Pediatric critical care medicine: Planning for our research future

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Objective: To introduce to the pediatric critical care medicine community a new program in pediatric critical care medicine at the National Institutes of Health.

Data Source: Summary of literature review and conference proceedings.

Data Synthesis: At the National Institute of Child Health and Human Development (NICHD), a new program in pediatric critical care and rehabilitation research has been established in the National Center for Medical Rehabilitation Research. The program is directed by a pediatric intensivist and is focused on developing research toward improving long-term outcomes in pediatric critical care and on incorporating pediatric rehabilitation medicine as a partner in this goal. To provide strategic direction for the new program, the NICHD sponsored a planning conference May 3–4, 2002, at the NICHD in Bethesda, MD. The conference invitees represented a broad range of pediatric critical care medicine clinical and research interests, expertise, and career stages. It also included individuals with expertise in rehabilitation research.

Conclusion: The composition of the new program, including its link to physical medicine and rehabilitation, is discussed. In addition, recommendations by the conference participants and program director are provided to foster the development of more randomized, controlled clinical trials and to develop successful clinician scientists in pediatric critical care medicine. (Pediatr Crit Care Med 2003; 4:196–202)

Key Words: physical medicine and rehabilitation; pediatric critical care medicine; research

The field of pediatric critical care medicine has evolved rapidly in the last 20 yrs, and the mortality rate for critically ill children has decreased dramatically (1, 2). As pediatric critical care medicine matures, the development of research capacity to increase the specialty's knowledge base emerges as a critical issue. Our specialty will need to define a body of research unique to the critical care of children (3). In addition, as more children survive critical illness and as more medically fragile and disabled children are living longer, there is increasing need to undertake research that evaluates long-term outcomes after pediatric critical care.

This report focuses on the research-related issues and opportunities in both pediatric critical care medicine and rehabilitation practice identified by a group of experts at a recent conference sponsored by the National Institute of Child Health and Human Development (NICHD) at the National Institutes of Health (NIH). Within the NICHD, a new program in pediatric critical care and rehabilitation research has been established in the National Center for Medical Rehabilitation Research. The program is directed by a pediatric intensivist, and is focused on the development of research linking critical care and rehabilitation interventions. Such research efforts should provide a knowledge base for improving long-term outcomes in pediatric critical care and in incorporating pediatric rehabilitation medicine as a partner in this agency.

Linking Physical Medicine and Rehabilitation in Pediatric Critical Care Medicine

The research interests, issues, and methods germane to physical medicine and rehabilitation (PM&R) and pediatric critical care medicine are quite complementary. There are many fundamental differences between the two fields, including the clinical paradigm, the research unit of analysis, the functional domains of focus, and the time scales of interest. There is common interest, however, in the same children: survivors of critical birth disorders, injuries, or illnesses who—looking forward—have many years of life and function once the life-threatening condition has been ameliorated.

PM&R utilizes the paradigm of functional hierarchies recently updated by the World Health Organization as the International Classification of Function (4). Whereas pediatric critical care medicine operates primarily at the levels of disease and impairment (with research focus primarily at the level of molecule, gene, and organ system), PM&R focuses at the level of disability (activity and handicap participation), with research more focused on the measurement and improvement of function, activity and participation, and data gathered in study of the child, the family, and the environment. The time scales of interest to pediatric critical care medicine are frequently measured in minutes, hours, or days (e.g., the immediate impact of a treatment for shock), whereas the span of interests in PM&R may extend for months or years (e.g., long-term functional consequences of...
critical illness and pediatric intensive care unit [PICU] treatment that determines ultimate work productivity and outcomes in the adult).

Research methods and data analysis may be quite different for the two fields. Research questions in the field of pediatric critical care medicine may lend themselves to randomized, placebo-controlled clinical trials that utilize parametric statistical methods, although barriers to randomized clinical trials are well known (5). PM&R research frequently utilizes population-based models, and single-subject repeated-measure designs, requiring nonparametric statistical treatment with methods drawn from behavioral and educational statistical methods, including Rausch analysis and multivariate approaches (6).

