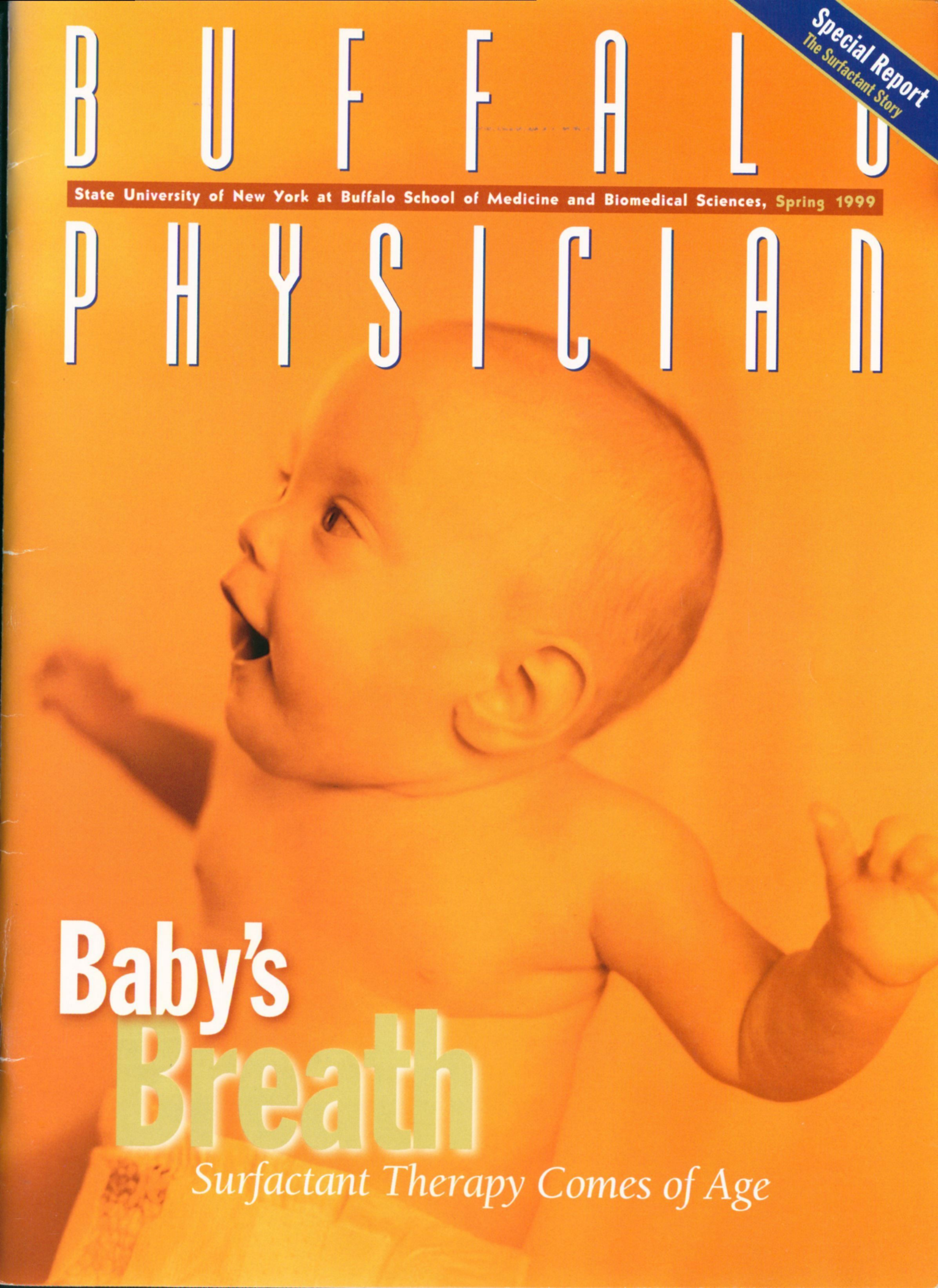
BUFFALO PHYSICIAN

State University of New York at Buffalo School of Medicine and Biomedical Sciences, Spring 1999

Special Report
The Surfactant Story



Baby's Breath

Surfactant Therapy Comes of Age

BUFFALO PHYSICIAN
Volume 33, Number 4

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Buffalo Physician is published quarterly by the State University of New York at Buffalo School of Medicine and Biomedical Sciences and the Office of Publications. It is sent, free of charge, to alumni, faculty, students, residents, and friends. The staff reserves the right to edit all copy and submissions accepted for publication.

Letters to the editor, address changes or other correspondence should be addressed to: The Editor, *Buffalo Physician*, State University of New York at Buffalo, Office of Publications, 136 Crofts Hall, Buffalo, NY 14260. We can also be reached by phone at (716) 645-6969; by fax at (716) 645-2313; or by e-mail at bpnotes@pub.buffalo.edu

Dear Alumni and Friends,

BY NOW YOU SHOULD HAVE RECOVERED from the pictorial extravaganza, featuring your new dean, in the winter issue of *Buffalo Physician*. Now, as I travel around the countryside meeting alumni, I will perhaps have become a more familiar face.

Having just returned from such a trip (Houston, Dallas and San Antonio) it occurred to me that perhaps, as important as these excursions might be for maintaining contact with the school, they also represent marvelous opportunities for connecting alumni with others in the region. For example, in addition to getting together with classmates, more recent UB graduates are able to meet established alumni who just happen to live and work in the same area of the country. In Houston, where Robert Hall, class of 1948, hosted a dinner and reception, the graduation dates of alumnus representation spanned 56 years, including two graduates enrolled in the early years of their respective residency training programs. These residents were able to make contacts with established UB alumni—well placed and highly respected within the local academic and medical community, as well as nationally. In turn, the more "chronologically challenged" alums had opportunities to compare their experiences at UB with those of the more recent graduates.

At our Dallas meeting, hosted by Ken Altschuler (Class of 1952), the represented dates of graduation spanned 46 years and provided similar networking opportunities, as did our subsequent meeting in San Antonio, hosted by Bradley Aust (Class of 1949), where two alumni were able to join the Dean's Advisory Council for a reception and dinner. Clearly, this kind of local networking is something we should try to encourage and facilitate through these events. Indeed, as we plan to repeat the Texas circuit of visits on a more regular basis, hopefully the word will get out about these affairs yielding even greater turnouts—and consequently, enhanced networking opportunities.

Spurred on by the success of these recent meetings, we are planning additional outings to include California and Florida. Please be receptive to any of the forthcoming invitations to participate in one of these gatherings. I look forward to meeting with as many of you as possible. It is particularly gratifying to meet former students but it is also great fun to trade anecdotes with pre-1963 graduates. Although my chair tenure in Buffalo began in 1974, I was also at UB and actively teaching, between 1963 and 1967 (in fact, it is a little-known fact that I personally crafted many of the pathology exams during that time). Accordingly, I feel I know at least some of the students from that era as well.

If we don't have an opportunity to meet on one of these future trips, I hope to see as many of you as possible at the upcoming Spring Clinical Day, which is scheduled for the first weekend in May. See you there!

John R. Wright, MD
Dean, School of Medicine and Biomedical Sciences

Dear Fellow Alumni,

I KNOW MANY ALUMNI HAVE NO IDEA how the Medical Alumni Association is governed, so this letter is my attempt to change that. The Governing Board oversees the various activities of the association. It consists of three officers, seven to nine active members, the immediate past president, three emeritus members and regional members representing alumni from outside Western New York. The board has several committees that oversee finances, medical student affairs, alumni awards and Spring Clinical Day/reunion activities. The purposes of the Medical Alumni Association (as stated by our Bylaws) is to promote the general welfare of the medical school, to advance the cause of medical education, to instill a fraternal spirit in the student body and to sustain that spirit among its alumni.

The Governing Board meets ten times per year, in addition to the annual business meeting during Spring Clinical Day. Dues-paying members are invited to attend meetings and are encouraged to notify board members or the alumni office of their interest in becoming involved.

It has been my honor to serve as the president of the Medical Alumni Association this year. I would like to acknowledge the support and help received from Mrs. Nancy Druar, the association's administrative assistant. She has had a particularly arduous year with our offices being moved and telephones being changed multiple times, as I am sure anyone who has tried to contact the office knows. Despite these hardships, she has sustained all the good works of our organization with much grace. I will pass the gavel to Richard Collins, '83, on May 1, 1999, at Spring Clinical Day. I hope to see many of you there.

Elizabeth L. Maher, MD
President, Medical Alumni Association

BUFFALO PHYSICIAN

VOLUME 33, NUMBER 4
SPRING 1999

COVER PHOTO BY PAUL FRANCIS

PICTURED ON THE COVER is nine-month-old Kristie Ponter, who was born at 23 weeks and weighed 1.4 pounds. She developed respiratory distress syndrome and was given surfactant shortly after her birth, according to her parents, Joelle and Rick Ponter of Gasport, New York. At her last checkup, Kristie weighed over 10 pounds.

The Surfactant Story

by S. A. Unger

Photos by Paul Francis

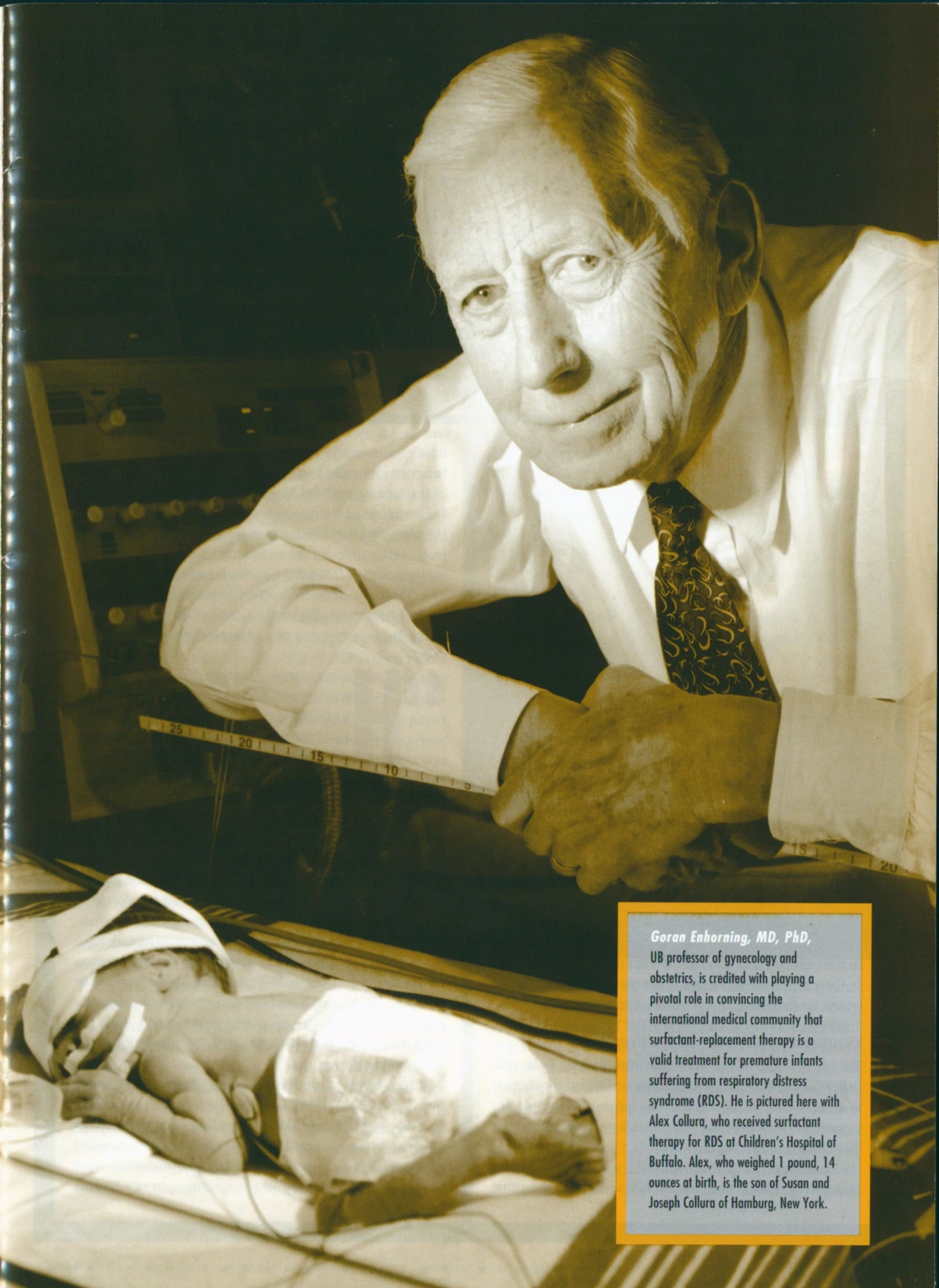
Buffalo's historic role in surfactant therapy, and the man who led the way

"It hurt me to see that when infants were born too early and had difficulty breathing, really nothing could be done about it. They were just left to die."

