

LEE E. FARR LECTURE

Sowing the Seeds for a Career in Medicine: Reflections and Projections

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Dr. George Lister delivered the following presentation as the Lee E. Farr Lecturer on May 8, 2011, which served as the culmination of the annual Student Research Day at Yale School of Medicine. He is the Chair of Pediatrics at the University of Texas Southwestern Medical School and Pediatrician-in-Chief at Children's Medical Center of Dallas. In his lecture to the medical students, who had just completed their research theses, Dr. Lister discusses his own work on sudden infant death syndrome (SIDS[†]), demonstrating the complexity of clinical research and proving insight into the traits required of physician scientists. Committed to medical education and recognized by several awards for his mentorship, he ends the talk by imparting valuable advice on future physicians.

Dr. Lister is the Robert L. Moore Chair of Pediatrics at the University of Texas Southwestern Medical School and Pediatrician-in-Chief at Children's Medical Center of Dallas. He received his MD at Yale University and was a pediatric resident at Yale-New Haven Hospital and a

fellow at the University of California, San Francisco (UCSF) and the Cardiovascular Research Institute, where he became interested in post-natal adaptation to hypoxia. He joined the Yale faculty in 1978, where he rose to Professor of Pediatrics and Anesthesiology and founded the Section of

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[†]Abbreviations: SIDS, sudden infant death syndrome; UCSF, University of California, San Francisco; NICHD, National Institute of Child Health and Development; NIH, National Institutes of Health; SPR, Society for Pediatric Research; CVRI, Cardiovascular Research Institute; ICU, intensive care unit; PI, principal investigator; ALTE, apparent life-threatening event; MRI, magnetic resonance imaging; CT, computed tomography

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Critical Care and Applied Physiology, serving as its Chief for more than 20 years before moving to the University of Texas Southwestern. In 1992, Dr. Lister was appointed by the National Institute of Child Health and Development (NICHD) to chair the steering committee of a national study of the Collaborative Home Infant Monitoring Evaluation, a program intended to reassess home monitoring of infants at risk for sudden infant death syndrome (SIDS). This research resulted in a major reduction in home monitoring and was the basis for complete revision of the American Academy's recommendations.

Dr. Lister is deeply committed to the careers of students, residents, and fellows. He directed a National Institutes of Health (NIH)-funded training program in Critical Care Medicine for 20 years; helped initiate the Society for Pediatric Research (SPR) Student Summer Research Program; participated actively in teaching programs in Eastern Europe through a number of international organizations; served as a clinical director of the MD-PhD program at Yale; and worked with colleagues in other countries to create student research opportunities. He has given national addresses on the "Development of the Academic Pediatrician" and the "Complexity of Education in the 21st Century." Additionally, Dr. Lister's teaching and expertise have been recognized through receipt of the Francis Gilman Blake Award and the Charles W. Bohmfalk Prize at Yale, a Fulbright Fellowship, the Distinguished Career Award of the American Academy of Pediatrics, the SPR Maureen Andrew Award for Mentorship, and election to the Institute of Medicine of the National Academies and the Academy of Medicine, Engineering, and Science of Texas. Most recently, he received the 2011 Joseph W. St. Geme, Jr. Leadership Award from the Federation of Pediatric Organizations, which honors role models in pediatrics. In the following lecture, Dr. Lister shares his own research experience and career development as a means of guiding and motivating future physician scientists.

LEE E. FARR LECTURE

I must admit that after I was invited to give the talk, I looked at the list of luminaries and had the distinct feeling that the wrong Lister was invited to give this Farr Lecture.

This is indeed a singular honor, and I wish to address my comments in large measure to the students. I would like to celebrate your imagination, your curiosity, and the qualities that you portrayed through that very special and defining facet of the Yale medical education, the Thesis. The influence of this experience (I do not mean my talk) and the process of exploration culminating in scholarly pursuit will affect the manner in which you approach medicine for the rest of your life, in ways that you cannot contemplate. However, to be true to the scientific principles, you will not be able to do the controlled experiment (for which your parents will be grateful) to prove that it has changed your life. As you look back, you will be astounded that you pursue the problems of your patients differently from many of your peers, which you will see as you enter the world with physicians who have been educated in other schools.

I have entitled my talk "Sowing the Seeds for a Career in Medicine: Reflections and Projections," and I would like to describe my experiences in education, research, and the care of patients, and how each realm has improved and enriched the other. I hope to convey the enjoyment of struggling with a complex problem (as many of you have well demonstrated today), the pleasure of being surrounded by students, and the lessons I have learned along the way.