Despite these differences, there are cooperative opportunities. One example of such an opportunity is the long-established National Pediatric Trauma Registry, which was launched in Boston as a collaborative project between PM&R and pediatric trauma surgeons in the 1980s and blended the interests and methods of both fields into an enduring project (7).

Administrative Barriers to Research

The administrative difficulties of research are well chronicled (6, 7). For example, often heard complaints include there is “never enough time,” “not enough money,” and routine undercompensation or perceived devaluation of effort. As we explore the administrative barriers to research, a microeconomics analysis of the forces affecting supply-and-demand curves was presented to describe the dynamics of research productivity.

The “law of demand” states that the quantity demanded rises as the real cost to the buyer falls. Importantly, the demand curve is viewed from the perspective of the buyer, in this case, the university or hospital. This relationship is summarized in Figure 1. The university will “buy” more research if the price/quantity of research (price per research quantity) decreases (shifting the demand curve). Factors reducing the price/research quantity include relative devaluation of the competing interests, such as teaching and clinical care (thus increasing the personnel pool available for research), decreasing personnel costs (e.g., reducing salaries, hiring younger employees), and increasing the ease of research, as it impacts the buyer. Importantly, pediatric critical care medicine researchers have little influence over these issues, and focusing too much on them wastes valuable time and energy.

The “law of supply” states that costs rise in the short run when production is expanded. The supply curve is viewed from the perspective of the seller, in this case, pediatric critical care medicine practitioners/faculty, who have substantial influence over these issues. This relationship is summarized in Figure 2. We can shift the supply curve (reducing the cost/quantity of research) by favorably improving efficiency, reducing personnel costs, creating a favorable work environment, reducing the development costs of researcher physicians, and increasing the marginal effect (e.g., increasing working hours).

One interesting and important supply curve issue is the development costs of producing a new researcher. Using the NIH K08 or K23 award (75% protected time for at least 3 yrs) as an example for analysis, it takes approximately 2.5 physicians working at 100% productivity (no nonclinical time) to support the development time of a new researcher. Thus, it is readily apparent that support for such development must be obtained from resources other than pediatric critical care medicine faculty. The NIH, and particularly, the new pediatric critical care and rehabilitation research program, may be a source of this essential support.

Overcoming Administrative Barriers to Research

Starting and maintaining a successful pediatric critical care medicine research program is more challenging than ever. A list of essential elements for success in pediatric critical care medicine research was identified from an administrative perspective. Although lessons may be learned from the business literature, which is rich in studies of change, leadership, and group dynamics, the analogies are at best incomplete for the value system of medicine that PM&R and pediatric critical care medicine share.

Implement and Reinforce Leadership Qualities in Researchers and Faculty

The art of leadership is becoming a more focused topic in both the business and medical arenas (8–11). Dealing with a group of physicians is a difficult endeavor and has been compared with herding cats or forcing eagles to fly in formation. Leadership is about asserting influence (not control) and empowering all those around the leader to achieve their full potential; this philosophy enables all members to have ownership in the success of any group activity. This crucial effort is facilitated by clearly delineating roles and delegating responsibilities, while maintaining respect between group members. Leadership in the research setting is the expression of supreme management, organization, and mentoring skills.

Drive Momentum Regularly

For any project or proposal, the team must be inspired daily to move forward, however small a step. Maintaining a high level of morale among physician researchers can be particularly challenging after the initial wave of enthusiasm wanes. Fatigue and the competition between clinical and teaching responsibilities for limited faculty and time resources are two readily identifiable factors.

Measure Progress Periodically

It is useful to have regular research meetings as a group to monitor forward momentum so that all of the members of the group are accountable to the progress of the project as a whole. Progress needs to be measurable (e.g., how many patients

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Figure 1. Research demand curve, buyer (university/hospital) perspective.

Figure 2. Research supply curve, seller (pediatric critical care medicine practitioners/faculty) perspective.
are enrolled in a study and what are the preliminary data. All projects should be managed in the plan-do-study-act cycle so well known in the business world. Differential reward systems may be used as a method to motivate the group.

