

December 2009

Bryan Larsen, PhD *Executive Director ICTCR*

Theodore Rooney, DO, FACP
Director of Clinical Research, Des Moines University

Ronald J. Torry, PhD
Drake Liaison to ICTCR, Professor, Drake University College of Pharmacy and Health Sciences

Joan McCleish, PhD
Mercy College Liaison to ICTCR, Mercy College of Health Sciences

Dale Andres, DO
Chief Medical Officer, Mercy Medical Center

Simon Geletta, PhD
Director of MIRIAM (ICTCR's Informatics Arm)

In This Issue

Cover story: Neonatal Intensive Care Unit Included in Research Network. Page 2: Children and research. Page 3: Local physicians' contributions noted.

About Us

The ICTCR facilitates patient-centered research through the combined strengths of its founders: Mercy Medical Center, and Des Moines University along with its partners Drake University College of Pharmacy and Health Sciences and Mercy College of Health Sciences and welcomes inquiries from interested clinicians and scientists.

For more information, please call (515) 247-4435.
www.iowatranslationalresearch.org

Mercy Neonatal Intensive Care Unit Joins the University of Iowa in a Major NIH Research Program

Dr. Dan Ellsbury (page 3) will be the site investigator for a program beginning early next year that links Mercy Neonatal Intensive Care Unit with the University of Iowa in a program of research designed to improve the health of low birth weight and premature infants nationwide. Only 16 sites around the country are part of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network and the University of Iowa represents one of the more recently added study sites. With the addition of Mercy Medical Center as a satellite site of the program at the University of Iowa, a larger number of the smallest infants from the State of Iowa will contribute to important medical knowledge of the most vulnerable of patients.

Dr. Ellsbury will be joined by Dr. Cary Murphy (page 3) and other NICU staff members in pursuing important data gathering and clinical trials organized by national leaders in pediatric research. The parent site at the UI is led by principle investigator Dr. Ed Bell who will have frequent interaction with the Des Moines center and will ensure that a variety of advanced educational opportunities will be made available to personnel at Mercy Medical Center. In addition to the medical staff who will be involved in this project, a nurse-coordinator will be named in the near future to assist with the complex tasks associated with multiple clinical studies which will be part of ongoing national studies.

The overall program which is sponsored by NIH is supported by a data center operated by (RTI) Research Triangle Institute (see web site for additional information (<https://neonatal.rti.org/about/network/cfm>). As a participant in this program, Mercy NICU will provide data on infants between 401 and 1000 g that will support several individual studies including: [1] a general database and detailed follow up of these infants at 18 months of age, [2] Observational studies of early sepsis, [3] clinical trials to evaluate induced hypothermia after 6 hours of age for prevention of neurological complications, [4] comparison of initial surgical approaches in necrotizing enterocolitis or perforation and [5] a pharmacokinetic study of myo-inositol administration in prevention of retinopathy of prematurity. As long as Mercy remains a participant, other studies may be added. Thus far, many landmark papers have been published as a result of the neonatal research network (see page 2 sidebar).

It bears noting that the addition of Mercy Medical Center NICU as a satellite center was not a trivial process and involved many months of planning, meeting with University of Iowa researchers and ultimately a site visit by NICHD program officers and RTI. The outstanding track record of Dr. Ellsbury as a leader in the data driven quality improvement operations of the Pediatrix Corporation was undoubtedly a strong factor in the ability of the our NICU to have the opportunity to play a role in nationally significant neonatal research – *B. Larsen*

Circulating beta chemokine and MMP 9 as markers of oxidative injury in extremely low birth weight infants. G Natarajan *Pediatr. Res.* 2010 PMID: 19755933

Synchronized nasal intermittent positive-pressure ventilation and neonatal outcomes. V Bhandari et al 2009 *Pediatrics* PMID: 19651577

Perinatal Systemic Inflammatory Response Syndrome and Retinopathy of Prematurity. BG Sood et al *Pediatr. Res.* 2009 PMID: 20032809

Predicting Time to Hospital Discharge for Extremely Preterm Infants. SR Hintz et al. *Pediatrics* 2009 PMID 20008430

