

SmartTots

Funding anesthesia research to ensure pediatric safety



Please join this effort and help ensure that, when we make decisions that our children must undergo anesthesia or sedation for surgery to improve their quality of life, we are not left questioning our decisions.



IARS

International Anesthesia Research Society

The IARS is a 501 c (3) non-profit. Tax Id: 34-0750348

Executive Summary

The International Anesthesia Research Society (IARS) is a non-political medical society founded in 1922 to advance and support anesthesia research and education. The IARS contributes more than \$1 million annually to fund anesthesia research and provides a forum for leaders in anesthesia research to share information and ideas.

The IARS mission is to encourage, stimulate, and fund ongoing anesthesia-related research projects that will enhance and advance the specialty and to disseminate current, state-of-the-art, basic and clinical research data in all areas of clinical anesthesia, including perioperative medicine, critical care, and pain management. The IARS is focused solely on the advancement and support of education and scientific research related to anesthesiology.

Twenty-six million people in the United States annually undergo medical procedures requiring anesthesia or sedation and more than one million are children. Non-clinical studies in juvenile animal models show that exposure to some anesthetics and sedatives is associated with memory and learning deficits and other neurodegenerative changes in the central nervous system. Insufficient human data exist to support or refute the possibility that similar effects occur in children.

To address the critical public health issues associated with the safe use of anesthesia and sedatives in young children, the IARS has partnered with the US Food and Drug Administration, and is working with multiple stakeholders (e.g. professional societies, academic research institutions, patient advocacy groups, industry and other government and nonprofit organizations), to address scientific and clinical gaps regarding the safe use of anesthetics and sedatives in children by funding innovative pediatric anesthesia research projects.

In September of 2012, the IARS and the FDA convened a workshop of more than 50 experts in anesthesia and pediatric medicine, as well as individuals involved in patient safety and advocacy to establish a consensus statement on how to communicate with doctors and patients regarding the issues raised by SmartTots. This statement has been endorsed by the IARS, the FDA and other key anesthesia related organizations.

Notably, all administration, fundraising, and operating expenses for the SmartTots initiative are paid for by the IARS with grant support from the FDA. As such, 100% of the funds raised go directly to support research.

Introduction

Founded by a dynamic, award-winning oratory and essay writer, Dr. Francis McMechan, the International Anesthesia Research Society (IARS) is the oldest professional society for anesthesiologists, with a remarkable 90-year history of serving the anesthesiology community. McMechan founded the IARS (originally the National Anesthesia Research Society) to promote research in anesthesiology and communicate research results. The year 1922 marked the launch of *Current Researches in Anesthesia and Analgesia*, the world's first major anesthesia medical journal, later to become known simply as *Anesthesia & Analgesia*.

Today, the IARS contributes more than \$1 million annually to fund innovative anesthesia research and provides a forum for leaders in anesthesia research to share information and ideas. The IARS, a non-political medical society, focuses on advancing and supporting anesthesia research and education initiatives.

The IARS mission is to encourage, stimulate, and fund ongoing anesthesia-related research projects that will enhance and advance the specialty, and to disseminate current, state-of-the-art, basic and clinical research data in all areas of clinical anesthesia, including perioperative medicine, critical care, and pain management.

Dedicated to advancing and supporting the anesthesiology field by encouraging and funding innovative anesthesia research and education projects, the IARS Awards and Grants Program, established in 1983, has contributed nearly \$12,000,000 to the worldwide anesthesia community, bringing more than 130 research projects from conception to fruition.

Need for Anesthesia Research

Each year, more than 26 million people in the United States alone undergo medical procedures requiring anesthesia or sedation (Community Health Network, 2012). Many of these procedures, which have improved the health, longevity, and quality of life of the U.S. population, would not have been possible without modern anesthetic techniques. Scientists have learned that general anesthesia consists of several components, including sedation, unconsciousness, immobility, analgesia (lack of pain), and amnesia (lack of memory). They have developed agents that can provide each of these elements separately, which enables anesthesiologists to tailor the regimen to each procedure and patient. Advances in cell biology, genetics, and molecular biology have transformed anesthesiology into an active area of research (National Institute of General Medical Sciences, 2012).

Anesthesiologists carefully monitor patients throughout surgery using electronic devices that continually display vital signs. Major advances in monitoring include the continuous measurement of blood pressure, blood oxygen levels, heart function, and respiratory patterns. These advances have dramatically improved the safety of general anesthesia and make it possible to operate on many patients who were previously considered too sick to undergo surgery (National Institute of General Medical Sciences, 2012).

Millions of dollars are being invested in advancing technologies and tools for surgery annually. However, before a child undergoes surgery or a procedure, they often must first undergo a course of pediatric anesthesia. Unfortunately, extensive research on the long-term effects of pediatric anesthesia in children has lagged behind that of other areas. The International Anesthesia Research Society (IARS) has partnered with the U.S. Food and Drug Administration (FDA) to raise awareness and funds for much-needed anesthesia research that will ensure pediatric safety.