**Learn Negotiating Skills.** Physicians in general may be perceived as ineffective or impatient negotiators. The pediatric critical care medicine leadership needs to learn to negotiate from a position of strength and to strive for any leader of the research group to understand and appreciate group dynamics. For example, disruptive behavior of a team member is usually better treated as a team problem rather than a personal issue. Second, group learning activities can further consolidate group cohesiveness. A recent review article in *Harvard Business Review* (15) examining cardiac surgical teams learning a new technique revealed that important skills for leaders to foster team learning include being accessible, seeking input from others, and being a “fallibility model.”

**Maintain Quality Management.** Quality management and performance improvement are integral parts of ethical practice in pediatric critical care medicine and PM&R. This value system should be central in any research carried out, and some research projects can easily be extensions of quality or performance improvement projects.

**Acquire Organizational Skills.** For any researcher, or support staff member, organizational skills are of paramount importance. Prioritization and delegation are especially crucial. The importance of obtaining operational efficiency for any process cannot be overemphasized. Even very complex processes in research can be diagrammed; helpful paradigms on the use of diagramming for operations management should be reviewed in available business literature (16).

**Cultivate Human Resources.** Networking and establishing relationships that benefit ongoing and future research is a critical task of investigators. It is important to build alliances with other divisions and disciplines for intra-institutional and multi-institutional collaborative work.

**Build Team Discipline.** The culture of discipline through the organization starts with the right people in the research staff group; people with intensity and diligence do not need a disciplinarian leader. The research program needs to retain a culture of discipline and dedication that should not be compromised, while sustaining a supportive, creative milieu.

**Encourage Program Integrity.** Scientific efforts without integrity in data, people management, and design are disastrous. Continuous reassessment to maintain integrity in the culture and structure of the project is vital. Coercive influences can quickly lead to corruption. In situations in which performance is inadequate, evidence of coercion should be vigorously sought. The Stockdale paradox, a well-known construct that mandates honesty with all around you, is summarized in the following philosophy: “retain the faith that you can and will prevail in the end, regardless of the difficulties, AND at the same time, confront the most brutal facts of your current reality, whatever they might be (17).”

### Barriers Intrinsic to Pediatric Critical Care Medicine Research

Multiple challenges face investigators attempting to perform research in the PICU. These challenges were discussed in detail, as they hamper the ability to design trials that will guide clinical practice. Currently, evidence supporting preventive and therapeutic interventions in critically ill children is generally weak (18).

The number of randomized clinical trials is very low, and most of these trials have used outcome variables of questionable importance. Before designing controlled experiments comparing one intervention with another, we need quality epidemiologic and descriptive studies to guide trial design. For many, if not most, common conditions in the PICU, these studies are lacking.

In general, mortality is a rare event in immunocompetent critically ill children, even in patients with the highest illness severity. Because of this, there is an urgent need to define other clinically important outcome measures for clinical trials. Duration of mechanical ventilation and PICU stay have associated costs, but they are of questionable value as outcome measures when deciding to study drugs or treatment strategies that may cause rare but clinically important complications. Assessment of functional status at PICU discharge is one area in which more research is needed, as it is likely to be the outcome measure used most frequently in future clinical trials. This outcome variable suggests an obvious link between pediatric critical care medicine and PM&R.

### Collaborative Clinical Research in Pediatric Critical Care Medicine: The NICHD Neonatal Network as an Example

Collaborative research in pediatric critical care medicine and PM&R is a necessity by virtue of the fact that our patient populations are diverse, and few, if any, institutions have a sufficiently
large patient population to study specific diseases or interventions in a reasonable time period. Although the foregoing is evident to all who consider the subject, there have been few attempts and even fewer successes at multi-institutional research in pediatric critical care medicine. One example of a successful multi-institutional pediatric research network is the NICHD Neonatal Research Network, now in existence for about 15 yrs. The NICHD Neonatal Research Network was created in response to the need for well-designed clinical trails in neonatology. Principal investigators design protocols that are evaluated by a steering committee and, after approval, studied at each of the network clinical centers. The data are stored and analyzed at a common data center. The network began in 1987 with seven clinical centers, and it now has 16 centers. The data center is located in the Research Triangle Institute in North Carolina. The funding mechanism used is a 5-yr cooperative agreement between NICHD, clinical centers, and the data center. Critical initial elements of networks are identified by the network’s program scientist as: 1) important problems that require collaboration to obtain an answer, 2) standardized, appropriate therapies, 3) clinical equipoise, and 4) the “right” principal investigators.