Well, how did I get to Yale? I would say by serendipity. My interview for medical school was not focused on medicine. We discussed exploration, curiosity, engagement, and poetry. The interviewer, whom I will mention in a moment, probed my willingness to commit to an interest and a passion and even the willingness to take a risk of not succeeding. So who was this? Donald Henry Barron, Professor of Physiology. To put Dr. Barron into perspective, an issue in 1969 of

the *Yale Journal* [1] was dedicated to him and he was viewed as a father of fetal physiology, at least on this side of the ocean. His teacher, Sir Joseph Barcroft from Cambridge, was viewed as the father of fetal physiology on the other side of the Atlantic. Barron worked as a student and then a colleague with Barcroft, and Barcroft's last book, *Researches in Prenatal Life*, was dedicated to Barron. Barron had also been the assistant dean for admissions at the School of Medicine. Thus, two points to make: my deep gratitude to Donald Barron for having the open mind to accept me as a medical student, and more importantly, for demonstrating so well that student can often be the colleague and teacher.

What did I find when I arrived? I found faculty who were accessible and invested in students. I found my own fear that I didn't know enough; I soon shed the trepidation and became certain that I did not know enough. I found faculty who valued curious and industrious learners. I want to be sure you all know these traits are not universal amongst faculty in medical schools; I certainly did not know that at first. I saw faculty who were helping students focus on figuring things out and not intent on drumming more information into their head. And I found my own amazement at the sheer talents of my classmates, at least two of whom have generously supported this student research program and may be in the audience. I was just dazzled by the students and soon recognized the value of those who surrounded me because I learned the most from them.

As a student, I had a series of enriching experiences, although they were not organized with any game plan or blueprint. At the time, these seemed serendipitous, but they were usually prompted by the watchful generous faculty so characteristic of the institution. I went to New Zealand to study rural care on a grant I received my first year. With the support of a senior faculty member, received a grant to conduct my Thesis in a laboratory of the Cardiovascular Research Institute (CVRI) at the University of California, San Francisco (UCSF), and had my

first publication from this experience. After residency here, I returned for fellowship at UCSF to try to develop clinical expertise in the field of pediatric critical care medicine that was neither defined nor consecrated at the time. From faculty, I received encouragement to try something new and returned to the CVRI because it was one of the premiere places at the time for research in fetal and newborn physiology. I also rediscovered how important Donald Barron was, not just to my career.

I then returned to Yale to establish a research laboratory and work in a field that captivated my interest. Again, by serendipity and certainly without advanced planning, I developed a training program. One Saturday morning while working in the laboratory, I received a phone call from two colleagues at Johns Hopkins who said, "George, we've got a fellow for you," to which I said, "I don't have a fellowship program," and in harmony they responded, "Now you do." That's one way to get started. One of those callers became the Chairman of Pediatrics at Utah and the Dean at University of North Carolina and the other the Chairman of Pediatrics at the University of Colorado, a collaborator, lifetime friend, and interestingly, second generation student of Barron's. You never know who is going to call and what opportunities might arrive at your doorstep. Answer the phone.

About 10 years later, I received another unexpected phone call. This was an invitation to a National Institutes of Health (NIH) Conference where I thought I was being asked to help critique a new study on the utility of home monitoring for infants at risk for sudden infant death syndrome (SIDS), but I was actually being asked to lead a program in an area that I knew virtually nothing about. In fact, at the time, I could hardly even spell SIDS. This serendipitous call was certainly a game changer for me, and yet provided another wonderful opportunity and challenge. What I would like to do now is to take a few minutes, not to discuss the whole SIDS program, but to explain how a problem that is seemingly quite simple is actually complex and engaging. I use this as an

example because you will confront many problems as physicians that you're told by others are very simple. However, when you explore and question what is thought to be known, the problem will become far more interesting and complex and make take you on a path you did not anticipate. I am going to take you rapidly through the background where the field of SIDS was about 25 years ago to get to a problem I found fascinating.

What was the interest in SIDS? SIDS was a serious problem with an unsolved mechanism. The challenge by 1990 was that contemporary management made no difference in frequency. There were many children dying of SIDS and many question marks about the cause and the value of new technology to monitor infants, but not a lot of success. In 1979, there were over 5,000 infants thought to die of SIDS and little difference in 1987. It was a third most common cause of death in infancy, and there was a very high rate in certain groups: about 1 per 1,000 in term infants, >3 times that rate in infants who were born very prematurely, two and a half times that rate in native Americans and about twice that rate in black infants. It was very common for infants who had been resuscitated from or thought to be at high risk for a life-threatening event to be admitted to the pediatric intensive care unit (ICU). Indeed, it was a plague that we did not know how to thwart, and the price to pay was high if one's assessment or management was wrong. Thus, the NIH had a high interest in SIDS.