In one breath, these are the words spoken by Goran Enhorning, obstetrician, as he talks about his motive for beginning his tortuous, but historic, quest to develop exogenous pulmonary surfactant 35 years ago. His hopes then, as they are today, were simple and straightforward: to alleviate the suffering and prevent the death of premature babies afflicted with respiratory distress syndrome (RDS), a condition that, previous to "the surfactant era," killed 70 percent of its victims.

In his next breath, Goran Enhorning, Swedish research physiologist and inventor, moves away from the realm of the heart and into the mind, where, with softly accented words, he struggles to translate into layman's language the scientific insights he has experienced throughout his controversial career, a career he is still fully engaged in at age 75.

Leaning forward in his chair in his office at the Children's Hospital of Buffalo, he explains that surfactant is a naturally occurring substance in the lungs that helps make breathing possible by decreasing surface tension at the airway-fluid interface in the alveoli. "Surface tension was described by LaPlace's Law—you know, P equals two times T over R, with P representing the pressure that must be generated to overcome surface tension, T, and R representing the radius of the alveolus . . ."



Goran Enhorning, MD, PhD, UB professor of gynecology and obstetrics, is credited with playing a pivotal role in convincing the international medical community that surfactant-replacement therapy is a valid treatment for premature infants suffering from respiratory distress syndrome (RDS). He is pictured here with Alex Collura, who received surfactant therapy for RDS at Children's Hospital of Buffalo. Alex, who weighed 1 pound, 14 ounces at birth, is the son of Susan and Joseph Collura of Hamburg, New York.

In talking with Enhorning, it becomes clear how his affinity for both basic science and medicine enabled him to make crucial contributions that kept the field of surfactant research alive in years past, when leading experts worldwide dismissed its viability. It also becomes clear that his work contributed to making Buffalo, New York, a hub for surfactant research—a place where world-class scientists converged in free-wheeling collaboration to help make real the dream Enhorning first envisioned many decades ago.

These scientists include Enhorning's long-time colleague and sometime rival Edmund "Ted" Egan II, MD, professor of pediatrics and physiology at the University at Buffalo School of Medicine and Biomedical Sciences. In the early 1980s, Egan and his collaborators—building on Enhorning's seminal work—spurred on a highly contentious international race to develop the first exogenous surfactant product. Today, despite the behind-the-scenes jostling that continues among these competitors, there are several surfactant products on the market and, as a result, the mortality rate for infants born with RDS has dropped to 5 percent.

This dramatic, innovative work has not ended in the clinic, however. As the 1990s draw to a close, Buffalo is equally noted for the contributions its scientists are making to basic research in the area of surfactant therapy—contributions that are leading the field into the 21st century, where it promises to impact a wide range of respiratory disorders affecting adults, as well as neonates.

Bruce Holm, PhD, associate dean for research and graduate studies at UB's School of Medicine and Biomedical Sciences, is one of the preeminent scientists recruited to UB in the late 1980s by Enhorning and Egan. Like many others worldwide, he readily acknowledges the pioneering contributions made by Enhorning, whose fortitude against all odds is now as well honored as his science. "If it weren't for Goran Enhorning, we wouldn't have the low neonatal mortality rates we have today," states Holm, "and we wouldn't have been able to develop our understanding of the science behind pulmonary surfactant to the extent we have. And, clearly, there's a good deal for the Buffalo medical community to be proud of regarding its contributions to surfactant therapy and research.

"But the surfactant story isn't over yet," he adds. "Even though it has already resulted in what would have to be considered one of the most dramatic breakthroughs in the past 50 years in terms of what neonatologists have in their repertoire for treating prematurely born infants, everyone involved believes there's much more to come."

Discovering How the Lungs Work—or Don't

To get a sense of the fortitude Enhorning, Egan and others needed to bring exogenous surfactant to where it is today—and to appreciate the promise it holds for tomorrow—it's necessary to go back to 1929, when the "surfactant story" begins.

That year, a pulmonologist named Kurt von Neergaard, who was living in Switzerland at the time, first espoused the theory that in order for the lung to function, it needed an agent that would coat the inside of the airway, particularly the tiny air sacs called alveoli (of which an adult human lung has about three million). He surmised that this coating would prevent the alveoli from collapsing during expiration, when they become very small. Working from an understanding of the Law of LaPlace, he deduced correctly that this agent causes surface tension in the lung to change its value and that the agent is composed of a phospholipid or protein.

"He became so frustrated trying to get his work published, he gave up," explains Enhorning. Medical historians often cite von Neergaard's finding as a classic example of a "premature discovery," as nothing was done with his promising line of research until the early 1950s, when Richard Pattle in England and John Clements in the U.S. independently rediscovered the concept of an alveolar surface-active material that came to be known as "surfactant."

"John Clements was and probably still is the biggest name in surfactant research," explains Egan. Working at the University of California at San Francisco, Clements, in the 1950s, was shoring up his reputation as a giant in his field by focusing on the problem of surface tension in the lung and the role surfactant plays in alveolar stability. His research in those early years was primarily basic, which put his career in perfect synch with the pioneering phase the science of lung physiology was undergoing at that time.

"You have to understand that during that era—between 1940 and 1965—scientists were just beginning to gain a sophisticated understanding of how the lungs work and how we control breathing by mixing gas and air," says Egan. "And in the 1950s, these studies were being led by two or three great centers in the United

"If it weren't for Goran Enhorning, we wouldn't have the low neonatal mortality rates we have today, and we wouldn't have been able to develop our understanding of the science behind pulmonary surfactant to the extent we have." — BRUCE HOLM

States, one of which was at the University at Buffalo, where key contributions were being made by Hermann Rahn, Leon Farhi and many others in our Physiology Department."

A spin-off of the basic research going on at UB and elsewhere during this time was that scientists began to develop a more sophisticated understanding of lung diseases and their etiology, according to Egan.

With the stage thus set, a giant leap in surfactant research took place in the late 1950s, when a pediatrician named Mary Ellen Avery was invited to complete a fellowship in the laboratory of Jere Mead, a Harvard University physiologist. "Avery and Mead were thinking about the premature babies who had a progressively more difficult time breathing and then died. Their lungs were totally collapsed and looked like livers, and they had the idea that maybe these babies were missing this lung surfactant," explains Egan.

Following through on this idea, Avery and Mead completed a complex project in which they studied the lung material of infants who died of RDS (then called hyaline membrane disease), compared with the lung material found in babies with normal respiratory systems who died of other causes. In a now-famous paper published in 1959, the researchers "showed that surface tension was higher in infants dying from RDS than it was if you got the lung material from infants dying from other causes," says Enhorning.

Based on their findings, Avery and Mead put forth the idea that babies who have RDS are surfactant deficient, in the same way somebody with diabetes is insulin deficient.

"This idea really sparked enormous interest," Enhorning comments.

"This was very esoteric science," Egan emphasizes. "It wasn't anything the great majority of physicians around the country had any training in; they didn't understand it. There simply wasn't a good paradigm for it."

Soon after publication of the Avery and Mead paper, the scramble was on to concoct an exogenous surfactant material and get it into the lungs of babies born with RDS. Around the world, research groups moved into action, hoping to be the first to produce a lifesaving substance that would put a stop to a disease that killed approximately 10,000 babies each year in the U.S. alone.

At about this same time, in 1961, Goran Enhorning had just completed a PhD in physiology at Karolinska Institute's Medical School in Stockholm, Sweden, where

Bruce Holm, PhD, associate dean for research and graduate studies at UB's School of Medicine and Biomedical Sciences, came from the University of Rochester in 1988. That year, he teamed up with Sadis Matalon, then a UB physiologist, to show for the first time that high concentrations of oxygen can damage the cells in the lungs that produce surfactant. Today, the innovative studies conducted by Holm and his UB collaborators continue to help define the forward edge of surfactant research worldwide.

in 1952 he had earned his medical degree. Upon graduation he was awarded a Fulbright scholarship to study at the University of Utah, where he began research into surfactant. Normally, Fulbright scholars are limited to a one-year stay, but an exception was made for Enhorning and his visit was extended for another year. During this second year, Forest Adams, a well-known surfactant researcher from the University of California at Los Angeles (UCLA), came to the University of Utah to lecture, at which time he was introduced to Enhorning. As a result of their meeting, Adams

arranged for yet another year extension for Enhorning and made a place for him in his lab at UCLA.

In Adams's lab, Enhorning continued work he had begun in Utah on an ingenious apparatus he called a bubble surfactometer, which he readily admits took him more than 15 years to fully develop. In the decades that followed, however, the bubble surfactometer would greatly enhance scientists' ability to run physical tests on surfactant preparations in order to assess their surface tension-lowering properties prior to *in vivo* studies.

Adams's lab also provided the setting for Enhorning to work alongside another young scholar, Tetsuro Fujiwara of Japan, who, like Enhorning, would go on to devote his career to the elusive goal of developing a surfactant-replacement product.

One of the requirements of Fulbright scholars is that they return to their country of origin for a minimum of seven years upon completion of their studies abroad. As a result, in 1964 Enhorning left Los Angeles to return to Sweden, but that was not the last he and Fujiwara would see of one another.

The Rush to Find a Cure

During the years that Enhorning and Fujiwara were studying in the U.S., the race had intensified among scientists who hoped to be the first to determine the active components of lung surfactant and to discover a replacement substance.

Foremost among the scientists exploring this problem was Clements in San Francisco, who, in collaboration with M. H. Klaus, was studying the biochemistry of surfactant. Using the limited testing technology they had available to them at the time, they concluded that the surface tension-lowering component of the material resided in its phospholipid, most specifically a biologically rare molecule called dipalmitoylphosphatidylcholine, or DPPC.

Convinced that DPPC was the active surface tension-lowering substance in surfactant, the San Francisco group then decided to take a step that remains controversial to this day.

"They took this DPPC material, which they had only tested in physical systems, not biologic systems," says Egan. "It looked like surfactant. Best of all, it was easy to make, easy to work with, and they were really convinced they had the 'guts' of it, so their next thought was, 'Let's test it in babies.'" Additional motivation to push ahead with testing had come in 1964, when a Canadian group, which had rapidly followed up on Clements's findings, published a paper reporting that they had found some improvement in babies with RDS who had been treated with a DPPC mist.

In 1965, therefore, with their new DPPC solution in hand, the Clements team boarded a plane for Singapore, where they had access to a large population of babies and could complete their studies quickly.

"They took aerosolized forms of DPPC and fogged it into the babies," recounts Holm. "And remember, these are the days before mechanical ventilation. The babies were in these plastic hoods, and they just put this mist of DPPC in the hood and that was the concept of ventilation. Looking back on it, most of the DPPC probably stuck on their hair and face. I'm sure almost none of it got in their lungs. If it had, it probably would have had some positive benefit. But they hadn't done any animal studies so, among other things, they didn't know how to deliver it correctly."

Upon returning, the group published a landmark 60-page paper in *Pediatrics* in 1967, concluding that exogenous surfactant was *not* efficacious for the treatment of infants with RDS.

"So here you have the biggest names in surfactant research saying that surfactant therapy doesn't work," says Egan. "And not only that, but concluding that surfactant deficiency was a *result* of RDS rather than the *cause* of it."

Once the paper was published, interest in surfactant-replacement research for RDS, in large measure, came to a sudden halt. "Clements's conviction alone and his stature in the academic community were such that the publication of this paper turned the entire field of surfactant research in the wrong direction for more than 10 years," Egan explains. Pausing, he adds, ". . . with the exception of one kind of idiosyncratic, brilliant intellectual who lived in Sweden and was an obstetrician by training."

"This Has Been Tried Before and Does Not Work"

Back in Sweden, with his bubble surfactometer in tow, Goran Enhorning was running some tests of his own. "DPPC was inexpensive, it was sterile, it didn't have any antigenic proteins, so it was appealing. If you could use DPPC, it would have been wonderful. But you couldn't. It was hopeless. I found that out with the bubble surfactometer," he recalls.

At this point, Enhorning turned to a pathologist named Bengt Robertson for help, and together the scientists experimented with various surfactant preparations, which they began early testing of on rabbit neonates. "What they found," Egan explains, "is that the rabbits lived longer and breathed better. But because the medical establishment was by now convinced that surfactant deficiency was *not* the cause of RDS, they had trouble getting their work published.

"I think people in the field ignored Goran's early work because he was producing evidence that was contrary to conventional wisdom, because he was up in

Edmund "Ted" Egan II, MD, UB professor of pediatrics and physiology and founder, president and CEO of ONY, Inc., holding a vial of the company's exogenous surfactant product, Infasurf. In the early 1980s—building on Goran Enhorning's seminal contributions—Egan worked with Robert Notter at the University of Rochester to develop the drug. Their efforts fueled a race among scientists around the world working toward this same goal.