Productivity of the network is enhanced by other identified crucial elements as well. These include stable funding of infrastructure, a central data safety and monitoring committee, access to large populations of subjects, and mechanisms for developing randomized clinical trials including a protocol review process. The origin of the NICHD Neonatal Network in response to rapidly changing perinatal practice, and the contrast between randomized clinical trial funding through the network model as contrasted with traditional NIH funding mechanisms, is outlined in two references (19, 20).

The conference faculty identified ten barriers to collaborative clinical research in pediatric critical care medicine and discussed possible solutions. The barriers identified are listed below.

1. Pediatric intensivists are not strong believers in the scientific method—much of our care is empirical, and evidence-based medicine has yet to have a major impact in altering practice.

2. Pediatric intensivists are busy and are generally clinically oriented. In an era and specialty driven by doing more for less, we feel that we do not have time to undertake research.

3. Competing studies sometimes vie for the same population.

4. Pediatric intensivists may not be the primary physicians for the patients in the PICU, making enrollment in research studies challenging.

5. Organization and patient composition (diagnoses, demographics) differ in each PICU, resulting in difficulty with both patient recruitment and adherence to research protocols.

6. The mortality rate in our patient population is low, and primary outcome variables other than mortality rate are problematic in clinical research.

7. Physicians often fail to enroll patients in studies and collect data, and the resources to hire research nurses are limited.

8. Financial support may be limited and difficult to identify. Even simple protocols may be expensive.

9. Multi-institutional research requiring interaction with the bureaucracies at each institution, from institutional review boards to clinical study offices, is viewed as a real barrier. Each institution is different, and as a result, operational overhead is magnified, even for simple studies.

10. Only a few investigators can receive meaningful academic credit and financial compensation for participating in a multicenter trial—limiting enthusiasm.

Although solutions for each of these barriers can ultimately be found, development of funded research infrastructure in a network would be an ideal way to enhance the likelihood of successful randomized clinical trials and accurate, large descriptive and epidemiologic studies to guide trial design.

Curriculum Development and Research

At the 1988 meeting of the Association of Medical School Pediatric Department Chairs, it was noted that the principal goal of fellowship training should be the development of future academic pediatricians. For pediatric critical care medicine, clinical work, teaching, and research continue to reflect the core values of academic medicine, but in recent years, economics, politics, and excessive administrative responsibilities have distracted many intensivists, resulting in their failure to thrive in the research arena. The fundamental question remains of whether pediatric intensivists are contributing to the further understanding of critical illness by enriching the academic milieu, obtaining extramural funding, collaborating, and training future physician scientists. At the 1988 Association of Medical School Pediatric Department Chairs meeting, a series of guidelines were established regarding research training in pediatric subspecialties and include:

1. Research training should begin as early as possible.

2. Applicants for fellowship training should be evaluated for their commitment to academic pediatrics.

3. Each fellow should have a mentor and research advisory committee.

4. All fellows should receive training in experimental design, statistical analysis, scientific writing, biomedical ethics, educational techniques, and grant preparation.

5. Training program directors should develop linkages to basic and clinical science disciplines/departments. Similar relationships should be developed with public health and behavioral science departments.

6. Graduates of fellowship programs should be prepared to initiate independent research and seriously compete for peer-reviewed funding.

An essential aspect of research training for fellows involves establishment of a research advisory committee similar to that for graduate students. Such a committee would be composed of experienced faculty research preceptors similar to a doctoral thesis committee who would provide research guidance for fellow trainees.