To work on a medical problem, it can be useful to read the initial case report. Many people know about the judgment of Solomon but they do not necessarily know the complete story as written in the biblical passage [2]: "Some time later, two prostitutes came to the king to have an argument settled. 'Please, my lord' one of them began, 'this woman and I live in the same house. I gave birth to a baby while she was with me in the house. Three days later, she also had a baby. We were alone; there were only two of us in the house. But her baby died during the night when she rolled over on it.'" Arguably, this is the first description of SIDS.

Now fast forward to the 1980s, and there were many proposed mechanisms for SIDS. The one that loomed largest was that apnea was the cause, avidly proposed by a pediatrician, Alfred Steinschneider. There were many other theories, including chronic hypoxia, facial positioning with asphyxia, regurgitation of milk, overheating, structural neural abnormalities, rhythm disturbances including a long QT syndrome, and infection and deficits in immunity.

So, what confounded the field of study? Here are some of the factors. A paper published in 1969 in the journal *Pediatrics* [3] proposed that, using impedance plethysmography, "continuous monitoring of respiration in small infants is now clinically feasible." That paper was followed in 1972 with a report by Steinschneider in *Pediatrics* [4] of five infants, two of whom died of SIDS, that stated, "These data support the hypothesis that prolonged apnea is part of the final pathway resulting in sudden death. . . . infants at risk might be identified prior to the final tragic event." Just to set the scene, a device was developed that could monitor respiration in infants, and then five infants in three families were described, three of whom were referred because of cyanotic episodes risk for dying, and two subsequently died. This was the genesis of the apnea hypothesis, and it was perfectly plausible that if a baby does not breathe for long enough time, he would die. However, the rationale for monitoring was not so simple. To point out the complexity and controversy, there was a lively correspondence in *Pediatrics*, which I have labeled Point and Counterpoint, and I want to share the charged exchange.

The Point [5]: "Conclusive proof that SIDS is preventable through the use of home monitors is lacking. The 'hardware' currently on the market is not well adapted. There's reason to be seriously concerned about adverse effects on parental behavior. There are many types of sleep apnea, both obstructive and nonobstructive." Indeed, many parents commonly turned off the monitors because they seemed to alarm randomly and became disruptive.

SIDS: Theories Compete in Profusion

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ORIGINAL ARTICLE
 Volume 338:1709-1714 June 11, 1998 Number 24

Prolongation of the QT Interval and the Sudden Infant Death Syndrome
Peter John Schwartz, M.D., Marco Stramba-Badiale, M.D., Ph.D., Alessandro Segantini, M.D., Paola Austeri, M.D., Giuliano Bosi, M.D., Roberto Giorgetti, M.D., Fabio Gracini, M.D., Ernesto Diego Marni, M.D., Francesco Perricone, M.D., Dario Rosti, M.D., and Patrizia Salice, M.D.

Figure 1. *New England Journal* headlines about SIDS.

The Counterpoint [6]: Steinschneider wrote, “These systems are of value in the management of infants having prolonged apnea and recurrent apneic episodes. Sufficient experience exists to justify our concern for the consequences. The authors recognize that . . . There must be a reversible point in the pathologic spectrum of SIDS.”

Upon review of the chaos of the literature at the time, I thought the smartest thing was said by Sylvia Limerick, Countess of Limerick, at a SIDS conference: “When theories compete in profusion then the experts conclude, in confusion, there’ll be flaws in all laws of this unexplained cause till the problem is solved by exclusion” [7].

To demonstrate the theories competing in profusion, I have extracted some of the *New England Journal* headlines about SIDS (Figure 1). The confusion was well documented by a statement from an NIH Consensus Conference in 1986 that “cardiorespiratory monitoring or an alternative therapy is medically indicated,” even though effectiveness of home monitors in reducing infant morbidity or mortality remained to be established [8]. The

ineffectiveness of home monitoring was demonstrated by the lack of change in the incidence of SIDS from 1984, once monitors became readily available, until 1989.

Why weren’t the monitors effective? Perhaps the hypothesis for the cause of SIDS was erroneous. Alternatively, the hypothesis was correct, but the monitors were flawed. Or, it was also possible that there was an eclectic group of mechanisms and any benefit related to apnea was too small to detect. Hence, we were left at this point with no proven means to assess breathing in infants but with apnea as the leading contender as the cause of SIDS.