"In the 1950s, these studies were being led by two or three great centers in the United States, one of which was at the University at Buffalo, where key contributions were being made by Hermann Rahn, Leon Farhi and many others in our Physiology Department."

— EDMUND "TED" EGAN II

Sweden and because he had very distinguished people openly pooh-poohing his work."

After years of having his work essentially blackballed by the scientific community, Enhorning finally met with temporary success in 1972. "The editor of *Pediatrics* who accepted the paper Robertson and I coauthored was an exception," recalls Enhorning, "and he invited me to follow up with an editorial on our work." Despite publication of this paper, however, Enhorning and Robertson again found their work ignored; between 1972 and 1976, few journals accepted their papers. "Papers we submitted were rejected with one line: 'This has been tried before and does not work,'" recalls Enhorning.

A year before publication of the paper in *Pediatrics*, Enhorning had moved to Canada to take a position at the University of Toronto. There, he continued collaborating with Robertson, who still lived in Sweden but made extended visits to Canada. "In 1973 and 1974, I did a study with Robertson I consider very important," says Enhorning. "We deposited surfactant in the pharynx of premature rabbit neonates, who inhaled it with their first breath, and X rays showed how it opened up their lungs. We published this study in 1975, and it was at that point that we started thinking about seriously testing it in babies." Toward this goal—and with publishing no longer an insurmountable hurdle—Enhorning and Robertson submitted a steady stream of papers on animal studies they conducted throughout the latter half of the 1970s.

It was during this time, in 1977, that Enhorning first published a paper describing, in depth, his bubble surfactometer, which has since become a staple tool used by scientists studying surfactant.

Based on the work Enhorning and Robertson were doing in the 1970s, researchers began revisiting the idea of creating a synthetic surfactant material. Some were once again testing the DPPC substance that Clements had unsuccessfully experimented with in the mid-1960s.

For example, in 1976 Fujiwara was back at UCLA and was working with Adams in an attempt to duplicate the Enhorning and Robertson studies by depositing DPPC in the upper airways of sheep. Frustrated with their results, they concluded that surfactant therapy didn't work.

"During a trip to Los Angeles that year, Robertson visited Adams's lab and was told about the frustrating results of the experiments. He told them that what they needed to use was natural surfactant from adult animals, not a synthetic material like DPPC. So they changed their techniques and then could confirm our studies," explains Enhorning.

Shortly thereafter, Robertson returned to Sweden permanently and Enhorning began collaborating with Fred Possmayer, a biochemist who worked in London, Ontario, at the University of Western Ontario. Their goal was to develop a surfactant material that would be safe to test in babies. "One of the big problems we had was that the raw material—the natural surfactant—was very difficult to get," Enhorning recounts.

To overcome this problem, Enhorning paid a visit to a local slaughterhouse in Toronto. "I got really lucky because one of the investigators working in research at the slaughterhouse had just had a baby who developed RDS, so

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— EDMUND "TED" EGAN II

Biochemist Fred Possmayer, PhD, of the University of Western Ontario in London, Ontario, collaborated with Goran Enhorning in the late 1970s to prepare a sterile and active exogenous surfactant product using material obtained from the lungs of large calves. It was this product that Ted Egan and Robert Notter used as a basis for developing Infasurf for treatment of neonates with respiratory distress syndrome.

he arranged for me to get lung lavage from large calves."

The surfactant material that Possmayer made using raw material obtained at the slaughterhouse was extremely active in terms of its surface tension-lowering properties; however, when they attempted to sterilize it with gamma rays or by autoclaving, this crucial activity was lost. "We felt this was due to its high protein content," says Enhorning, who by this time understood, as did all researchers in the field, that surfactant was a complex mixture composed of 90 percent lipids and 10 percent proteins. "In an attempt to rid the material of these proteins, we extracted the surfactant lipids and resuspended them in saline solution, and the material we obtained could then be autoclaved and sterilized without it losing its surface activity," he explains.

However, unbeknownst to Enhorning and Possmayer at the time, a few tiny apoproteins slipped through and made it into their experimental material. It wasn't until the mid-1980s that scientists made the critical discovery that these apoproteins of pulmonary surfactant, which have since been named SP-B and SP-C, are essential for an immediate expression of surface activity.

"Possmayer and I extracted the phospholipids from the material. By doing that, we thought we would get rid of the proteins, which we felt might be dangerous and which interfered with our attempts to sterilize the material," says Enhorning. "We thought we had removed all the proteins but, serendipitously, we hadn't. Later we found out that about 2 percent of the extract was made up of proteins that had slipped by when we analyzed its properties."

Once Enhorning and Possmayer discovered how to produce their sterile, active substance, they wrote about it extensively in journal publications.

Coming Around to Goran Enhorning's Idea

"By the late 1970s, everyone had come around to Goran Enhorning's idea of 10 years earlier: that it probably is surfactant deficiency that causes RDS," Egan explains. "The obvious next step, then, was determining what kind of surfactant-replacement therapy you're going to give. Basically, you have two options—synthetic and natural."

Egan, himself, entered the field of surfactant research at about this time. In 1977 he moved to Buffalo, where he had accepted a joint appointment as chief of neonatology at Children's Hospital of Buffalo and professor of pediatrics and physiology at the University at Buffalo's School of Medicine and Biomedical Sciences.

"Ted Egan was a physiologist who had some world renown for his work in lung-water clearance," explains Holm, referring to the process in which, at birth, a baby absorbs the liquid that fills its lungs and establishes breathing. "And as a neonatologist and chief of neonatology at Children's, he obviously was interested in developments with surfactant therapy."

Once in Buffalo, Egan set up his lab, where he conducted ongoing studies on sheep related to his research. Soon he met Robert Notter, a scientist who earlier in his career had given up a faculty position in chemical engineering at Pennsylvania State University in order to go to medical school, which he felt would better prepare him to pursue a consuming interest he had in lung surfactant. After he completed medical school at the University of Rochester, he stayed on as a faculty member, dedicating himself to his research.

"By 1980, Bob Notter had a synthetic mixture of surfactant that we both thought would work, and we decided that the best way to find out was to test it in my sheep," recalls Egan.

Egan and Notter were encouraged by a paper that had just been published in Cambridge, England, which reported that surfactant had been tested on babies with very good results. Based on the Cambridge study and others, they were acutely aware that groups around the world were hard at work in the ongoing race to develop their own surfactant products. They knew, for example, that Fujiwara had returned to Japan and was working there; that Clements was working in San Francisco; that Robertson had returned to Sweden, where he was continuing his research; that a group in San Diego was approaching the problem by extracting surfactant from amniotic fluids; and that Enhorning and Possmayer continued their work in Toronto.

It was with great anticipation, therefore, that Egan and Notter began their experiments in 1981. Notter had extensively tested his surfactant preparation in physical systems and had found it very promising. "We took this synthetic product and put it in preemie lambs that were surfactant deficient, and the results were disastrous," Egan recalls.

Frustrated with their lack of progress, Egan and Notter decided they needed to pull back and reassess their methodology because, as Notter pointed out, everything was looking good on his physical systems, so perhaps they needed to look at whether Egan's "experimental setup" was flawed. "In other words, he was saying to me, If we have good stuff, would we even recognize it?" Egan says. Thinking there was only one sure way to determine this, the scientists decided they would put their synthetic mixture aside and instead test a dose of whole surfactant taken directly from the lungs of an animal.

"We were simply looking for a positive control," Egan says. However, what occurred that day in March of 1981, when they tested the new surfactant mixture, was something Egan says he will never forget.

"It was stunning. It was probably as exciting a lab event as I've ever participated in. Surfactant-deficient sheep are pretty doleful animals, let me tell you. But when we gave them the surfactant Bob provided, they were acting like mature fetal sheep getting ready to be born. It was fantastic."

But the biggest surprise was yet to come. "I thought what we had used was whole lung surfactant as we had planned," Egan says. "But when it worked so well, I said, 'This whole surfactant is great!'" It was at this point that Notter informed Egan that what they were testing was an extract he had prepared based on the published works of Enhorning and Possmayer, an extract that he had slightly modified to his own specifications.

"There's no doubt that Enhorning and Possmayer were much farther down the road with their natural extract in 1981 than we were with our synthetic product. Until we ran this test, Bob was primarily interested in a synthetic product. But once this new extract looked so good and once I found out that there was almost no protein in it, I thought, 'We're home,'" Egan recalls.

It was from this point onward that Egan and Notter abandoned their quest for a synthetic surfactant and focused their efforts on refining a natural extract.

Which Way to Go?

All the scientists working on surfactant worldwide had come to this difficult junction in their research. Obviously a synthetic product was attractive: It would be easier to mass-produce, would be available in limitless quantities, could be more easily controlled for quality and could be patented and sold as a brand-name product, something that was sure to attract the needed support of pharmaceutical companies.

Natural products, on the other hand, while holding exceptional promise, posed very formidable challenges. "In 1980 we knew that natural surfactant was about 10 percent proteins and that one of these proteins was very large. Like the proteins in your blood, it clots, coagulates and you can't sterilize it; it has all kinds of problems," Egan explains. "So we were faced with two issues: if we were going to develop a natural replacement product, it had to be one that wouldn't hurt the patient, yet was hardy."

In 1983, despite these complications, the Buffalo-Rochester team of Egan and Notter and the Toronto team of Enhorning and Possmayer had each begun small, prospective placebo-controlled trials of natural surfactant extract to prevent RDS in preemies—at last marking the start of full-fledged efforts on the part of the two groups to test the drug in babies.

Two years later, both the Buffalo-Rochester group—now joined by clinicians Melinda Kwong and Donald Shapiro—and the Toronto group had completed larger randomized clinical trials, which they each reported on in the August 1985 issue of *Pediatrics*. Using what were similar extracts, they demonstrated that calf-lung

"We were simply looking for a positive control," Egan says. However, what occurred that day in March of 1981, when they tested the new surfactant mixture, was something Egan says he will never forget.

surfactant extract did prevent lung disease in premature babies and could significantly reduce the severity of respiratory disease.

"After seeing the results of these clinical studies, all of which were so compelling for this particular material, Ted took it on as a crusade to go out and see that it became widely available," recounts Holm. "Early on, he had offered the calf-lung surfactant, pretty much free, to pharmaceutical companies, but they had already committed to marketing products developed by other groups. Also, another reason why they weren't interested in the material was that it had been reported on in professional journals to such an extent it was considered to be in the 'public domain,' so it couldn't be patented.

"So this really was the genesis of the idea 'Let's go out and make and market our own product.'" In hindsight, Holm adds, "Remember, these were academic physicians with no background in commercializing a drug, and so they were too naive to know that they couldn't go through the FDA process without any financial backing."

What they did have, according to Holm, was "the best of intentions and a belief that what they were doing was for the greater good."

Determined to provide a parent company for his orphan drug—which has since been dubbed "Infasurf"—Egan founded ONY, Inc. (Ontario New York), in 1985 and set up offices in the Baird Research Center located near the University at Buffalo campus.

A Boost from Basic Research

While surfactant was entering its clinical-trial phase, other equally momentous developments were again taking place on the basic-science side of surfactant research.

Much of it centered on Bruce Holm, who in 1981 came to work in Notter's lab at the University of Rochester while pursing a doctorate in toxicology. Over the next seven years, Holm gained considerable recognition for a series of contributions he made to the field of surfactant.

In the mid-1980s, it was Holm and Jeffrey Whitsett, a researcher at the University of Cincinnati, who conducted a study that finally identified apoproteins as the mystery component in surfactant that enables it to be efficiently adsorbed by the lungs. In their paper, which was published in *Pediatric Research* in 1986, they were the first to show the functionality of the apoproteins SP-B and SP-C.

From the start, Holm was primarily interested in studying adult respiratory distress syndrome (ARDS) and its potential connection to surfactant. "No one had ever really wanted to study surfactant in adults," he explains. "Initial attempts to do so went nowhere because the dogma at the time was that surfactant deficiency was related to a quantitative deficiency—as in the case of premature babies—but not to a qualitative deficiency; therefore, the accepted belief was, 'It can't be part of the issue.'"

By the late 1980s Holm, who had admired Enhorning for many years, began to collaborate with the senior scientist and others on studies demonstrating a mechanism by which plasma proteins were shown to inhibit surfactant function. These findings, published in 1988 in the *Journal of Applied Physiology*, helped introduce the concept that surfactant-replacement therapy could be of benefit to a much wider range of lung conditions than just RDS.

