PTN POST JUNE 2012 • ISSUE 1

Leading the Way

Childhood Obesity: A Crisis for Health and Health Care

Obesity has almost tripled among young people in the United States over the past 30 years. In 1980, a mere 7% of children ages 6–11 and 5% of adolescents ages 12–19 were considered obese. By 2008, 20% of children and 18% of adolescents fell into that category. That's approximately 12.5 million young people grappling with issues related to excess weight.[1]

Childhood obesity is a serious medical condition. Former Surgeon General Richard Carmona underscored its negative impact, noting, "Because of the increasing rates of obesity, unhealthy eating habits, and physical inactivity, we may see the first generation that will be less healthy and have a shorter life expectancy than their parents."[2] This is because extra pounds in childhood can spawn health problems that were once confined to adulthood, such as high blood pressure and elevated cholesterol—two risk factors for cardiovascular disease. In fact, in a population-based sample of 5- to 17-year-olds, 70% of obese youth had at least one risk factor for cardiovascular disease.[3] Children and adolescents who are obese are also at greater risk for bone and joint problems, prediabetes, sleep apnea, and social and psychological problems such as bullying and low self-esteem.

Over the long term, obese kids are likely to become obese adults and are therefore more at risk for adult health problems such as heart disease, type 2 diabetes, stroke, and osteoarthritis. Overweight and obesity are also associated with increased risk for many types of cancer, as well as multiple myeloma and Hodgkin's lymphoma.

The spike in obesity and obesity-related disease has forced the U.S. health care system to juggle resources and shoulder the additional expense of tending to these patients. Nationally, the cost of treating obesity-related health problems totals $190 billion a year or 20.6% of U.S. health care expenditures.[4] Among young people, approximately $11 billion is spent annually on those with private insurance and another $3 billion on those receiving Medicaid.[5]

To curb skyrocketing spending and ensure optimal care for obese patients both young and old, more research is needed on obesity prevention and the therapeutic modifications required in the meantime to safely and effectively treat America's obese population.

1. http://www.cdc.gov/obesity/data/trends.html.
2. http://www.surgeongeneral.gov/news/testimony/childobesity03022004.html.
3. Freedman DS, et al. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. Journal of Pediatrics 2007;150(1):12–17.
4. Cawley J, Meyerhoefer C. The medical care costs of obesity: an instrumental variables approach. Journal of Health Economics 2012;31(1);219–230.
5. Thomson Medstat Research Brief: Childhood Obesity: Costs, Treatment Patterns, Disparities in Care and Prevalent Medical Conditions, 2006, found at: http://www.medstat.com/pdfs/childhood_obesity.pdf.

How Do We Dose Effectively in Obese Children?

Overweight and obese children often are excluded from pediatric studies, leading to critical gaps in scientific and clinical knowledge that put this ever-growing population at risk. Using the wrong dose of a drug could limit its efficacy or expose an obese child to possible drug-related toxicity.

Unfortunately, typical drug dosing guidelines based on patient weight are often inadequate for these kids because of their altered body composition, physiology, and related changes in drug metabolism and distribution. For example, children who are obese can have different proportions of lean and fat body tissue and altered liver and kidney function, which can affect the drug absorption, metabolism, and elimination, respectively. Because of such differences, specific dosing recommendations for this population are desperately needed so that pediatricians can be sure that they are delivering the best and safest care possible to every patient.

The PTN plans to create an evidence base for the formulation and dissemination of such recommendations. A project team will conduct a literature review to develop a drug database that will inform dosing for obese children. They will also identify major gaps in this knowledge base and outline recommended study methods for the U.S. Food and Drug Administration to use in filling these gaps. Finally, the team will develop a web-based resource tool for the broad dissemination of present and future dosing guidelines for obese children. Using this systematic and thorough approach, the PTN hopes to understand how drugs behave differently in obese children and make any dosing changes widely available to pediatricians taking care of obese children.

PTN Overview

Danny Benjamin, MD, PhD, MHS, Lead Principal Investigator

Welcome to the first issue of The PTN Post, a bimonthly newsletter designed to keep you informed about key issues in pediatrics and the work of the Pediatric Trials Network (PTN).

The PTN is filling critical gaps in medical knowledge about how best to treat young people with drugs and devices used every day in pediatricians' offices and hospitals around the world. We hope that this newsletter will inform and engage our readers, thereby adding to the momentum behind our effort to improve medical care for infants and children.