As more than 1 million infants and young children undergo surgical procedures requiring anesthesia annually in the United States alone, parents are faced with one of the most difficult decisions they could ever have to make and that is if their young child should have surgery. The issue becomes more complicated due to concerns about a child's response to general anesthesia or sedation.

According to *Defining Safe Use of Anesthesia in Children* by Bob Rappaport, MD, R. Daniel Mellon, PhD, Arthur Simone, MD, PhD, and Janet Woodcock, MD, a paper published in the *New England Journal of Medicine* on April 14, 2011, "Anesthetic agents are commonly used for a variety of medical procedures in infants and children, but little is known about their effects on the developing brain. **A growing body of data from studies in animals suggests that under certain circumstances, such as prolonged anesthesia, these drugs could adversely affect neurologic, cognitive, and social development of neonates and young children.** We believe that these findings should be of concern to the scientific and medical communities."

SmartTots Research Initiative

To address the critical public health issues associated with the safe use of anesthesia and sedatives in young children and provide parents and doctors with the information they need when faced with such a dilemma, the IARS and the FDA have created a research initiative called SmartTots.

SmartTots-funded research will help determine if any particular anesthetic or sedative drugs pose hazards to young children, design the safest anesthetic and sedative regimes, and potentially foster the development of new anesthetic and sedative drugs. Recent studies have shown an urgent need for research into the potential risks of using anesthesia and sedation on the development of children under age four.

"Every time you get anesthesia during surgery, there's a risk. But there may be a special risk for children under four," said Dr. Michael Roizen, chair of the executive board for SmartTots. "SmartTots will allow us to learn how to give anesthesia and perform surgery safely on children under the age of four."

Animal studies done by the FDA's National Center for Toxicological Research and several university investigators have shown that anesthesia and sedative exposure can cause harmful

neurological changes in young rats and mice. Commonly used anesthetics caused widespread loss of nerve cells and abnormal behavior. FDA studies in non-human primates found similar neurological problems. Alternatives to the medications typically used in children who require general anesthesia are few and do not represent a realistic alternative.

“If you could postpone surgery for those under the age of four, that would be fine,” said Dr. Roizen. “But for most procedures, you can’t delay them because they are important for the child’s development and health.”

SmartTots Consensus Statement on Patient Safety

SmartTots released a consensus statement in December of 2012 regarding the safety of anesthetics and sedative agents administered to infants and young children. This statement was the end product of a scientific workshop on September 10, 2012 at the FDA White Oak Campus in Silver Spring, Maryland, which convened experts in anesthesia and pediatric medicine, as well as individuals involved in patient safety and advocacy.

The consensus message is intended to enable immediate awareness and education for parents and physicians while research studies look for more definitive data to either prove or disprove the existence of real and clinically relevant risks to children. SmartTots is actively securing funds for new and ongoing investigations that will help close research gaps and ensure the identification of safe anesthetic treatments.

After a full day of data review and evaluation, the Workshop successfully resulted in a consensus statement which has been endorsed by key organizations within the field including:

- American Academy of Pediatrics (AAP)
- American Society of Anesthesiologists (ASA)
- European Society of Anaesthesiology (ESA)
- International Anesthesia Research Society (IARS)
- Society for Neuroscience in Anesthesiology and Critical Care (SNACC)
- Society for Pediatric Anesthesia (SPA)
- US Food and Drug Administration (FDA)

Consensus Statement

Each year, millions of young children require surgery and other procedures for serious or life-threatening medical conditions or to improve their quality of life. Anesthetic and sedative drugs are widely used to help ensure the safety, health, and comfort of children undergoing these procedures. However, increasing evidence from research studies suggests the benefits of these agents should be considered in the context of their potential to cause harmful effects.

Previous research in young animals and children has raised concerns that exposure to commonly used anesthetics may produce adverse neurobehavioral effects. However, these studies had limitations that prevent experts from drawing conclusions on whether the harmful effects were due to the anesthesia or to other factors, including surgery, hospitalization, or pre-existing conditions. Furthermore, the findings in children have been mixed, with some studies of infants and young children undergoing anesthesia or sedation finding long-term deficits in learning and behavior, while others have not.

Clearly, additional research is urgently needed to identify any possible risks to young children. In the absence of conclusive evidence, it would be unethical to withhold sedation and anesthesia when necessary. Instead, healthcare providers should do the following:

- Discuss with parents and other caretakers the risks and benefits of procedures requiring anesthetics or sedatives, as well as the known health risks of *not treating* certain conditions
- Stay informed of new developments in this area
- Recognize that current anesthetics and sedatives are necessary for infants and children who require surgery or other painful and stressful procedures

Statement Testimonials

“As an organization dedicated to the health of children, the **American Academy of Pediatrics** naturally wanted to play a role in developing the consensus message on this important safety topic,” said Dr. Thomas McInerney, AAP president. “Anytime a child undergoes a surgical procedure requiring anesthesia or sedation, parents will have questions about possible risks. Additional research is urgently needed to expand what we know about the health effects of anesthesia. Meanwhile, the Academy encourages parents to be educated about the risks and benefits of anesthesia and surgical procedures performed on their child.”