"While we were off doing clinical studies, Holm was working with researchers throughout this area—in Buffalo, Rochester, Toronto and London, Ontario—to find out that you can inhibit lung surfactant, which was a brand new concept," explains Egan. "They were showing that surfactant plays a role in lung diseases, not just when it is missing, but when it becomes deactivated by things seeping into the lungs that don't belong there and which start tearing up the surfactant, making it terribly difficult for people to breathe. We began to see it as being similar to autoimmune diseases, where the body turns on itself."

In 1988 Holm also teamed up with Sadis Matalon, who was then a physiologist at the University at Buffalo, and others to publish a study that showed for the first time that high concentrations of oxygen can cause changes in Type II pneumocytes, the cells that produce surfactant.

"Obviously, this was really very important because we use oxygen as an essential therapy for treating lung diseases," explains Egan, who notes that, today, the 40-year-old Holm is recognized as "one of the world's leading experts on oxygen toxicity."

"Not only did Holm and Matalon document that oxygen can damage cells in the lungs that make surfactant, but they also showed that if you give an animal surfactant, it will speed its recovery, diminish the injury or even prevent it," he adds.

While studying oxygen toxicities, Holm also refined a technique for isolating the Type II pneumocytes. This was a very important development, as well, according to Enhorning, because "more and more, physiologists are studying disease at the cellular and molecular level."

Critical Mass Converges in Buffalo

As the years passed, it became increasingly clear that, philosophically, the Buffalo-Rochester group had much in common with the Toronto group and that, together, they stood apart from other groups worldwide. Most important, they shared the philosophy that *both* lipids and proteins must be included in surfactant preparations if they were to produce optimal results. Further-

Robert Notter, MD, gave up a faculty position in chemical engineering at Pennsylvania State University to earn a medical degree, which he felt would better prepare him to pursue a consuming interest he had in lung surfactant. In the 1980s, as a faculty member at the University of Rochester, he collaborated with Ted Egan at the University at Buffalo to develop the surfactant drug Infasurf.

"It's this cell-biology aspect that will take us to the next level. The philosophy shouldn't just be 'Okay, we can keep them alive.' That, of course, is very important for the physician, but, for a scientist, you always want to go one step farther; you want to see if you can prevent this from happening in the first place."

— BRUCE HOLM

more, they felt strongly that both SP-B and SP-C must be present because their research had shown that the two apoproteins work synergistically.

In contrast, in the late-1980s Clements's group in San Francisco, which had by then partnered with Burroughs Wellcome, was developing a synthetic preparation called Exosurf that was composed primarily of DPPC and contained no protein. In turn, Fujiwara's group in Japan, which had partnered with Abbott Labs, was testing a patented product called Survanta, manufactured from a mince of whole cow lung, supplemented with synthetic phospholipids and neutral lipids, but containing only trace amounts of the SP-B apoprotein.

Given the long years of collaboration between the Buffalo-Rochester-Toronto researchers, it came as no surprise when Egan successfully recruited Enhorning to Buffalo in 1986, followed in 1988 by Holm, who came from the University of Rochester to complete a postdoctoral fellowship at UB, during which time he worked with Enhorning and others to continue his novel work on surfactant inhibition.

There's So Much at Stake

Once the randomized clinical trials were completed on Infasurf in 1985, Egan initiated the process whereby he hoped to win Food and Drug Administration (FDA) approval for the drug. Immediately, he was told by the FDA that in order for Infasurf to be considered for approval, controlled studies of it had to be completed. "This meant some of the babies would get surfactant and some of the babies would get nothing," recalls Egan. "So I said, 'I can't do that.'" Egan's appeals to the FDA to make an exception to their rule did not meet with success. As a result, he decided to delay controlled clinical trials until other surfactant drugs came on the market, at which time he could compare one surfactant to another.

In 1990, his wait ended when Exosurf was approved by the FDA and debuted as the first surfactant drug available in the U.S., followed closely by Survanta in 1991.

In the intervening years, while waiting for Exosurf to come on the market, Egan made Infasurf available to all babies in Buffalo who needed it, something he was able to do while Infasurf was classified as an "investigational new drug." This strategy was given a boost in 1989, when the FDA gave Egan's company, ONY, Inc., permission to charge for Infasurf so that costs for its development could begin to be recouped. However, the FDA gave the company permission to do this with the stipulation that it upgrade its manufacturing facilities to meet the requirements for a commercial venture. The only way to get the needed equipment in a timely manner was for the owners of the company to guarantee a loan, which Egan did personally after buying out the other owners.

"I was placed in a position where I felt we had developed something that was really a super therapy but which, because it wasn't a mainstream commercial venture, was about to be abandoned," Egan says. "I thought about my own motivation up to this point—why I went into this in

the first place—and I felt it really didn't do any good to develop an optimal product and then watch it die."

In 1989, therefore, Egan gave up his position as chief of neonatology at Children's Hospital of Buffalo and went to a part-time status at the hospital in order to fully devote his energies to ONY, Inc.

When Exosurf came on the market in 1991, Infasurf finally entered the clinical-trial phase for FDA approval, as studies were conducted in which the two drugs were compared. To facilitate this process, ONY, Inc. formed an alliance with Forrest Labs, which has its headquarters in New York City. With Forrest Labs providing the personnel and financial resources needed for this costly process, FDA trials of Infasurf were completed between 1991 and 1994, with all data submitted to the agency by 1995.

In 1995, when it looked like Infasurf would finally make it out the other end of the FDA pipeline, Egan's plans hit yet another snag and were ground to a halt. When the FDA approved Survanta in 1991, it designated it an "orphan drug" because it was determined to be the first pharmaceutical of its kind. "Being designated an 'orphan drug' by the FDA puts you in a category that gives you some tax breaks and provides you market exclusivity against similar or same drugs for seven years. It's like having a patent for that period of time. What happened in 1995 was the FDA decided that, under the orphan-drug rules, Infasurf was the same drug as Survanta. That doesn't mean that we are the same drug, like a generic drug, but just that we are a 'similar' drug," Egan explains.

The effect of this ruling, therefore, was that Infasurf had to stay off the market until 1998, since Survanta had made its debut in 1991. Despite repeated requests for the FDA to change its ruling, the decision held fast. Today, Egan simply says, "What it came down to with the FDA is that both drugs came from cows."

Holm is emphatic about the difference between Infasurf and the Survanta and Exosurf products. "In our opinion, and in the opinion of many scientists, the most effective surfactant drugs are those that contain the lipids as well as the two apoproteins B and C. Our studies have shown that these two proteins work synergistically and that, of the two, B is the most important. Exosurf contains no proteins, and in the Survanta preparation only minute amounts of the B protein are present, while Infasurf contains it in quantities normally found in healthy mammals."

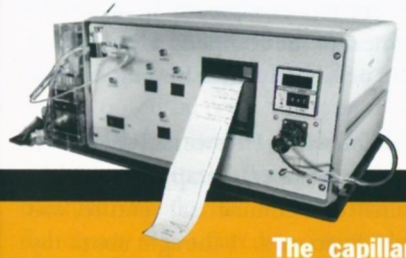
To demonstrate what he calls "a night-and-day difference" between protein-based surfactant drugs and those containing no proteins, Holm points out that as soon as Survanta became available, "Exosurf rapidly lost its majority share of the market, which tells you what the clinicians using the two drugs are finding. We feel that Infasurf's inclusion of *both* apoproteins makes it a drug with notable differences when compared with Survanta and one that defines the 'next generation' in surfactant drugs."

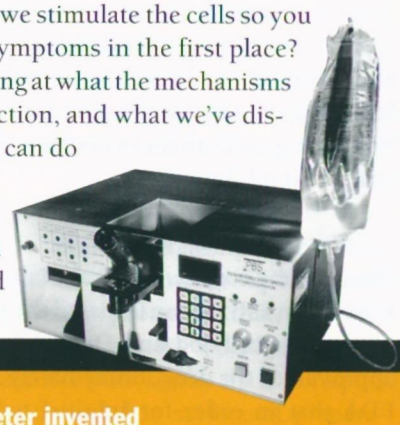
On July 1, 1998, the exclusivity clause for Survanta expired, and Infasurf finally became an FDA-approved drug. What would have otherwise been a banner day in the history of Infasurf, however, was clouded by yet another obstacle. In 1994, Abbott Laboratories claimed Infasurf infringed on Survanta's patent, and hearings on the ensuing case began in June 1998.

Despite the ongoing legal battles *(see article, page 13)* Egan is convinced that as Infasurf becomes widely available to physicians working on the front line in neonatal intensive care units, it will win a significant share of the market through its own merit. "Physicians are looking for the best product," he says, "and any margin of improvement will be huge because there's so much at stake."

The Stage Has Been Set

Throughout the 1990s, scientists in the informal Buffalo-Rochester-Toronto research network have continued to pursue independent interests, as well as to collaborate with each other on groundbreaking studies that have helped define the leading edge of surfactant research worldwide. "We're looking at cell-directed therapies now," Holm says. "We know that surfactant can take care of many of the symptoms of lung disease and that it has reduced infant mortality related to RDS to 5 percent, down from a high of 70 percent in the 1960s. So now what we want to do is take a step back and ask ourselves, Can we stimulate the cells so you can never get the symptoms in the first place? That involves looking at what the mechanisms are for cellular function, and what we've discovered is that you can do pharmacological manipulations, particularly with oxidant stress, and





The capillary surfactometer (left) and bubble surfactometer invented by Goran Enhorning. The former is being used to study the potential role of surfactant dysfunction in asthma.

you can prevent this damage from occurring *in vitro* and *in vivo*."

Citing a series of diverse investigations that build on surfactant research, Holm talks about studies ongoing at UB whereby researchers are hoping to find improved ways of treating ARDS, pulmonary dysplasia and hypoplastic lung from congenital diaphragmatic hernia. Referring to the latter condition, he says, "For example, we have shown that the blood-flow problem that exists there and the stiffness of the lung can be corrected by giving exogenous surfactant. But the lungs are still small, so we've been doing things directly to the Type II cells in this and other injuries. By tweaking those cells and putting mechanical stressors and growth factors in, lo and behold, we're finding we can grow the lung back to normal size in two weeks *in vivo*.

"So, we're branching out, and it's interesting because it's all growing out of surfactant," he adds. "It's this cell–biology aspect that will take us to the next level. The philosophy shouldn't just be, 'Okay, we can keep them alive.' That, of course, is very important for the physicians, but, for a scientist, you always want to go one level farther; you want to see if you can prevent all of this from ever happening in the first place."

Enhorning couldn't agree more and has headed off on his own to again champion a controversial theory in which he contends that surfactant dysfunction contributes to symptoms of asthma. To assist in the elucidation of his new theory, he has again invented an apparatus, which he calls a capillary surfactometer. "I feel the capillary surfactometer is the most important work I have done; I think it has the most promise," he states matter-of-factly.

Egan is following Enhorning's new studies with great interest and says, "Goran has this fascinating, very innovative theory about asthma and, again, he's going against the tide, he's way out in left field. He's challenging conventional wisdom and almost *nobody* thinks he's right because he's saying that the reason why asthmatics have a tough time getting air is not because there is a spasm of the muscles of the airway and not because the airway is clogged with inflammation, but because they have surfactant dysfunction. And you better watch him, because he may be right again."

Fortunately, history may not repeat itself for Goran Enhorning. "Some people *are* looking at what Goran is saying and have approached us about doing some studies in asthma and respiratory syncytial virus," Holm reports.