For two decades, it has been recognized that formal courses in research need to be added to medical school curricula and that national guidelines need to be developed to define the infrastructure for the conduct of and training for research. In pediatric critical care medicine, daily activities provide a wealth of clinical stimuli for research. However, such clinical “light bulbs” can only move toward fundamental discoveries by providing future physician scientists with research training. Basics of such a research curriculum should include the ability to critically review the literature in the field of interest, to define the research questions related to the field of interest, and to know how to identify, design, and in-
terpret appropriate data sources for investigating the research question raised.

For academic pediatric critical care medicine, three imperatives are obvious. There is a need for 1) increased hypothesis-driven research, 2) increased emphasis on extramural funding, and 3) formal research curriculum development. Pediatric critical care medicine fellows need to be provided with training in the methods of basic, clinical, and outcomes research. In addition, fellows should undertake and complete a specific project while interacting and collaborating within an appropriate intellectual environment.

Several institutions have established formal research training programs. One stellar example is at the University of Colorado Health Sciences Center. This program offers a formal, structured, rigorous training experience in clinical investigation or health services–related research. (http://www.uchsc.edu/clinicalscience). Track 1 of the program focuses on clinical investigation, whereas track 2 of the program focuses on health services research. The curriculum for both tracks includes topics in pediatric research, clinical epidemiology, biostatistical methods, ethics, regulation, and human subjects and practical application of molecular and cell biology techniques for the clinical investigator or, alternatively, an introduction to health services research.

Short of a formalized local institutional program for training in research, most institutions have a multitude of resources available to facilitate composition of an ad hoc program. Such resources include institutional review boards and resources for exploring funding. The NIH Guide (http://grants.nih.gov/grants/index.cfm), the COS funding alert system (fundingalert@cos.com), and Science magazine’s Next Wave link (http://nextwave.sciencemag.org/) are readily available starting points. The General Clinical Research Centers (http://www.ncrr.nih.gov/clinical/cr_gcrc.asp) represent the major focus on the National Center for Research Resources, which provides support for clinical research, research infrastructure, biomedical technology, and comparative medicine. General Clinical Research Centers support patient-oriented research, epidemiologic and behavioral studies, outcomes-based research, and health services research. The centers provide resources to local investigators, including experimental design, statistical consultation, clinical research nursing, database assistance, and ancillary coast support, all of which may be of value in training and in conducting clinical research.

An initiative for a national research curriculum for pediatric critical care medicine might be compared with a recent similar initiative introduced by the Pediatric Section of the Society for Critical Care Medicine for PICU resident education (www.picourse.org) or the pediatric critical care medicine Web site (http://pedsccm.org/).

Last year, Russell Chesney, president of the American Academy of Pediatrics encouraged “all groups involved in medical education to collaborate on the development of a curriculum in research methodology for pediatric trainees that introduces core skills of designing, conducting, and interpreting child health research.” Because clinical medicine, and in particular, the intensive care unit, are so inexorably linked to the laboratory, the opportunities for designing and conducting research in critical care are innumerable.

Obviously, many reforms are needed: academic healthcare centers require revitalizing in terms of cost accounting; payment of graduate medical education dollars must go directly to teaching hospitals; the NIH budget must be increased and allocated in such a fashion that pediatric critical care medicine investigator-initiated investigation is realistically supported; and comprehensive healthcare reform must underscore the ethical medical value system that supports clinical research. For fellows who become seriously engaged in such a process, the new NIH-funded educational loan repayment program (http://www.lp.nih.gov/about/extramural/index.htm#pediatric) represents an excellent source of support for those who pursue research careers in basic or clinical sciences.

Research as a pathway to truth is time consuming, usually difficult, and routinely expensive. On the other hand, it is fun and provides a diversion from the clinical stress of intensive care medicine, some protection from burnout, and importantly, a perspective about practice that cannot be gained in another way. If pediatric critical care medicine is to continue to develop as a recognized, respected participant in academic medicine, it must invest serious, consistent, disciplined research training to foster the development of the future pediatric critical care medicine physician-scientist.