“Recent studies have raised concerns about the safety of anesthetics for our pediatric patients, as they are at a critical developmental period,” said Dr. Nancy Glass, **Society of Pediatric Anesthesia** president. “However, definitive answers regarding the effects of anesthesia in children remain inconclusive. While the experts continue to investigate treatments and develop these important answers, it’s important that the medical and scientific communities work together to communicate our knowledge in a unified message, with patient safety at its core.”

“The **International Anesthesia Research Society** is fully committed to supporting the urgent fund raising and research agenda that are represented by SmartTots,” said Dr. James Ramsay, co-chair of the SmartTots Steering Committee and past chair of the IARS Board of Trustees. “It’s imperative we work together to scientifically determine the safest way to care for our youngest patients as they undergo necessary procedures requiring sedation or anesthesia.”

SmartTots Objectives

SmartTots is a multi-year collaborative effort designed to increase the safety of anesthetic drugs for the millions of infants and children who undergo anesthesia each year. Research funded through SmartTots investigates multiple aspects of existing anesthetics and their administration, including dosage and exposure. Findings from these studies will establish the development of new practice guidelines and anesthetic drugs. Data, outcomes and best practices generated by SmartTots will be placed in the public domain. Additionally, findings will also help determine strategies for mitigating and managing negative affects on the developing brain and encourage development of new anesthetic drugs that are safer for children.

SmartTots Research Requirements

SmartTots has its own Scientific Advisory Board (SAB) established with the sole purpose of reviewing grant applications for pediatric anesthesia research projects. This group, made up of leading anesthesiologists and researchers in the field, review grant applications and select only the best science to receive funding.

As determined by the SAB, SmartTots funds research focused on three fundamental areas:

1. What is the spectrum of general anesthetic agents, sedatives, surgical procedures, and/or opiates that cause developmental neurotoxicity? What are the doses, durations, and frequencies of exposure? What are the most vulnerable periods of development?
2. Are there short- and long-term neurocognitive, emotional, behavioral, and/or social outcomes resulting from exposure to anesthetic agents?
3. What approaches can be taken to prevent or mitigate developmental anesthetic neurotoxicity?

The SAB has developed stringent eligibility requirements and specific guidelines for applicants to follow when the Request for Proposal period is open.

Timetable and Use of Funds

To fund the type of research necessary to ensure pediatric safety during surgery, we have estimated that we need to fund \$30 million of research over the next 20 years. While the private/public partnership with the FDA was signed in 2011, fundraising activities were launched in 2012. An infusion of \$200,000 from the IARS and funds raised thus far has allowed SmartTots to fund two research projects in 2012. SmartTots is now offering two grants at \$200,000 (paid over a two-year period) in 2013.

IARS and SmartTots Leadership

Board of Trustees

The IARS board of trustees provides oversight of all IARS financial, operating, and programmatic activities. Board members sit on various committees including the Steering Committee developed to manage the day-to-day operations of the SmartTots research initiative.

Executive Committee

Debra A. Schwinn, MD - Chair
Seattle, Washington

Davy C.H. Cheng, MD - Secretary
London, Ontario, Canada

James G. Ramsay, MD - Past Chair
Atlanta, Georgia

Denise J. Wedel, MD - Journal Liaison
Rochester, Minnesota

Alex Evers, MD - Treasurer
St. Louis, Missouri

Makoto Ozaki, MD, PhD – Member-At-Large
Shinjuku, Tokyo, Japan

Members

Emery N. Brown, MD, PhD
Boston, Massachusetts

John F. Butterworth, IV, MD
Richmond, Virginia

Keith A. Jones, MD
Birmingham, Alabama

Colleen Koch, MD, MS, MBA
Cleveland, Ohio

Santhanam Suresh, MD
Chicago, Illinois

Christian P. Werner, MD
Mainz, Germany

SmartTots Steering Committee

The SmartTots Steering Committee provides the day-to-day management of the initiative and consists of IARS board members, FDA staff, and other key partners from the field.

James Ramsay, MD, Co-Chair
Bob Rappaport, MD, Co-Chair
Emery Brown, MD, PhD
Igor Cerny, PharmD
Alex Evers, MD
Robert Nelson, MD, PhD

Merle Paule, PhD
Debra Schwinn, MD
William Slikker, Jr., PhD
Christian Werner, MD
Tom Cooper, Staff

SmartTots Executive Board

In addition to the oversight provided by the IARS Board of Trustees and the day-to-day management provided by the Steering Committee, SmartTots has a fundraising executive board chaired by well-known and respected anesthesiologist Dr. Michael Roizen. The sole focus of the executive board is to raise awareness and funds for the initiative. The board is made up of philanthropists from both inside and outside the medical field.

Board Members

Michael Roizen, MD, Chair
David Abramson
Mehmet Oz, MD
Kelly Posner, PhD

Mark C. Rogers, MD
Ned Russell
George Stephanopoulos

Research Evaluation

All grant awardees are required to submit two reports: a progress report and an end of project report detailing how the money awarded was utilized as well as outcomes of the research. Reporting includes any changes made to the original methodology proposed as well as an explanation of goal achievement. The Scientific Advisory Board reviews progress reports and final reports to evaluate the success of the research project. Results of all research are made available to the public.