The principal investigators (PIs) who were part of this study had different views of the problem and different approaches to monitoring. A reasonable starting point was to develop a schematic to highlight the hypothesis and unproven assumptions, which is shown by Figure 2. Based on the contemporary data, SIDS seemed to have a predilection for three groups of infants: those with an apparent life-threatening event (ALTE), siblings of SIDS victims, and premature infants. The prevailing hypothesis

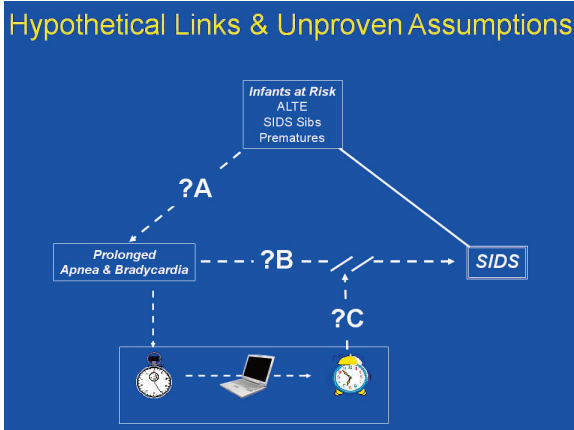


Figure 2. A schematic highlighting the hypothesis and unproven assumptions about SIDS.

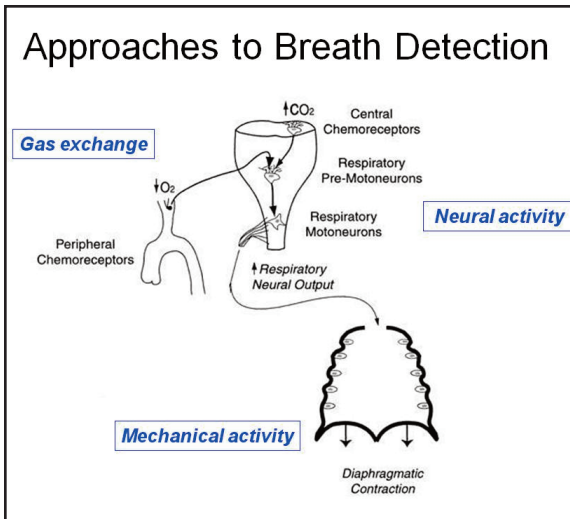


Figure 3. Approaches to breath detection.

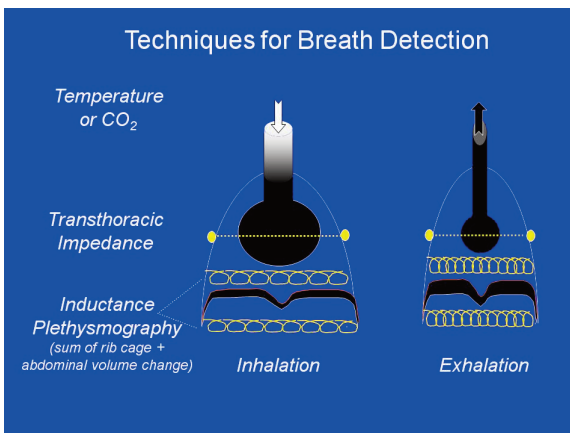


Figure 4. Some of the common techniques available at the time for detecting a breath.

(A) was that these infants had prolonged apnea or bradycardia. The rationale for monitoring was that the apnea or bradycardia (B) caused SIDS, and that a monitor with an alarm (C) could intercept the life-threatening event by either arousing the caregiver or the infant. The schema outlined a credible approach to the problem, but hypothesis A was more formidable than I imagined. At our first meeting, each PI presented slides with respiratory patterns, and all I saw were wavy lines but could not tell what the figures represented. When I showed the data to colleagues and asked them to explain what they saw, each scratched his head and professed being bewildered; even educated guesses were not concordant. Indeed, when we formally analyzed 80 respiratory traces only 20 percent of the time was there agreement among the seven PIs, and only 4 percent of the time was there agreement among all. I first thought this might be caused by less than precise data collection, but quickly realized the disparities might have a more complicated root cause. Thus, our first major challenge was to determine a valid means to detect and analyze a breath. Figure 3 shows that one might use a different strategy depending on the feature of breathing — neural activity, mechanical activity, or gas exchange — that is to be scrutinized.