Career Development and Research Training of Junior Faculty

Attitudes and values about research are often developed during fellowship. Few programs consistently provide high-quality research training to fellows in pediatric critical care medicine. The situation is similar in pediatric rehabilitation medicine. The reasons for this deficiency have been discussed but can be summarized in three elements: 1) lack of a scientific culture within the fields, 2) lack of scientific mentors and role models, and 3) lack of nonclinical time due to a lack of research training support.

One recent innovative strategy in this area is the establishment of an institutional research advisory committee for the purpose of overseeing an intramural peer review process. The aim of such a functional body is to allocate seed money, research nurses, and data managers to young investigators (fellow and fellows). Institutional funds are used to support the work of beginning investigators. Hard costs are about $250,000 in one program. The committee is especially useful in its function in the mentoring role for divisions without a research tradition. Included in committee membership are the institution’s core of research personnel: nurses, epidemiologist, statistician, administrator, and medical director.

In developing research capacity, the junior faculty career level is a vital link. In a model of pediatric critical care medicine that equates 13 service weeks per year with a full-time academic intensivist position, it is often difficult to foresee the development of research as a prominent career choice. A model of junior faculty development in pediatric critical care medicine is presented from Dallas for junior faculty seeking a research-oriented career. Clinical time is 8–10 wks/yr, irrespective of funding support, for 3–4 yrs. Mentoring relationships within and outside the division of pediatric critical care medicine have been developed and are available to new junior faculty, with these relationships beginning during the job interview process. Junior faculty are encouraged to pursue graduate school basic science courses. Finally, periodic communication and feedback are formally provided. Careful thought and planning are essential to facilitate the retention of these young investigators within the field of pediatric critical care medicine if suc-
cessful development of clinician scientists is to be achieved.

Innovation, Intensity, and Research

Many of the advances in medicine have come from persistent, detailed observation and from innovative ideas arising from the immersion of the investigator in poorly understood clinical realities (21). To the extent that the observed disparities and questions are translated into sound laboratory and clinical experiments, the potential for the enrichment of medical and scientific knowledge has seemed unlimited.

For example, cardiopulmonary bypass came about because a surgical resident watched a woman die of a pulmonary embolus. He was struck by the thought that this patient might have survived if a way existed to drain venous blood from her body, oxygenate it, and return it to her circulation while her body dealt with the embolus. Dr. John Gibbon took this thought to the lab and made it his life’s work. Despite many barriers, and the extreme reluctance of his mentors, he persevered and developed such a device, which was first used for an 18-year-old woman in 1953 to repair an atrial septal defect. From these beginnings, cardiopulmonary bypass revolutionized cardiac surgery. As an offshoot, extracorporeal life support was also developed—again with much persistence, little funding, and continual criticism. Today, >24,000 patients failing conventional therapy have received extracorporeal life support outside of the operating suite. Applications of this method to new patient populations continue to develop.

What are some of the characteristics of innovators? How do innovative ideas and the researchers from whom they spring survive, because many are not well accepted in the beginning? Three “outlook paradigms” are identified that suggest the inner landscape and motivation of innovation. 1) Robert Kennedy: “Some men see things as they are and say ‘sic’ ‘Why?’ I dream things that never were and say [sic] ‘Why not?’” 2) Nike: “Just do it.” 3) Star Trek’s Captain Kirk: “To boldly go where no man has gone before.” Intensivists, provoked by the responsibility to direct the care of the desperately ill, get ideas. PM&R physicians, provoked by the responsibility to maximize outcomes for patients with underlying medical fragility and residual disability get ideas. Given the energy and tenacity to pursue these ideas, old dogma will be questioned and new paths explored. Should these investigators find themselves in an administrative environment supportive of innovation, research will be productive. In addition, experience and encouragement intuitively seem useful to bring innovative ideas to fruition.

What will preserve innovation in medicine? A value system that supports the discovery process is essential. Remembering and applying the scientific method is important and should be a daily habit in caring for children with critical illness and injury. Laboratory and clinical investigations are of equal importance and should be translated one to another, whenever possible. An important task of research leadership is to ensure this balance in funding and effort.