We welcome your input about topics of interest for future issues. Please contact us with your suggestions via the PTN website (**https://pediatrictrials.org/contact-info**). We look forward to hearing from you.

Taking the Guesswork Out of Pediatric Weight Estimation: A PTN Study to Validate the Mercy TAPE™

The Mercy TAPE in action

A child's weight is often necessary to ensure the delivery of age-appropriate, weight-based care, but many times a suitable scale is not available. In developed countries, the use of scales may be impractical, such as in cases of emergency or trauma or in instances where children are encumbered by casts, tubing, hoses, or other medical equipment. In undeveloped countries, health care settings may lack a scale altogether. Therefore, methods for obtaining accurate weight are needed around the world.

Numerous methods for estimating weight on the basis of age and/or length have been evaluated in children. However, most of these strategies do not perform well in children at the extremes of weight, thus putting them at risk for under- or overdosing of medicines.

To address these limitations, investigators at Children's Mercy Hospitals and Clinics in Kansas City, Missouri, have developed and validated a weight estimation method (the Mercy Method™), which uses measurements of arm length and upper arm circumference to predict weight. A partial weight is assigned to each measurement, and addition of the partial weights that correspond to the child's arm length and upper arm circumference provide an estimated weight for that child. Because the Mercy Method performs well both in children who are underweight and those who are overweight/obese, it outperforms many of the other weight estimation methods that are currently used in practice.

From this method, a simple paper-based device (the Mercy TAPE) was developed to facilitate weight estimation without the need for additional external references. A study examining the Mercy TAPE is the first device trial to be undertaken by the Pediatric Trials Network. The TAPE study has successfully completed enrollment of 625 evaluable patients and did so in less than two months. The PTN team attributes this impressive enrollment rate to the efforts of the lead investigator Susan Abdel-Rahman, PharmD (Children's Mercy Hospitals and Clinics), the principal investigators Ian Paul, MD (Milton Hershey Medical Center) and Laura James, MD (University of Arkansas Medical Center), and the study personnel at each of the three participating institutions.

Results from the TAPE study are expected in 2012.

Susan Abdel-Rahman, PharmD: Lead Investigator for the Mercy TAPE Study

1. DESCRIBE YOUR ROLE AT CHILDREN'S MERCY HOSPITALS AND CLINICS.

I'm an independent researcher, an attending on the Clinical Pharmacology consult service, and a professor in the Department of Pediatrics.

2. DESCRIBE YOUR RESEARCH INTERESTS.

My research focuses on two somewhat disparate areas: pediatric drug disposition/action (or pharmacokinetics) and fungal genetics. The primary goal of my work in pediatric pharmacokinetics is to optimize drug dosing in children. My fungal research uses molecular tools to describe the epidemiology and natural disease course of a common fungal infection in children. My research team is also developing and adapting moderate throughput approaches for the screening of new and existing chemicals for antifungal activity.

3. HOW DID YOU BECOME INVOLVED WITH THE TAPE STUDY?

We were working closely with the World Health Organization on its **"Make Medicines Child Size"** initiative. As we formulated pediatric dosing recommendations (nearly all of which are based on weight), we realized that many of the children for whom the recommendations were being targeted live in regions of the world where accurate, calibrated scales are simply unavailable. This knowledge served as the impetus to investigate a weight estimation method that can be used in almost any context.

4. HOW MIGHT THIS MEASURING DEVICE IMPROVE PEDIATRIC CARE?

The Mercy TAPE will allow us to deliver more accurate doses of medicines to children in need, whether in emergency/critical care settings in the United States or in resource-restricted community settings overseas. Given its accuracy, the Mercy TAPE can also be used to track weight and nutritional status of children in resource-restricted communities.

5. WHAT ARE THE NEXT STEPS IF THE STUDY IS SUCCESSFUL?

If successful, the next steps involve evaluating how best to integrate the device into practice. We are also in the process of collecting data that will permit modification or refinement of the TAPE for special populations, such as newborns and children with Down syndrome.

The Pediatric Trials Network (PTN) is made possible by the Best Pharmaceuticals for Children Act (BPCA). The BPCA, first enacted in 2002, provides mechanisms for studying on- and off-patent drugs in children. Visit us on the web at www.pediatrictrials.org.

The Pediatric Trials Network is supported by The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, and U.S. Department of Health and Human Services.