Figure 4 shows a cartoon demonstrating some of the common techniques that were available at the time for detecting a breath. One technique used a thermistor placed at the nose or mouth to measure the temperature of expired gas. Alternatively, one could use an infrared probe that detects carbon dioxide, often referred to

as an end-tidal CO₂ monitor. As we exhale, the carbon dioxide pressure rises rapidly from 0 to a value close to that of arterial blood, because there is nearly complete equilibration between CO₂ in alveolar gas and arterial blood. Another technique, called the trans-thoracic impedance, is measured between two electrodes placed across the chest. This is the method that is used in most hospital rooms today. It produces the wavy lines commonly seen on monitors and was the basis for the monitors that children were sent home with before our study. I once thought the size of the wave correlated with the volume of the breath, but the device is constantly readjusted internally to be able to see a breath. Another available device, inductance plethysmography, uses two elastic bands, one around the chest and the other around the abdomen. When a subject takes a deep breath, either the chest wall is expanded circumferentially or the abdomen is expanded as the diaphragm descends and pushes the abdominal contents out. Thus, the sum of the volume change in the thorax and the abdomen is equivalent to the volume of a breath.

Here are examples that show breathing patterns using two of these techniques. Figure 5 shows comparison between the inductance and the impedance device, both with a pattern of “breath, no breath, and a breath,” or concordance between techniques. However, when we examine similar data in the infant at another time (Figure 6), we see “breath, no breath, breath” using inductance, but no breath using impedance. The infant is perceived to be breathing by one device and not by the other. Of course the alarm would go off for the impedance device, which is exactly what happened to thousands of families whose infants were monitored. Another confounding factor is the presence of airflow ob-

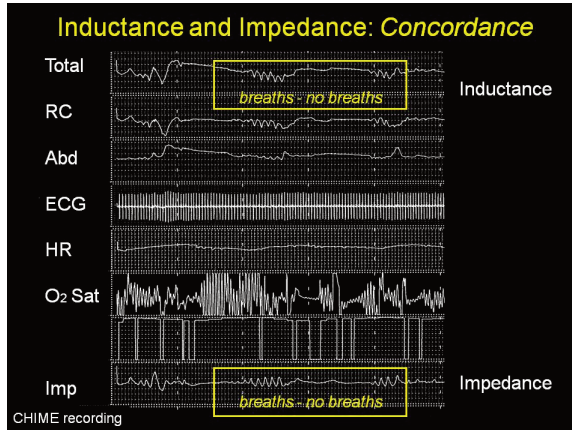


Figure 5. Comparisons between the inductance and impedance device, both with a pattern of “breath, no breath, and a breath,” or concordance between techniques.

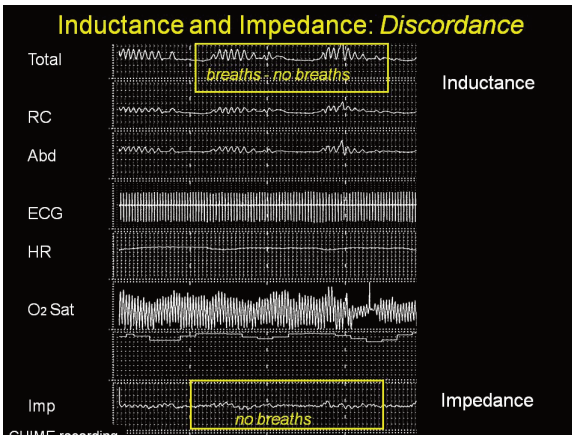


Figure 6. “Breath, no breath” using inductance but no breaths using impedance, demonstrating discordance between techniques.

struction, which is quite important for the infants we studied: a) using inductance plethysmography, there will be no net air entry detected and no net increase in chest plus abdominal volume, i.e., apnea; and b) with impedance, the rib cage can appear to be expanding even though there is little or no air entry, i.e., no apnea.

In other circumstances, the devices provided data that made it difficult to determine when a breath was initiated after a period of apnea, so it was complicated to know how long the apnea lasted. The difficulty is that a breath is not a fixed volume. We know that in quiet breathing, a breath is 5 to 6 milliliters per kilogram, but a breath could be 4mL per kg or even less. So, to detect a

breath in a baby, one has to have some arbitrary threshold that is acceptable. We also found considerable disparity when we compared the end-tidal CO₂ tracing and the thermistor. Sometimes the CO₂ concentration increased appropriately with an expiration, but we did not see much of a change in the thermistor temperature. This may have occurred because the temperature deviation in the thermistor depends on how long inspired gas is retained in the thorax, and thus is warmed. If an infant breathes fast or pants, the expired air may not be very warm, and if the breathing is slower, the air warms to body temperature. In contrast, CO₂ increases somewhat independently of the exhaled volume as long as the breath exceeds dead space, but some other factors may create a tracing with a slow indistinct increase.