In pediatric critical care medicine and PM&R, there are many opportunities to expand our horizons, and there are many people able and willing to think outside the box. Presently, the danger is that time, money, and personnel are eroding. As clinical workloads rise, the energy and availability of innovators fail to transcend the barriers to research. The elimination of negative incentives and the creation of specific rewards to innovators is imperative.

Pediatric critical care medicine and PM&R have seen dramatic improvements in outcomes since their beginnings. How did this happen without large-scale, randomized, controlled trials? This is best understood through a model described in the business literature as “lead user innovation” (22). Essentially, the process entails investors developing breakthrough discoveries in the laboratory and at the bedside by making changes that improve the outcomes on a real-time basis. A lead user is a person who needs a product, strategy, or technology before it is available or widely used. Lead users will use a technique, product, or strategy before it is validated because they have a unique necessity to do so. This necessity, the mother of innovation, is unique to lead users. Presumably, these innovations could be tested at a later date by randomized, control trials or by other formalized research methodology, but frequently, they are not. For example, fluid therapy was developed by lead user innovations. Years later, a randomized, control trial was done in Dengue shock syndrome, and it showed 100% survival regardless of what type of fluid therapy was used (23, 24).

Critical care abounds with examples of innovation driven by lead users. Nitric oxide was considered an industrial toxin. A researcher described endothelial relaxant factor and then hypothesized that this factor was nitric oxide. A number of lead users administered this gas to children dying of persistent pulmonary hypertension of the newborn. The children survived (25). The FDA approved use of this industrial toxin. After many more years, industry-funded randomized, controlled trials affirmed what the lead users had already demonstrated and disseminated the findings to other lead users in PICUs all over the country. At the present, nitric oxide is commonly used. The NIH, following its mission to improve care for the citizens of the United States, is now interested in sponsoring studies of its use in mechanically ventilated premature infants.

Another illustration comes from the evolution of treatment for acute lung injury or acute respiratory distress syndrome. This pathologic entity was first described after World War II, often referred to as traumatic wet lung, and eventually, Da Nang Lung, and many other names (26, 27). The term acute respiratory distress syndrome was described in the 1970s when mechanical ventilation modalities were evolving, and the confusion created by the use of the word “adult” in describing the entity was acknowledged. An early reference to the use of continuous positive airway pressure as a method of respiratory support appeared as early as 1909 (JB Downs, unpublished observations, September, 2002) (27, 28). Dr. Jack Downs described using an anesthesia ventilator and manipulating its valves so that a small amount of ventilator pressure remained at the end of exhalation (known today as positive end-expiration pressure) (29). The practice
became widespread, and thousands of patients were saved. Eventually, ventilator manufacturers added a positive end-expiration pressure valve in response to the demands of lead users. Many years later, the NIH ARDSnet trial used formalized methodology to study this problem in an effort to make mechanical ventilation both safer and better understood by healthcare practitioners.

In 2003, it is time to support multicenter, randomized, controlled trials, with the network format being used to ensure adequately powered studies. Because mortality rates are so low, morbidity and disability have become more appropriate outcome measures. Contemporaneous with the increased use of multicenter, randomized, controlled trials in our field, lead user innovation must be encouraged and preserved if the best possible outcomes are to be attained for children with complex illnesses. Developing mechanisms that support lead users and more traditional research is the most productive avenue for expanding research capacity in pediatric critical care medicine and PM&R.

Conclusion

This new program in pediatric critical care and rehabilitation research within the National Center for Medical Rehabilitation Research represents an exciting and important opportunity to advance the science and practice of pediatric critical care medicine and improve outcomes of infants and children with life-threatening conditions. As a field, we are indebted to Dr. Duane Alexander, director of the NICHD for recognizing the critical need for the development of clinical scientists in our discipline. We also welcome the opportunity to build important new collaborations with our colleagues in pediatric rehabilitation.

Finally, our field has already begun to benefit from this new program. In November 2002, two requests for applications, one in the area of pediatric cardiopulmonary arrest and the other addressing respiratory failure, were posted and generated considerable interest via the R21 funding mechanism. We look forward to a steady stream of important funding opportunities targeting both clinical trials and career development.

REFERENCES