GCRC Director

Currently the GCRC is supporting approximately 45-50 projects and receives one to two new applications per month. These include studies conducted by R01 funded research scientists as well as young faculty.

With a commitment to providing a rich environment for mentored patient-oriented clinical research, two GCRC physicians have recently received K-23 awards: Debbie Jones, MD, Pediatric Nephrology, and Pedro Velasquez-Mieyer, MD, Pediatric Endocrinology.

We look forward to continuing our support for these and other new investigators.

Upper left, Pam McClendon, RN, prepares for blood draws in the GCRC lab. Above right, Kathy Pitts, RN, programs the DEXA computer for a bone scan. Lower left, two beds in the small ward on the GCRC.

Nurse Director Teresa L. Carr

For months at the end of 2004, tenants of the William F. Bowld Hospital had been leaving for new destinations on campus. The GCRC was on notice to vacate the facility by the end of Jan. 2005. New space was in the process of being built-out at Methodist University Hospital replete with 12 private exam rooms, a cold room, a room to house the DEXA scanner, a small ward, an exercise equipment room, a laboratory, a bionutrition/patient educational area, eight administrative offices, a nurses' area, a conference room and a reception area.

While some of the space was already configured, other areas required major renovations, such as the cold room, the ward and the core lab. After the move a temporary lab was set up. Tanning beds were in place for Dr. William Rosenberg's blinded 12-week UV study that would eventually enroll 50 adult subjects. There was Dr. Jaquelyn Fleckenstein's Hepatitis C clinic and Dr. Kitabchi's diabetes prevention study, ACT NOW. Other long-standing diabetes studies Look Ahead and EDIC, had scheduled visits, as well as Dr. Dagogo-Jack's peer-to-peer diabetes motivational study, CDIP.

The first quarter of 2005, was a whirlwind. In addition to the clinic visits, there were carpenters, electricians, telephone service reps and Methodist University Hospital personnel checking on the progress. And there were meetings with more of the same. Through it all, GCRC Nurse Director Teresa L. Carr directed the nursing staff, oversaw the remaining build-out, cleaned, put up supplies, persuaded, cajoled, and improvised. In all she demonstrated both her ability to get the job done and what it takes to be a team leader. When interviewed, she said she enjoys seeing people come together and help each other out. For the Nurse Director problems are just opportunities waiting for a solution. Who better to oblige?

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Our Mission…

- **To make available to medical scientists the resources necessary for the conduct of clinical research.**
- **To provide an optimal setting for controlled investigation by clinical scientists.**
- **To learn more about normal and abnormal body function and about the cause, prevention & cure of human disease.**
- **To encourage, develop, and maintain a corps of expert clinical investigators.**
- **To support funded investigators and give a start to unfunded investigators.**