Where did this leave us and what did we learn? Judging the adequacy of ventilation was not such a simple task. The reason that investigators were not agreeing was not because one group was clever and others were not. Rather, the fundamental process of breathing is darn hard to detect and quantifying a breath is even more difficult, especially in a baby. Why? The timing of detection influences the results. Some devices detect the change from inspiration to expiration; some detect early expiration; and some detect expiration to inspiration. Moreover, there are different thresholds for detection. Some techniques are quantitative and some are qualitative with respect to the volume of the breath. In addition to the differences that result from various techniques, there is can be disparity in interpretation. Interestingly enough as we began to search for a means to track breathing in infants, we realized that investigators were measuring different qualities of a breath none of which were perfect, and we had to come to some resolution. Recognizing the utter complexity in detecting a breath and judging whether it was adequate was an epiphany for me. I had been watching infants breathe for years, but finding a means to measure with validity while an infant was at home was an informative and challenging journey.

Even with a single method for breath detection, one needs to have some agree-

ment on what constitutes a breath because there are decisions to be made regarding the threshold and interpretation of the data. Accordingly, we examined inter-rater reliability to judge the duration of apnea and quickly learned two important lessons: 1) it's better to have technicians than investigators judge data; they follow rules more consistently; and 2) there is an effect of training, which is shown by progressive improvement in judging respiration with a second data set. I am pleased that we ultimately developed a valid, well-tested, and consistent method to detect and record respiration in infants at home and to distinguish whether apnea was from airway obstruction or disordered control (central apnea).

With the appropriate methods, we studied over 1,000 infants for over 700,000 hours to test our set of hypotheses. Our subjects included 306 healthy term infants, 152 infants with an ALTE, 178 siblings of SIDS victims, and 443 premature infants. An ALTE had been defined as any episode that was frightening to the observer and that was characterized by some combination of apnea, (central or obstructive), color change (cyanosis, pallor, plethora), marked change in muscle tone (usually limpness), choking, or gagging. We included these groups of infants because they were thought to have a far higher than normal incidence of sudden infant death. We reasoned if we were going compare breathing activity amongst these putative "at-risk" infants, we had to know the breathing patterns in presumed healthy infants. We specifically included healthy term infants because we knew that families who had babies at home on monitors reported that they were constantly turning the monitors off because they were alarming when the infants looked fine, possibly because these were false alarms and the monitors detected apnea when it did not exist or that even healthy babies have episodic breathing with prolonged periods of apnea. The monitors that were in common use at the time were detecting apnea when it exceeded 20 seconds, the "conventional threshold." With the aid of a group of experts in respiratory physiology, we then cre-

ated what we called “extreme thresholds” for apnea and bradycardia, based on postnatal age because we thought it would unconscionable to have a monitor on an infant believed to be at high at risk for SIDS with no alarm. With trust in the integrity of our data and established thresholds for an alarm, we first asked whether these infants “at risk” were indeed susceptible to prolonged apnea or bradycardia (as shown by the large question mark). In our hypothetical construct, the monitor detects apnea or bradycardia, starts a stopwatch, initiates a computer recording and triggers an alarm that wakes either the caregiver or the baby to intercept the event.

The overall findings can be summarized in a single figure (see Figure 4 of reference [9]) that shows the frequency of extreme apnea or bradycardia in all infants studied. The frequency in healthy term infants serves as the reference value in contrast to the other groups of infants. It was apparent that the increased frequency of extreme events occurred before 43 weeks post-conceptual age (about 2 weeks post-term). The younger the infants, the higher the frequency of events, but interestingly enough, by 43 weeks, event frequency decreased and there was no difference among infant groups, including those who were born prematurely, in the frequency of extreme events when compared to health term infants.

From these data we concluded the following. There was an increased incidence of extreme events only in preterm infants and only to 43 weeks post-conceptual age (about 2 weeks post-term). There was no difference in extreme events in children with an ALTE or SIDS siblings compared to health term infants. There was a very high frequency of obstructed breathing, which we were able to detect with our methodology, and a very high incidence of conventional events in all infants including healthy term babies, which is likely the reason parents commonly turned off the monitors.