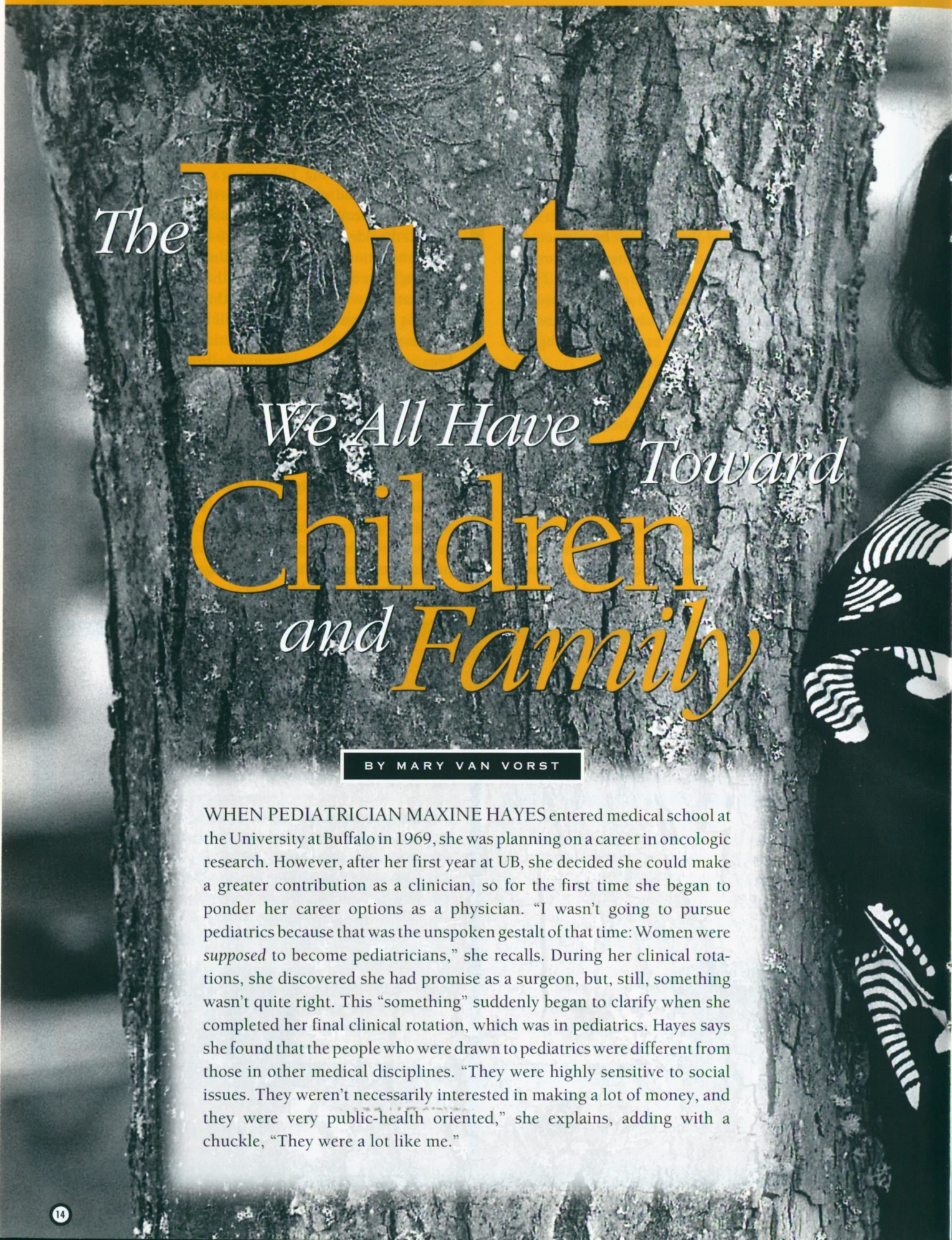
"But, really, the big battle has been won, and that battle was getting enough evidence out there to finally convince the international medical community that surfactant-replacement therapy is a valid treatment for premature infants. That set the stage; now the science will continue to develop." +

The Progress of Infasurf

In the courts and new clinical trials

When the Food and Drug Administration (FDA) approved Infasurf in July 1998, ONY, Inc., and Forrest Labs implemented a licensing agreement which stipulated that ONY, Inc., would manufacture Infasurf and Forrest Labs would market it under its label. Despite this progress, ONY, Inc., still faced a legal challenge from Abbott Laboratories, which in 1994 claimed Infasurf infringed on the patents of its surfactant drug, Survanta. A trial was held in the summer of 1998 in the District Court in Buffalo. "To be honest, Abbott is a 13-billion-dollar-a-year company and their attitude toward a multimillion dollar lawsuit is very different from that of a 20-employee embryonic company," says Edmund "Ted" Egan, MD, ONY's founder, president and chief executive officer, who is also a professor of pediatrics and physiology at the University at Buffalo School of Medicine and Biomedical Sciences. In September 1998, the jury in the case ruled in favor of Abbott Laboratories, but a final judgment has not been entered and appeals are expected to extend the legal dispute well into 2000. Commercial sales of Infasurf await resolution of the lawsuit, according to Egan.

Meanwhile, Infasurf continues to make impressive inroads in the scientific arena. In January 1999, *Critical Care Medicine* (Vol. 27, No. 1) published a study led by Douglas F. Willson, MD, of Children's Medical Center of Charlottesville, Virginia, in which it was shown that pediatric patients who received the drug for a spectrum of respiratory disorders demonstrated rapid improvement in oxygenation and, on average, were extubated 32 percent sooner and spent 30 percent less time in the pediatric intensive care unit than control patients. "The success of surfactant replacement therapy in newborn infants with respiratory problems is well established now, so scientists are looking at its efficacy for children beyond the neonatal period," says Egan, who was a coauthor of the study. "While these findings are very encouraging, a larger, blinded, controlled trial is necessary, and this is something that's being planned before recommendations can be made for use of surfactant in pediatric patients with respiratory failure," he adds. +



The Duty We All Have Toward Children and Family

BY MARY VAN VORST

WHEN PEDIATRICIAN MAXINE HAYES entered medical school at the University at Buffalo in 1969, she was planning on a career in oncologic research. However, after her first year at UB, she decided she could make a greater contribution as a clinician, so for the first time she began to ponder her career options as a physician. "I wasn't going to pursue pediatrics because that was the unspoken gestalt of that time: Women were *supposed* to become pediatricians," she recalls. During her clinical rotations, she discovered she had promise as a surgeon, but, still, something wasn't quite right. This "something" suddenly began to clarify when she completed her final clinical rotation, which was in pediatrics. Hayes says she found that the people who were drawn to pediatrics were different from those in other medical disciplines. "They were highly sensitive to social issues. They weren't necessarily interested in making a lot of money, and they were very public-health oriented," she explains, adding with a chuckle, "They were a lot like me."

"EVERY CHILD HAS A RIGHT TO A GOOD birth, AND AFTER THAT A CORE OF GOOD PREVENTIVE HEALTH SERVICES.

THESE INTUITIVE PROMPTINGS eventually compelled Hayes to redefine her career goals, and in the two and a half decades since graduating from UB, she has gone on to become not only one of the more prominent pediatricians in the United States, but also a public health advocate widely recognized for her dedication to policies that promote maternal and child health. Today, Hayes is the assistant secretary of community and family health for Washington State's Department of Health, where she oversees a staff of more than 200 and manages an annual budget of over $300 million (70 percent of the Department of Health's budget).

Maxine Hayes's push to succeed can be traced back to her childhood in Jackson, Mississippi. Raised in the segregated South of the 1950s and '60s—where she says there was literally a railroad track separating blacks from whites—she grew up poor, but admits she never knew it. "My family taught me there was nothing I couldn't do," she says.

In addition to poverty and racism, Hayes remembers battling the specter of sexism in high school, as well, and reflects, "I guess I was always trying to prove girls could do things boys could do, and do them better. It tickled me to death when I was valedictorian of my senior class and a boy came in second."

It was during her high school years that Hayes was singled out by an African American women's service club, LINKS, Inc., which every year took under its wing one promising African American girl or boy from each of the three public high schools in Jackson. The women in this club introduced their young charges to art, music and literature. Also, to compensate for segregationist practices that banned blacks from fine restaurants, the women hosted elaborate social dinners in their homes, taking the opportunity to teach etiquette to Hayes and the others. Among the women in the club was a graduate of Spelman College in Atlanta who, over time, became Hayes's mentor. Convinced Hayes would flourish in the all-girls' setting at Spelman, the woman encouraged her to apply. When the college responded with an offer for a scholarship, Hayes was on her way to Atlanta.

While at Spelman, where she majored in biology, Hayes won a Charles Merrill scholarship to study abroad in Vienna for a year, an opportunity whose timing would lead to events that would alter her life's path in ways she never could have imagined at the time. By choosing to go abroad and opting to study outside her major, Hayes delayed her graduation by a year. And that year—1968—was a momentous one marked by the assassinations of both Robert Kennedy and Martin Luther King, acts of violence that resulted in political upheaval and calls for change. One fallout from that tumultuous year was that the country began to examine its college and post-graduate entrance policies for minorities. As a result, the extra year Hayes added to her undergraduate studies put her in the right place at the right time when medical schools began working to attract minority students. When she had entered Spelman, Hayes's goal had been to eventually earn a PhD in biology or cytology; however, in 1969, when recruiters from UB's medical school offered her a scholarship, she accepted it, turning down a scholarship to Harvard because she wanted to dedicate her career to finding a cure for cancer and UB's affiliation with Roswell Park Cancer Institute strongly appealed to her.

Hayes says she has long had an appreciation for the social context of medicine. "We physicians need to have a role in impacting policies," she contends. "We need to ensure that the technical knowledge brought to healing is such that it gets to the root causes of why people are sick in the first place, things such as poverty and social disparities."

"I felt there was a reason why all of that happened, and that attending medical school was going to provide me with an opportunity to do something for my community and the greater good. As the saying goes: 'To whom much is given, much is also required,'" Hayes says. "I had classmates in my biology classes at Spelman who would have given anything to go to medical school. But they graduated on time and were not given that opportunity. That all turned around in one year, and I have always felt it was for a reason."

After her first year in medical school, Hayes spent a summer working as a medical extern at a family health clinic in Mississippi. It was there that she realized her family had shielded her from the stark realities in her home state, as that summer she not only wrote prescriptions for medicine, she wrote prescriptions for food. "I began to see all the social ills and to realize that having the

SO MUCH OF WHAT WE SPEND IS **wasted** ON TRYING TO CURE THINGS THAT COULD HAVE BEEN PREVENTED."

technical knowledge of medicine was not going to be sufficient," she recalls.

Following graduation from UB in 1973, Hayes pursued her postgraduate training in pediatrics at Vanderbilt University Hospital in Nashville and at Children's Hospital Medical Center in Boston, finishing in 1976. In 1977, she went on to earn a master's degree in public health at Harvard University. She then returned to Mississippi, where she established a primary care family health clinic on the outskirts of Jackson, becoming the first and only pediatrician in Rankin County and serving a population of some 60,000.

Word of Hayes's success in her Mississippi clinic began to circulate among public health professionals and, in 1985, "out of the clear blue," she says, she received an offer from Children's Hospital and Medical Center in Seattle to serve as medical director for the Odessa Brown Children's Clinic, which delivers primary care to a predominantly low-income population in central Seattle.

Hayes accepted the offer and moved West, leaving her home state but not its problems, which she soon discovered to be much the same in Washington State, except that instead of poor rural families, there were poor inner-city families.

Hayes says her move to Seattle was nothing short of culture shock. Though soft-spoken, she acknowledges, "I'm very intense, very competitive—a Type-A personality.

"When I arrived in Seattle, the first thing everybody noticed was my intensity, and people in the Northwest are definitely not intense. I was amazed you could be so productive and casual at the same time." Over time, as people got to know her, she says, "They told me, 'Loosen up,' so, now, Birkenstocks are definitely part of my wardrobe, and I carry a backpack at all times, even on the rare occasion when I'm wearing a business suit. I've been won over!"

During her three years as medical director at the Odessa Brown Children's Clinic, Hayes worked to expand its mission. In addition to seeing patients herself, she set up educational programs for unemployed single mothers, established a sickle-cell screening program and advocated for policies that ensured better access to health care for foster children.

Hayes's dedication and organizational talents caught the attention of Jule Sugarman, one of the founders of Headstart and then-secretary for the Department of Social and Health Services for Washington State. Sugarman had a vision for children's health in Washington and needed a pediatrician who had credibility in the private community to go to work in the public sector. In 1988, he successfully recruited Hayes to come to work with him for the express purpose of getting a bill passed in the legislature that would launch a maternity care access program called First Steps. "I'm not asking for your life, only two years," she recalls him saying in response to her hesitation to leave a job she loved. Sugarman, who had already gotten Children's Hospital to agree to "loan" Hayes to the state for that period of time, told her: "Go and get this bill implemented, and then you can go back." What really hooked Hayes, she says, was when he asked her, "How long do you want to take care of kids one by one and deny the opportunity to take care of every single one of them?"

Because her original appointment was to be temporary, Hayes decided to stay in her home in Bellevue, a suburb east of Seattle, and make the daily three-hour round-trip commute by vanpool to the state capital of Olympia. That was 10 years ago, and she's still at it. Hayes, a single mother of two boys, ages 12 and 16, starts each day at 5:30 a.m. Carpooling by van allows her time to work en route and frees her to spend time with her sons after her busy days, which usually include a visit to the gym, where she says she follows "a very disciplined exercise program."

Hayes's initial appointment in 1988 was as director of the Division of Parent-Child Health Services, and one of her first accomplishments was to help win passage of the First Steps legislation as Sugarman had hoped she would. In 1990, she was promoted to assistant secretary of Parent-Child Health Services, and three years later she moved into her current position as assistant secretary of community and family health.

Hayes believes her most important contribution to public health is her ability to solve problems. "I see opportunities where others see challenges," she says. Last year she created a new office in her division, called the Office of Community Wellness and Prevention. By targeting the pediatric population, in particular, this office strives "to approach chronic disease by looking at common risk factors, such as tobacco, physical inactivity and nutrition, especially as it relates to obesity," Hayes explains. Another innovative idea she implemented was to position the state's Women, Infants and Children (WIC) program as a counterpart to existing chronic disease prevention programs. "When you look at chronic diseases, you realize you can begin to intervene against many risk factors for these diseases in childhood by focusing on good nutrition," Hayes notes. "Our health department is the only one in the country where you'll find this 'upstream' approach to chronic disease prevention."