Outcome of term infants using apgar scores at 10 minutes following hypoxic-ischemic encephalopathy. AR Laptook et al *Pediatrics*. 2009 PMID: 19948631

Validation of the Functional Status II questionnaire in the assessment of extremely-low-birthweight infants. D DaCosta et al 2009 *Dev Med Child Neurol* PMID: 19459909

Stability of neuromotor outcomes at 18 and 30 months of age after extremely low birth weight status. M Peralta-Carcelen 2009 *Pediatrics* PMID: 19403482

Cytokines associated with bronchopulmonary dysplasia or death in extremely low birth weight infants. N.Ambalavanan et al 2009 *Pediatrics* PMID: 19336372

Impact of postnatal corticosteroid use on neurodevelopment at 18 to 22 months' adjusted age: effects of dose, timing, and risk of bronchopulmonary dysplasia in extremely low birth weight infants. D Wilson-Costello *D Pediatrics* 2009 PMID: 19204058

Patent ductus arteriosus therapy: impact on neonatal and 18-month outcome. JC Madan et al *Pediatrics* 2009 PMID: 19171637

Twin gestation and neurodevelopmental outcome in extremely low birth weight infants. R Wadhawan et al 2009 *Pediatrics* PMID: 19139085

Timing of elective repeat cesarean delivery at term and neonatal outcomes. AT Tita 2009 *New Engl J Med* PMID: 19129525

This array of articles, almost all of which are from 2009 show the range of clinical discovery made by the Neonatal Research Network. Many of these are practice – changing and illustrate the power of research networks.

Involvement of Children in Medical Research

The landscape for including children as participants in clinical research studies began changing significantly in 1998 when the NIH published new guidelines regarding the appropriate involvement of children in clinical trials as it was recognized that many treatments that might be of value to children and infants lack data on safety and efficacy specifically determined in children. It was noted that many physicians who had limited or no data on which to base treatment of children would have to use their best clinical estimations in applying drugs or treatments on data obtained from adults despite the fact that children may have different responses to these therapies.

The changes in NIH guidelines came as a result of Congress addressing the relative exclusion of children from research approximately two years prior. NIH responded in several ways to promote clinical research involving children (persons less than the legal age of consent) in valid clinical trials.

The slowness to embrace research involving children is understandable and may have been born of concern about the vulnerability of children to exploitation due to their lack of maturity, their potential fragility and their possible limited capacity to understand research. Indeed, rules concerning human subjects' research (45 CFR 46 Subpart D with parallel regulations in the title covering FDA-regulated research at 21 CFR 50 Subpart D) specifically singles out children as a class that is accorded special protection (as are pregnant women and their fetuses and prisoners). Researchers may have in the past tended to err on the side of extreme caution, but concern that children may be missing benefits of medical discoveries and Federal directives have brought about changes. The Institute of Medicine of the National Academies published a major treatise in 2004 and other books have followed. The subtitle to a 2006 volume "*Children in Medical Research – access versus protection*" by Lainie Friedman Ross really encapsulates the heart of the matter. The fall 2009 AAHRP newsletter (*AAHRP Advance*) noted that among the 7 IRBs that were newly accredited by AAHRP (Association for the Accreditation of Human Research Protection Programs Inc.) three were for children's hospitals which they interpreted as indicating escalating levels of clinical research involving children.

With the Federal guidance to be more inclusive of children in research, IRBs have worked to operationalize the rules that allow 4 kinds of research on children. These include [1] Research involving minimal risk, [2] Research involving greater than minimal risk with foreseeable direct benefit to the minor, [3] Research with greater than minimal risk with no direct benefit to the child but benefit to society, and [4] Research that is otherwise not approvable but may be approved by the Secretary of DHHS. While the categories that may be approved are spelled out in regulation, IRBs tend to struggle with what is actually meant when applied locally. An interesting report was published by Shah et al in *JAMA* in 2004 in which 188 IRB chairs were polled to determine their interpretation of minimal risk in children (81% considered a single blood draw as minimal risk but 23% considered allergy skin test as minimal risk). Understanding of benefit also differed from person to person.