Although we did not find that any infants except those born prematurely had prolonged apnea or bradycardia, sometimes one gets lucky in a study and new insights are provided. We superimposed our data on the

published data that provides the age at which there is peak incidence of SIDS [10]. For a term infant, the peak incidence of SIDS was about 52 weeks, and the peak incidence was at an earlier age in preterm infants — the more premature, the younger the age at peak incidence of SIDS. It was readily apparent that the peak incidence of SIDS was far later, by weeks, than the peak incidence of apnea and bradycardia. Thus, these additional data provided strong inference that the apnea and bradycardia in these infants was not the immediate precursor to SIDS, a difficult concept to have accepted at the time because of the prevailing view that the apnea frequently observed in infants was the cause for SIDS.

Just about at the time these studies were initiated, there was the observation in the United Kingdom that infants who succumbed to SIDS were found much more frequently on their stomach than on their back. Following review of the available data in 1992, the American Academy of Pediatric issued an official recommendation to its members to advise supine sleeping position [11]. The NIH subsequently held a consensus conference, which I attended, that recommended that infants be placed on their backs for sleep and soon thereafter launched a public campaign to promote this practice. The incidence of SIDS began to decrease within 2 years. I certainly will not take credit for immediately embracing the recommended change in sleep position, but I was quite interested in studying the relationship between position and cardiorespiratory events. To address that, we used a small device known as an accelerometer that could be placed on the sleeping infant’s back to distinguish prone for supine position.

With the dramatic reduction in SIDS that was associated with the recommendations for supine sleep position, the next problem was how to have those recommendations embraced by families in certain ethnic groups, particularly African-Americans, where incidence of SIDS remains high and non-supine sleep is also relatively high. This has been a major focus of the work by Eve Colson, who is on the faculty at Yale. Be-

cause the adoption of supine sleep position in black infants has lagged behind white infants, Colson, in a recent paper [12], derived the sobering estimate that from 1997-2002, 719 lives would have been saved if the recommendations would have been followed and supine sleep position had been employed for black infants at the same pace as the white infants. It is very interesting to learn how research gets translated into public policy and where the sources of resistance reside and challenging to change practice. While there has been substantial reduction in SIDS, numerous questions remain to be answered. I hope this brief reflection on a rocky journey shows how difficult but fascinating and gratifying pursuit of a serious problem can be.

I would like to spend the concluding time commenting on some of the lessons that I have learned during my career, regrettably more than once. I address these thoughts particularly to you, the students, in anticipation that these might be useful thoughts when you take your hard-earned knowledge and curiosity to the bedside of your patients.

First, surround yourself with people smarter than you, then look over your shoulder. I commented earlier but want to emphasize how much my classmates taught me, perhaps as much as my professors did because I was more willing to expose my ignorance to them. I also cannot stress enough the importance of the students, residents, and fellows who have worked with me and taught me many new things. One needs to have an open mind to learn from the student, and today's activities are a great example of that.

Next, the intersection of what afflicts the patient and what challenges the physician to me creates excitement and the bond for the doctor-patient relationship. This is fundamental to the world of medicine, and I hope a lesson that I hope I never forget. It has been said by people far smarter than I and far more established in the medical field but the privilege and opportunity to learn from your patient and be invested in the same problem that your patient suffers from is really the beginning of being a physician.

Take mastery of your education now; no one else will. What do I mean by that? Instead of asking your residents or your attending what to do, consider a problem, propose an approach and a rationale, and request affirmation or a rationale for an alternative. It is very easy to ask someone what to do; it is a little bit harder, particularly when you might be tired, to propose your ideas, but it is your best opportunity to learn. You will not learn from being told what to do. You will learn from carefully considering a problem and understanding why you arrived at a particular conclusion. Thus, every patient interaction represents that opportunity to learn.

Do not ignore an observation just because you disagree with the explanation. I read this wonderful excerpt from a book [13] by Robert Adair, the Sterling Professor of Physics at Yale, that captures this notion. He commented on risk of preconceived notions as follows:

"In all sports analysis it's important for scientists to avoid hubris and pay careful attention to the athletes. Major League players are serious people who are intelligent and knowledgeable about their livelihood. Specific operational conclusions held by a consensus of players are seldom wrong, though since baseball players are athletes not engineers or physicists their rationale may be imperfect. If players think that they hit better after illegally drilling a hole in their bat and filling it with cork they must be taken seriously. The reasons they give for their improvement, however, may not be valid." The point is that your patients are going to tell you things and there is a high risk of dismissing what they describe because we do not believe the explanation. Do not ignore what they have to tell you. Figure out the reason.