Hayes says she has long had an appreciation for the social context of medicine. "We physicians need to have a role in impacting policies," she contends. "We need to ensure that the technical knowledge brought to healing is such that it gets to the root causes of why people are sick in the first place, things such as poverty and social disparities." She is particularly adamant on the

CONTINUED ON PAGE 26

MEDICAL SCHOOL

New Health Care Business Center Opened

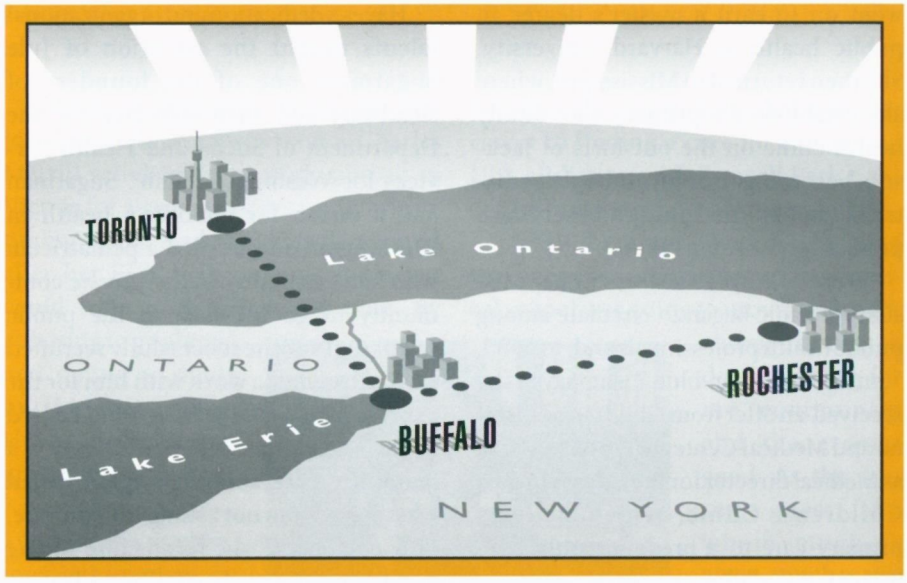
— Capitalizing on marketable products and processes that develop from research

Imagine Buffalo, Rochester and Ontario as an internationally recognized corridor for innovation in health care, with the University at Buffalo a critical component. That's the vision that led to the formation of the new Health Care Business Center (HCBC), a joint venture between UB and the Health Care Industries Association that will allow the region's health-care industry to capitalize on marketable products and processes that develop from research projects at UB, Roswell Park Cancer Institute, Kaleida Health and the Catholic Hospitals.

According to the Health Care Industries Association, a nonprofit organization designed to support and promote the regional health-care industry, this corridor, dubbed the "Lake Affect Region," represents the fourth-largest medical development market in North America, with more than 100 research institutions, 265 medical manufacturers and 95 hospitals.

Strategically located in Cary Hall in the School of Medicine and Biomedical Sciences on UB's South Campus, the HCBC serves as a focal point for fostering new opportunities between local companies and UB researchers—whether they are in medicine, dental medicine, pharmacy, engineering, management or arts and sciences. "Locating the Health Care Business Center at the hub of medical research at UB is key," says Luke Rich, vice president for regional development for the Empire State Development Corp. In the past six years, 35 percent of the inventions registered with the UB Office of Technology Transfer have been in the area of health care. But, explains Rich, getting to the next step—where an invention is refined, adapted and marketed—is hardly automatic. "Traditionally, the difficulty with academic research is in moving it from the paper or project stage to the product stage. That's a complicated process, and that's where the Health Care Business Center can really help," he says.

By Ellen Goldbaum



MIKE GELEN

"Traditionally, the difficulty with academic research is moving it from the paper or project stage to the product stage. That's a complicated process and that's where the Health Care Business Center can really help."

The HCBC will work closely with the UB Business Alliance's new marketing manager and with the UB Office of Technology Transfer. Also, with state funding obtained through the efforts of Assemblyman Robin Schimminger, the HCBC has been able to hire Rebecca Weimer, an experienced technology-transfer liaison who worked for 10 years at MDS Matrx, most recently as director of the international department. "Hiring someone who understands how to transfer the research and knowledge gained by the research community at UB and Roswell to companies that can turn them into products, grow new jobs and expand is one of the most important functions of the new Health Care Business Center," says Rich.

Together with Mary Ellen Rashman, executive director of the Health Care Industries Association, Weimer will strive to maximize networking between and among UB health-care researchers and industry. For both researchers and business professionals, she says, the key

to a flourishing health-care sector in Western New York is networking. "The whole foundation of the health-care industry is networking. People like to do business with people they know and like," she emphasizes.

To that end, the HCBC is putting out the welcome mat for both local and regional health-care companies and to UB researchers. "The more we learn about how professors work and develop research, the better we will be at connecting them with business people," she adds. "This is a hotbed of opportunities for collaboration; we've got to make sure that starts happening, with the goal of keeping business in Western New York."

The most pressing goal of the HCBC is to start to turn around the venture-capital climate in Buffalo, according to Weimer. To that end, the HCBC, in cooperation with Rand Capital, Inc., sponsored the "First Western New York Venture/Equity Forum" March 3–4, 1999, at the Hyatt Regency in downtown Buffalo.

Efforts now are also under way to bring in venture capitalists from outside Western New York to listen to presentations on the strength of the local health-care market in order to convince them to invest in local companies and start-ups. "We are putting together a program that will bring a focus to this area as a health-care mecca," Weimer says. In addition to presentations by officials from major investment firms, a technology showcase will demonstrate the great variety of medical products being developed locally and at UB, some of which are available for licensing.

In recognition of the fact that most start-ups form with an emphasis on engineering expertise, as opposed to business skills, the HCBC is creating a Business Development Program. Composed of Health Care Industries Association members, it will provide a resource for new businesses in the areas of marketing, financial planning, human resources and regulatory issues.

With the cooperation of all the major health-care institutions, as well as UB, HCBC has developed an economic-development proposal and submitted it to the office of New York State Governor George Pataki.

To date, feedback has been positive, reports Weimer. "There's a really exciting feeling about this. Everybody has signed off on it, including UB, Roswell Park, Kaleida Health and the Catholic Hospitals. Everybody's on the same page."

For further information on the Health Care Business Center, contact the center by telephone at (716) 829-3888 or by fax at (716) 829-3885. ✚

In Memoriam

Edith E. Sproul, 92, professor emeritus of pathology

Edith E. Sproul, 92, professor at the UB School of Medicine and Biomedical Sciences and associate chief cancer research pathologist at Roswell Park Cancer Institute, died January 19, 1999, at Roswell Park after a brief illness. Sproul was renowned for her work with George Papanicolaou of the Cornell University Medical School in New York City, which led to development of the pap smear.

Sproul received her medical degree from the Columbia College of Physicians and Surgeons. Before coming to Buffalo, she was a professor of pathology at the Columbia Medical College and later was chief executive officer of the Department of Pathology of the American University in Beirut. While in New York, she was the first to describe the relationship between general thrombophlebitis and pancreatic cancer and the first pathologist to describe the histological characteristics of early prostatic cancer. Along with Charles Gutman of Mt. Sinai Hospital in New York, she discovered the association between prostatic cancer and the prostate specific enzyme acid phosphatase. Sproul was a founding member of the pathology committee for the Eastern Cooperative Oncology Group and a member of the American Association for the Advancement of Science. She is survived by her husband, Arnold Mittelman, professor emeritus of surgery at Roswell Park and UB. ✚

Jael Sabina Sobel, 63, professor of anatomy and histology

Jael Sabina Sobel, 63, professor of anatomy and histology in University at Buffalo's School of Medicine and Biomedical Sciences, died December 5, 1998, of breast cancer.

A native of Israel, Sobel came to the U.S. in 1944 and graduated from Cornell University in 1957. She received a master's degree from Columbia University and a doctorate in zoology from the University of Wisconsin at Madison in 1964.

She completed a postdoctoral fellowship at the Sloan Kettering Memorial Institute for Cancer Research in New York, where she was one of the first scientists to successfully fuse a cancer and non-cancer cell.

In 1970, Sobel returned to Israel to perform research and teach at Tel Aviv University. She returned to the U.S. in 1977, working at the University of California for two years. She came to UB in 1979 as an assistant professor, performing research in embryology. Sobel's teaching duties included medical and dental students, who voted her outstanding teacher in 1983. Survivors include two sons, Daniel and Jeremy, and an extended family in Israel. ✚

MEDICAL SCHOOL

New Places, New Faces

—CHANGES COME TO THE SOUTH CAMPUS

THOSE WHO THOUGHT they had finally mastered the intricacies and idiosyncrasies of the Cary-Farber-Sherman complex in the School of Medicine and Biomedical Sciences may need yet another new mental map.

Michael Bernardino's arrival as vice president for health affairs, with responsibility for overseeing the university's health sciences schools and revamping the medical school's clinical practice plan, has set in motion a series of office and departmental relocations.

Also, a new abbreviation—BEB—has been added to the South Campus lexicon; it refers to the Biomedical Education Building, known since its construction in 1982 as the CFS addition. The Biomedical Education Building is not to be confused with the Biomedical Research Building (BRB), the campus's newest structure, which was completed in 1996.

The following is a summary of significant changes on the campus, all of which were completed in January 1999.

Vice President's Wing

The first floor of the south wing of the Biomedical Education Building, formerly housing Dean John Wright and the medical school support staff, has been transformed into the vice president's wing. This suite of offices now houses Bernardino and his secretary, along with the staff of the newly formed UB Associates, the medical service organization that will provide centralized accounting, management and legal services for the clinical practice plan.

The assistant vice president and general counsel, the assistant vice president for resource management (for health affairs), the chief operating officer for the practice plan and the medical compliance officer for the practice plan are also located here.

BY LOIS BAKER

Dean's Wing

Wright and his staff have moved into the first floor of the BEB's north wing, above the atrium, in an area formerly occupied by student study carrels and the medical admissions office. The study area is now located on the third floor of Farber Hall, while medical admissions has moved downstairs to the ground floor, into the former student locker area. Student lockers have been decentralized throughout the building.

Bruce Holm, associate dean for research and graduate studies, and his staff have moved into offices across the hall from Wright's suite, in renovated space used formerly for a staff lounge and a small conference room. The Lippshutz Conference Room occupies the remaining space in this wing.

Medical school development and alumni affairs offices, formerly located on the BEB's first floor in what is now the vice president's suite, are now located on the first floor of Cary Hall.

Relocation of Communicative Disorders and Sciences

The Department of Communicative Disorders and Sciences (CDS) moved from Park Hall to the South Campus in late December 1998, although it remains aligned academically with the College of Arts and Sciences. The move unites the department's various components on one campus: Its Center for Hearing and Deafness, a UB Center of Excellence, which concentrates on basic research into the neurobiological and environmental causes of deafness, has been located in Parker Hall on the South Campus since 1987.

CDS faculty offices now are located on the first floor of Cary Hall, in space formerly occupied by the Department of Biophysics, which merged with the Department of Physiology in 1997. That combined department is headquartered in Sherman Hall.

The Speech, Language and Hearing Clinic now occupies the ground floor of the BEB, which formerly housed the University Physicians Office. The Center for Hearing and Deafness will remain in Parker Hall.

Standardized Patient Center

In 1998, UB's School of Medicine and Biomedical Sciences was designated a regional center for testing medical students in basic clinical skills, medical history taking and patient interaction, using standardized patients (persons trained to simulate actual patients for use in medical education).

To accommodate this new function, the school renovated space on the second floor of Cary Hall into a Standardized Patient Center, which contains examination rooms equipped with video cameras to record student performance, as well as observation rooms for faculty monitors. ✚

New Faculty and Staff

NEW FACULTY AND STAFF have arrived on the South Campus in recent months. Several individuals have come on board to staff UB Associates, which will administer the clinical practice plan (see winter 1999 issue of *Buffalo Physician*), while others were hired to fill vacancies at the School of Medicine and Biomedical Sciences.

Office of Vice President for Health Affairs

Kathy R. Lamb, assistant vice president and general counsel, is a nurse practitioner and holds a law degree from Syracuse University School of Law. She came to UB from the Rochester law firm of Harris, Beach and Wilcox, L.L.P., where she was a partner in the Corporate/Health Care Practice Group. Prior to working at Harris Beach and Wilcox, Lamb was a partner with Falk and Siemer, L.L.P., of Buffalo, handling corporate healthcare issues. She also has served as a health-care attorney with Hancock and Estabrook in Syracuse and a litigation associate with Jaeckle, Fleischmann and Mugel in Buffalo. Her UB duties include handling legal issues involving the clinical practice plan and administering contracts with the teaching hospitals.