IRBs that review protocols related to research in children require someone with appropriate expertise with children to review protocols and when children are of sufficient age, the assent of the child to participate in the research (meaning active assent and not just lack of objection) is also required. For neonatal research, the Federal regulations include neonates of uncertain viability in the paragraphs of Subpart B with pregnant women and fetuses rather than in the Subpart D which refers to children. Viable neonates, even if the viability is supported by medical means are included with children and are covered by the language of Subpart D.

Featured Researchers:

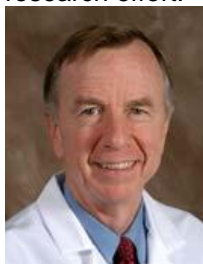
From Page 1:



Dan Ellsbury, MD, (Mercy NICU) will be serving as the Site Principle Investigator for enrollment of patients into the Iowa Cohort of the Neonatal Research Network.



Cary Murphy, MD will work with patients in the Neonatal Research Network as clinical studies are coordinated at the Mercy NICU and the University of Iowa NICU as part of the larger national research effort.



Dr. Ed Bell is the Principle Investigator for the UI center of which Mercy NICU will be a satellite center.

IMPACT!!: *A colleague recently asked me about the meaning of Journal Impact Factors, wondering if this is just an advertising ploy or if there was some real value to the concept.*

It is an intuitive notion that an article in a journal will be deemed to have had a measurable impact if the article is quoted by someone in another place.

Most published authors have enjoyed the little flash of enjoyment when they see their work quoted by someone else, and this experience is usually a random occurrence. But it need not be. In the information age, computers can “read” the bibliographies at the end of all published papers and tally the number of times articles are cited. It stands to reason, then, that the impact of a journal article could somehow be measured by how many times it gets cited. And by extension a journal’s impact could be measured by how many times that journal’s articles are cited.

Originally the concept of “impact” was developed by Eugene Garfield who himself has had a tremendous impact on the business and science of citation and management of literature references. Garfield established an enterprise known as Institute for Scientific Information. But now impact evaluation is the domain of Thompson-Reuters which has acquired ISI and the Journal Citation Report is published by Thompson ISI. In addition to information about citation counting there is a wealth of other information about scholarly publication that may be obtained on the ISI website: (www.isiwebofknowledge.com.)

Of course, if one wants to count citations, issues immediately arise that would influence the ability to compare one journal to another. So there are rules that have been established in the field for how impact factors are calculated. Is impact simply the raw number of times articles from a journal get cited? How long is the look-back period for counting citations (older articles should have more time to be cited than newer ones, for example.) Another influencing factor is the size of a field, so that if immunologists outnumber mathematicians, there may be seeming greater impact for immunology journals. Can the system be gamed by quoting yourself as often as possible?

So briefly, the rules established by Thompson ISI for their reporting gives a journal an impact score that is calculated for a 2 year look back period, though a 5 year factor is also now available. Articles from a given journal cited during the previous 2 year window will be tallied and divided by the number of articles published by the journal in its index years (impact for 2009 is based on citations from 2007 and 2008). The impact represents the rolling average of citations for the journal’s contents during the look back years. Not every published item gets counted, so while articles, reviews, notes and proceedings may be counted, letters and editorials may not, though editorials with long reference lists might be counted.

The impact factor has become very important to journals, and journals that have high impact factors definitely make their factors known because it is assumed that authors will want to put their best work in the highest ranked journals. Criticisms of the system exist and other kinds of impact measures are used by the experts in the field. The idea of an impact factor can also be applied to individuals and some universities evaluate their faculty on the basis of how often their work gets cited.

Statement of Purpose

The ICTCR is a research enterprise that facilitates productive research collaboration between its partners by sharing intellectual and infrastructure resources for the purpose of advancing patient-centered research that seeks better health for our communities and education and research opportunities for our faculty, staff, students and trainees. We believe the comprehensive training of medical students, residents and other health care professionals must be accompanied by a working knowledge of clinical research methods and best practices and that the best way to accomplish this is through active research endeavors. The ICTCR is dedicated to ethical and compassionate care for all individuals who participate in clinical research studies and actively supports the principles of autonomy, beneficence and justice in clinical research programs.