When I was a fellow, one of my mentors taught me that many people discard data point if they do not fit an analysis, but one ought to embrace the outlier because it may provide the novel insight into the problem. We often dismiss what does not fit our preconceived idea and are even coached for examinations just to pursue the familiar

elements. With your patients, you should not dismiss elements that do not fit. Rather, try to reconcile them.

In the ICU, which is where I practiced, I often commented that we not predict the future, only the past. More than one time a resident has gone to tell a parent or a patient about a procedure that is going to be performed, or a magnetic resonance imaging (MRI) or computed tomography (CT) scan that will be done at a particular time, and then it is postponed. That delay may be incidental to the physician but huge to the patient. Do not promise a patient or a family what you cannot deliver. My view is the only thing you can really promise is your presence and attention, but that will mean an awful lot to your patients.

Speak to families and patients in clear language. They will appreciate understanding what you have to say. I remember hearing an ear, nose, and throat surgeon ask a patient to raise his uvula. I hope the point is clear.

Next, find out what someone is seeking before giving advice. The friend may be asking an opinion about a surgeon, but that surgeon is operating, as you speak, on a family member of your friend.

The value of teaching is that it forces you to learn. Even as interns you are going to be in a position to teach others. This will be the greatest opportunity to figure out what you truly understand.

The value of writing clearly is that it helps you understand what are thinking. A clear manuscript is likely to be read, and a clear manuscript is most likely to be read rapidly. What you write is associated with your name forever, so make it the highest quality possible.

The successful scholar is not one who gets everything accepted, it is the one who responds to criticism and keeps trying. For those who have just presented your work, know that there are many Nobel Prize winners who have had manuscripts rejected or who have had grants turned down. They learn from the experience and the critique, they improve the document, and resubmit it. To emphasize the point, here is a summary statement for Christopher Columbus: This

project requests two years of support for equipping a small fleet of vessels for westward voyage from Spain beyond the Azores to the Indies. The entire basis of this proposal rests on the thesis that is yet unproven that the world is round. Disapproval is recommended based on the lack of scientific merit.

To finalize my comments, in your career try to make decisions thoughtful, then figure out how to make your decisions work. I have many students come to me wanting to know how to make the right decision about their educational plans. I often ask them to reflect back on the choices they made up to this point that are wrong. They usually look at me with a blank stare. It is not that they have been geniuses by making perfect choices. Rather, successful people take a step forward, learn from experience, and figure out how to get the most from their decisions. They are surprised they have taken the right steps, but actually it is because of their adaptability not just the decision-making. To end, one of my favorite authors said the covers of this book are too far apart, and I think that's a good signal to complete this presentation. I thank all of you.

REFERENCES

1. Nahum LH. Donald Henry Barron. *Yale J Biol Med.* 1969;42(3-4):130-8.
2. The Bible. 1 Kings 3:16-19.
3. Daily WJ, Klaus M, Meyer HB. Apnea in premature infants: monitoring, incidence, heart rate changes, and an effect of environmental temperature. *Pediatrics.* 1969;43(4):510-8.
4. Steinschneider A. Prolonged apnea and the sudden infant death syndrome: clinical and laboratory observations. *Pediatrics.* 1972;50(4):646-54.
5. Bergman A, Beckwith B, Ray CG. The apnea monitor business. *Pediatrics* 1975;56:1.
6. Steinschneider A. Nasopharyngitis and prolonged sleep apnea. *Pediatrics* 1976;58:1.
7. Firstman R, Talan J. *The Death of Innocents.* New York: Bantam Books; 1997. p 318.
8. National Institutes of Health Consensus Development Conference on Infantile Apnea and Home Monitoring, Sept 29 to Oct 1, 1986. *Pediatrics.* 1987;79(2):292-9.
9. Ramanathan R, Corwin MJ, Lister G, et al. Collaborative Home Infant Monitoring Evaluation (CHIME) Study Group. Cardiorespiratory events recorded on home monitors: Comparison of healthy infants with those at increased risk for SIDS. *JAMA.* 2001;285(17):2199-207.

10. Malloy MH, Hoffman HJ. Prematurity, sudden infant death syndrome, and age of death. *Pediatrics*. 1995;96:464-71.
11. American Academy of Pediatrics, Task Force on Infant Positioning and SIDS. Positioning and SIDS. *Pediatrics*. 1992;89:1120-6.
12. Colson ER, Rybin D, Lister G, et al. Trends and factors associated with infant sleeping position: the national infant sleep position study, 1993-2007. *Arch Pediatr Adolesc Med*. 2009;163(12):1122-8.
13. Adair RK. *The Physics of Baseball*. New York: Harper & Row;1990. p 3.