Tony Campanelli, formerly assistant vice president for fiscal affairs in the UB School of Medicine and Biomedical Sciences, has joined the staff of the vice president for health affairs as assistant vice president for resource management.

Patrick J. Dinicola, chief operating officer of the clinical practice plan, holds an MBA from Cornell University Graduate School of Business and Public Administration. Most recently, he was senior vice president for finance and administration at Trico Products Division in Buffalo; prior to that he spent three years at Trico's Texas Division. He also has held financial management positions with Frontier Corporation, Computer Consoles, Inc., and Schlegel Corporation, all of Rochester.

Maryann O'Brien, compliance auditor, holds a degree in medical records administration from Daemen College and is in the master's degree program in health services administration at D'Youville College. Before coming to UB, she was a full-time instructor in the Health Information Technology Program at Trocaire College.

Brian W. Murphy, formerly a research physicist in the UB Department of Nuclear Medicine, now directs the Health Professions Information Technology Partnership. His group manages educational software development for the health-sciences schools and provides information-technology support.

Tim Bleiler is an instructional designer and software developer for the Information Technology Partnership. He came to UB from the University of Iowa, where he developed several types of instructional programs, including software to study head and neck anatomy, and simulations of human temperature regulation. He is developing a program that can be customized to teach histology.

Brian Schroeder is a computer artist and multimedia designer for the Information Technology Partnership. He is a 1996 graduate of UB's fine arts program.

Kimberly Krzemien, who is legal assistant to Kathy Lamb, formerly was with the firm of Cooper and Cooper in Hamburg.

Dean's Office

Carolyn Hamilton, assistant dean for minority affairs, fills the vacancy created by Maggie Wright's retirement. She will help recruit and retain minority medical and graduate students and secure funds to support these efforts. Hamilton was assistant director of admissions at the University at Albany before coming to UB; prior to that she held the same position at SUNY at Delhi. She also spent nine years as Educational Opportunity Fund advisor at Stockton State College in Pomona, New Jersey, and has taught Afro-American history and culture courses at both Stockton State College and Saginaw Valley State University in Michigan. Hamilton graduated from SUNY at Oneonta and holds a master's degree from Atlanta University and a doctorate from the University at Albany.

Sandra Drabeck, formerly assistant dean for resource management for the School of Health Related Professions and the School of Nursing, has moved to the School of Medicine and Biomedical Sciences to become its assistant dean for resource management. A UB economics graduate, Drabeck has been at UB for nine years. She also has served as assistant to the provost for budget and personnel administration.

Thomas Martin has been appointed director of Laboratory Animal Research Facilities. An Australian, Martin formerly was director of the animal-care program and a senior lecturer at the University of South Wales, the most senior position in Australia in laboratory animal medicine. He has extensive experience with a range of species and has practiced as a veterinarian in several countries, including England and Iran. He holds a doctorate in veterinary pathology from the University of Sydney and an MBA from New York University. He is a research professor in the UB Department of Pathology, working in the areas of serological diagnosis, neurological effects of bacterial endotoxin, and orthopedic repair using biocompatible and bioabsorbable collagen.

HOSPITAL NEWS

Area Catholic Hospitals Merge and Restructure

—Preserving and Fostering a Mission of Compassionate Care

Consider the situation of Western New York's Catholic hospitals three years ago: They and their sister secular hospitals could be likened to cardiac patients living with multiple risk factors while fearing the occurrence of a major life-threatening event at any time. Their risks were empty beds, rising costs, an aging and declining population and the mandating of shorter inpatient stays and more outpatient treatments by managed care.

The "event" came in 1997 in the form of a one-two punch: passage of the Health Care Reform Act of New York State followed by passage of the Balanced Budget Act by Congress. Under the Health Care Reform Act, hospitals in the state lost their guaranteed payments from health insurers and moved into a free-market environment virtually overnight. The Balanced Budget Act introduced sweeping changes in the Medicare and Medicaid programs, including a reduction of $258 million in payments to Western New York health-care providers through the year 2002. Without dramatic intervention, the prognosis for Catholic hospitals, like many other hospitals, was a sure, slow decline.

By Lois Baker

Merger was the treatment of choice and the process, which was formalized in February 1998, appears to be a life-saver. Today, the Catholic Health System (CHS) is on the road to recovery.

The merger that created the new system is described as a "virtual merger" in that member institutions will share revenues, and all CHS services and functions are combined under a central administration, much the same as a full-asset merger. However, the system's religious sponsors—the Sisters of Mercy, Daughters of Charity, Franciscan Sisters of St. Joseph and the Diocese of Buffalo—retain their assets.

The 18-member, system-wide board of directors includes representation by organizational entities that govern the hospitals: Catholic Health East (formerly Eastern Mercy Health System), Daughters of Charity National Health System, and the Diocese of Buffalo.

A key remaining question, however, is, How long will the process take to transform CHS into a fully integrated health-care delivery system? "Five to seven years, if everything goes well," predicts Dale St. Arnold, president and chief executive officer of CHS. "Do I think we can do it? Yes. It's been done other places. The challenge here is the pace of change in the health-care environment; it's very, very fast. We're trying to accomplish in a few years what other communities have been working toward for 10 or 15 years," he adds.

Plans for merging Western New York's Catholic-affiliated hospitals and their multitude of outpatient services began in 1996. Common roots and missions made theirs a natural coalescing, but not necessarily an easy one, given the fact it involved 10,000 employees, 7,000 jobs and 1,700 physicians. "Ocean liners don't make sharp turns," notes St. Arnold.

The creation of CHS, along with that of Kaleida Health, has reverberated throughout Western New York, challenging the community's capacity for change. But St. Arnold emphasizes there really has been no other alternative for the region's hospitals, given the local, state and national health-care climate. "I don't think there was any question of what we should do. Otherwise, it would have been a case of waiting to see which institution was the last standing, based on financial depth, and nobody had a lot of financial depth. Everybody kept their head above water, but never very far above water. There is still a fair amount of unsettledness, but at least we can control the changes so they match the needs of the community," he says.

John Wright, MD, dean of University at Buffalo School of Medicine and Biomedical Sciences, lauds the merger, saying anything that stabilizes the regional health-care environment is good for the medical school and the region at large. "Their moving together to act more as a unit will help avoid duplication and will presumably strengthen each individual unit. It gives us the opportunity to better coordinate our efforts, which is a positive step."

Wright says he expects the school's current medicine and family medicine residencies to remain in the Catholic system, but notes that some changes could occur. "We know we will be required to reduce the size of our residency program. How it will affect the Catholic system and our other

partners, however, is not entirely clear at this time," he says.

"Perhaps more noteworthy is the fact that we have many volunteer faculty within the Catholic system who are very important to us," he adds. "The new configuration of the system will determine how that works out, as well."

St. Arnold also emphasizes the importance of maintaining an educational function in the system. "Physicians like to teach," he says. "They like to demonstrate their abilities, and it helps to keep them sharp. Our challenge is to determine how to serve that function in a period of diminishing resources."

ANSON LIAW

THE CREATION OF CHS, ALONG WITH THAT OF KALEIDA HEALTH, HAS REVERBERATED THROUGHOUT WESTERN NEW YORK, CHALLENGING THE COMMUNITY'S CAPACITY FOR CHANGE. BUT ST. ARNOLD EMPHASIZES THERE REALLY HAS BEEN NO OTHER ALTERNATIVE FOR THE REGION'S HOSPITALS, GIVEN THE LOCAL, STATE AND NATIONAL HEALTH-CARE CLIMATE.

As initially structured, the CHS comprised six hospitals and nearly 100 health and health-related services, including family health centers, diagnostic facilities, home care services, nursing homes, adult residences and behavioral health programs. In 1998, the system served an estimated 1.1 million outpatients and 44,780 inpatients.

While the hospitals continue to carry out their mission, St. Arnold and his board have set to work securing the system's financial stability. "We've finished a very thorough analysis of what we have in this organization," he says of the first year's accomplishments. "It was like pulling together several households into one. In addition to that, we are addressing the question of where we want to take the organization."

One of the first mandates was to define and correct redundancies in the system. This effort began with an assessment of facilities and services in Lackawanna and South Buffalo. The analysis lead to the decision to redefine the roles of that area's two Catholic hospitals—Mercy Hospital and Our Lady of Victory (OLV) Hospital—both full-service institutions located two miles apart.

The plan calls for concentrating medical and surgical acute care and maternity and pediatric services at Mercy, while transforming OLV into a center of excellence for ambulatory, clinical and rehabilitation hospital services, partnering with Baker Victory Services. OLV already was a major component of the region's comprehensive head trauma system, serving as the primary in-hospital rehabilitation unit. A similar assessment will be completed at Sister's Hospital in North Buffalo, Kenmore Mercy Hospital in Kenmore and St. Joseph Hospital in Cheektowaga.

In Batavia, St. Jerome Hospital and Genesee Memorial Hospital, which were affiliated with CHS through Genesee Mercy Healthcare, spun off from the original group of hospitals and had been negotiating its own merger for the past three years. In February 1999, CHS announced that sponsorship of St. Jerome Hospital will be transferred to the Genesee Memorial Hospital Group, ending the 82-year sponsorship of the hospital by the Sisters of Mercy and removing the Batavia hospitals from CHS.

Also, a tentative contractual relationship has been dissolved between CHS and the Health System of Niagara, which was comprised of Mount Saint Mary's Hospital in Lewiston and Niagara Falls Memorial Medical Center. This development, which came about due to the breakup of the Health System

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"Helping Hands" for Young Cancer Patients

Over the past 30 years, there has been a dramatic increase in the number of childhood cancer patients experiencing long-term remission and cure. Through research and new clinical breakthroughs, almost three-quarters of today's newly diagnosed children will be treated successfully and resume their everyday lives.

BY COLLEEN KARUZA

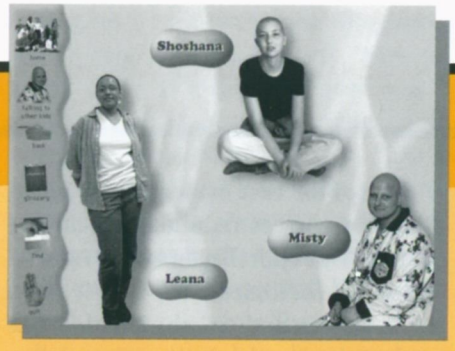
Left behind by these many lifesaving advancements is a lengthy trail of research data and study results—information easily accessed and understood by health-care professionals, scientists, medical-scientific writers and others "in the know." But what if the information seeker is a 10-year-old leukemia patient, or her parents, siblings, teachers or friends?

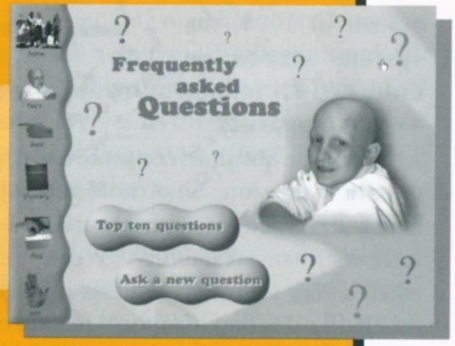
"The information is available to cancer patients and their families, provided they know how to properly access, correctly interpret and effectively personalize it," says Michael A. Zevon, PhD, chair of psychosocial oncology at Roswell Park Cancer Institute (RPCI). "Indeed, the first battle in a family's war with cancer—and cancer is a family's war—begins with the search for helpful, if not definitive, answers on all aspects of the disease."

Traditionally, patient information takes the form of written materials and face-to-face meetings with health-care professionals and families. An innovative technology that is moving beyond this framework to help meet the information needs of patients and their families is multimedia–based computer–assisted learning. Multimedia programs are being used more often in settings that require rapid, efficient transfer and learning of complex information. In an active dialogue with the computer, a variety of audio, text, video, graphics and animation components are integrated to provide the individualized, on-demand information needed to engage and enlighten the user.

Zevon and RPCI psychologist James P. Donnelly, PhD, have developed the "Helping Hands" project, a program that harnesses the educational potential of computer technology, enabling young patients, their families, peers and teachers to gain the information and skills needed to help the patient return to the routines of daily life.

"Helping Hands" provides cancer facts at an age-appropriate level and coping models designed to help manage the potentially devastating emotional aspects of the disease. A family with a newly diagnosed child, for





Pediatric oncology patients and their families can access patient information via a new multimedia, computer-assisted learning program at Roswell Park Cancer Institute.

example, will be able to look up other families whose child is receiving treatment at RPCI. The family can watch and listen as others describe and share their thoughts on effective coping. Selecting from a menu of specific topics, the family can view a presentation of the same family discussing the selected topic. The family will have the option of making personal contact with the computer family. This support can be important to the newly diagnosed patient and family.

What if the family wants specific information on blood counts? The program will illustrate the various blood components, explain their functions, define terms and provide a printed guide to understanding the importance of the child's hematologic status during treatment.

"Helping Hands" comprises three specific modules: the Pediatric Patient Module, the Parent Module and the School Module.

The Pediatric Patient Module has programs for children both over and under age 12. In the first interaction with the program, the child is asked his or her name and age. This information is used to respond to requests in an age-appropriate manner; that is, the computer will only access displays written at the child's reading and comprehension levels. "Today's young person has a comfort level with computers that makes this technology particularly appealing to them," says Zevon.

A menu of choices is then presented. Topics are available that will guide the child through the hospital experience, and provide medical information, coping strategies and the chance to meet other kids who have "been there," and answer the top 10 most frequently asked questions.

The Parent Module is an adult version of the Pediatric Patient Module, with two additional topics: Managing Your Life from the Hospital and Talking with Your Children. The School Module instructs teachers and classmates about cancer in the context of the psychosocial aspects of growing up.

This project would not have come this far, explains Donnelly, without the help of many individuals, most notably students from UB's Department of Art. "In 1995, Professor Anthony Rozak provided the initial technical assistance on the program's conceptual design and helped make critical hardware and software decisions." Since the inception of the project, Robin Sullivan, also of UB's Department of Art, has coordinated the continuing recruitment and involvement of UB art students. Using Macintosh computers, the students have translated the ideals of pediatric patient and family education conceived by the Psychology Department into a prototype that is currently being evaluated.

The psychologists have also recruited consultants from RPCI's pediatric and adolescent families, making the effort a true collaboration. Rounding out the team are the Roswell Park Alliance and the many donors whose generosity provided fundamental support for the project.

For more information on the "Helping Hands" project, contact Dr. Zevon at (716) 845-3052. ✚

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of Niagara, has resulted in Mt. Saint Mary's continuing as a contractual partner with CHS, while Niagara Falls Memorial Medical Center is pursuing an alternate affiliation.

The result is a leaner system composed of five hospitals and further consolidation of services is sure to follow. "We want to continue to organize our services around specific disease entities," explains St. Arnold. "For example, we are going to be looking at where the best places are for cardiac diseases. We may have one location doing knee replacements, while concentrating neurosciences in one or two hospitals," he says.

"Our decisions will be based on where the specialists are and how to align equipment, people and buildings to get our inpatients and outpatients back to health and to keep them well," he adds.

The net effect, St. Arnold says, should be a streamlined system with enhanced quality of care and cutting-edge computer technology that will free staff to spend more time with patients and less time on record keeping.

"The goal is to create enough surplus so we can make reinvestments," he says. "The challenge is the pace of change in this environment. We are going at warp speed into the future without the necessary tools to deal with this pace."

How has the merger been received? St. Arnold says the answer depends on whom you ask. "I think the business community wonders if this merger will actually lead to cutting costs. We've tried to demonstrate that we're moving in that direction." With that said, St. Arnold notes that health costs in Western New York are already among the lowest in the nation.

The community in general is supportive, he feels. "The merger helps preserve and foster Catholic health care in this region. People are very strongly behind that. If there are fears, they are of getting lost in a large system and of losing track of our mission to provide compassionate care.

"However, I think people are beginning to realize that by Catholic hospitals coming together, we can reduce overhead costs and redundancies and free up resources so we can do an even better job of fulfilling that mission." ✚

CGF Health System Renamed Kaleida Health

On January 20, 1999, Western New York's largest health-care system announced a new corporate identity. Known by the interim name of CGF Health System for the past two years, the merged entity created from the union of the Children's Hospital of Buffalo, Buffalo General Health System, Millard Fillmore Health System and DeGraff Memorial Hospital, is now Kaleida (pronounced Ka-ly-dah) Health.

The name is derived from the word kaleidoscope. Kaleida—from the Greek words "kalos," which means "beautiful," and "eido," which means "shape"—suggests the system's spectrum of health-care professionals, facilities and services, according to John E. Friedlander, Kaleida Health's president and chief executive officer. "Like a kaleidoscope itself, the strength and promise of Kaleida Health comes not from a single color or pattern, but from the ideal combination of skills and services by the thoughtful union of diverse parts."

Kaleida Health and its various entities include five hospitals, four long-term-care facilities, the region's largest home health-care service and numerous primary-care and outpatient facilities. The organization employs more than 12,500 people, and its medical/dental staff includes nearly 2,000 practitioners. ✚

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subject of children. "Every child has a right to a good birth, and after that a core of good preventive health services. So much of what we spend is wasted on trying to cure things that could have been prevented." In particular, Hayes has a strong personal commitment to reducing unintended pregnancies "because I think child-health battles begin with whether or not a child is wanted."

Hayes has been widely recognized for her vision for public health and, in 1995, she was elected to a two-year term as president of the National Association of Maternal and Child Health Programs, a honor of which she is especially proud. "Having had an opportunity to take that organization into a period of leadership for kids at a federal level was one of the most satisfying things I've done," she says.

Presently, Hayes serves on the American Public Health Association's Children's Health Task Force and has been appointed to the National Research Council and the Institute of Medicine's Board on Children, Youth and Families. In July 1998, she was named acting health officer for the Washington State Department of Health.

"I'm humbled by the fact that people tell me I have the ability to talk about the duty we all have toward children and family in a language that others can understand," she says.

In 1997, Hayes's ability to clearly set forth her vision won her an invitation to be a featured speaker at Harvard University's celebration of the 75th anniversary of its School of Public Health. This past December—at the invitation of Donna Shalala, secretary of Health and Human Services—she joined a 30-person delegation representing the U.S. at a binational conference in Jerusalem, Israel, held to promote international cooperation in advancing women's health issues.

In further testimony to the impact she has made in her field, Hayes was notified in 1995 that she was on the short list for the post of Surgeon General in the Clinton Administration. She has also been offered a number of other federal positions, all of which she has so far declined. "I feel Seattle is a great place to raise kids, and because I'm a single parent, I'm more inclined to stay put. Once my boys are out of high school, I feel I will be more inclined to pursue some of the more global, international interests I have," she says.

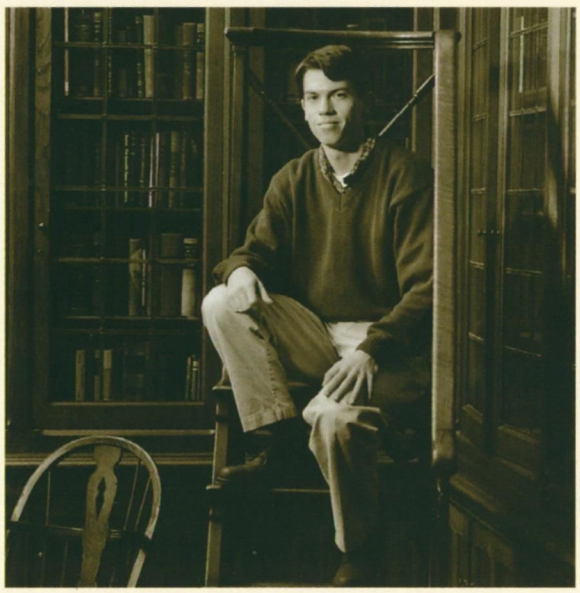
Considering Hayes's uncompromising belief in putting children first—at home, in her city, state and nation—one senses that the larger, "more global" issues she chooses to turn her attention to in the future will benefit in no small part from her compassion and dedication. ✚

Alumni Scholarship Makes a Difference

BY MARA MCGINNIS

For Jesse Cone, a first-year student at the University at Buffalo School of Medicine and Biomedical Sciences, the Medical Alumni Association Scholarship is making "all the difference in the world" to his education.

The scholarship, made possible by the generosity of alumni through their reunion class gifts, is providing Cone with $16,000 over four years for his medical school education. Recipients are selected by the admissions committee according to considerations of financial need and academic merit based on the incoming students' applications.



Originally from Pavilion, New York, Cone has been interested in medicine since high school. As an undergraduate at UB, he became intrigued by the connection between biology and English as studies of life and graduated in 1998 with a bachelor's degree in English.

"I was very pleased to receive the scholarship," says Cone, who is the oldest of six children. He explains that since he comes from such a large family, his parents are unable to support his education financially.

"I was accepted to other medical schools but this scholarship made it possible for me to go to UB with the least financial difficulty later on in my career." By alleviating some of the financial pressures of school, he says the scholarship is allowing him to work less and spend more time on his studies.

Donald Copley, MD, past president of the Medical Alumni Association, founded the scholarship program in 1993 with the help of John Naughton, MD, former dean of the medical school. "Dean Naughton and I were aware that first-year students were struggling financially, and so we decided to coordinate class reunion gifts for a scholarship," recalls Copley. "There was—and still is—a great degree of enthusiasm among the UB medical school community about the program.

"We as alumni share a universal feeling of concern for the first-year medical students. The sentiment is amplified when we come back [to the school] and think about how they are just beginning to face the challenges that we have already conquered."

Several UB medical students have received financial support through the Medical Alumni Association Scholarship, which, in recent years, has not had a high level of visibility. This year, however, Medical Alumni Association president Elizabeth Maher, MD, reinvigorated the program. "The reality is that students are begging for loans, and the obligation to pay those loans back often keeps young physicians from doing the kind of work they really want to do since it may not offer them the reimbursement they need," says Maher. "There has been a significant decline in state support for medical education, and we as fellow physicians and graduates of UB need to take some responsibility for making medical education more affordable."

Copley, now an emeritus member of the Medical Alumni Association, is impressed by the determined effort Maher has made to strengthen the scholarship program he first envisioned. "I couldn't agree more with Dr. Maher that we should be doing more for the young students. We need to recognize the impact we can have on the overall life of a future physician."

The decline in state support for medical education has only emphasized the need for such a scholarship, adds Copley.

Mary Glenn, development officer in the medical school, says steps are being taken to ensure that the scholarship program continues in future years. "We are raising awareness about the scholarship fund by increasing its visibility to alumni and making it easier for those who would like to designate funds toward it," explains Glenn. "Beginning in 1999, we also hope to start publishing an annual report of the fund that also would highlight each year's scholarship recipient."

Cone appreciates the generosity of the alumni and says he would like to thank them and make them aware of what an incredible difference it makes. "Realistically, from a financial perspective, the scholarship allows me to be in medical school." He also feels the scholarship program helps to preserve a sense of tradition at UB. "It has influenced and encouraged me to carry on that tradition by giving back to UB when I become a physician."

K.C. KRATT

A STUDENT'S PERSPECTIVE

The Role of the Patient in Medicine

—A PERSONAL PERSPECTIVE

AT AGE 15, I WAS ON THE GRAND ISLAND HIGH SCHOOL track team and an avid athlete. As my second season progressed, I was periodically awakened in the night by a crushing pain in my chest, which I disregarded, attributing it to weight lifting. Over time, however, I also began having a hard time breathing whenever I exerted myself. I felt like something was restricting my heart from beating, and eventually I had to quit track practice and rest. After a few weeks, the pain in my chest worsened and I found myself being rushed to the Children's Hospital of Buffalo.

By the time I arrived at Children's, I was doubled over from the pain in my stomach and chest. After receiving a physical exam from the emergency room resident, I was immediately introduced to the concept of a nasogastric tube. The nurse pumped out of my stomach what seemed like gallons of dark red blood. I recall a sense of relief that the hospital staff had found the problem and that I would be able to return to practice soon. But that wasn't the case.

BY JAMES J. MEZHIR

I was admitted to the hospital, began vomiting blood every few hours, and over the course of the next two days underwent a barrage of tests. I remember very clearly the day the chief of pediatric surgery and a group of short- and long-coated doctors entered my room to tell me my diagnosis.

"You have tumors in your chest and stomach, Jimmy," I was told.

"Are they malignant or benign?" I remember asking.

"I am afraid they are malignant, and we have to go in and take them out."

Curious to know what any human being in my situation would want to know, I asked, "Where did they come from?"

The surgeon's response was one I will never forget: "I am the best at what I do. I have written books and trained at the Mayo Clinic. All I can tell you is that you have had a run of bad luck, Jimmy."

And my luck didn't necessarily improve.

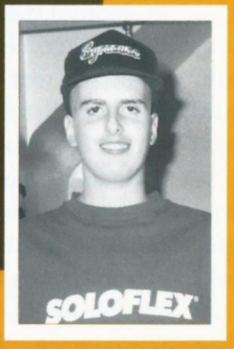
After starting my second year of medical school this fall, I sent for my medical records. When I sat down to read all about the 17 hours of surgery I underwent and the treatment that followed, I felt a mixture of emotions. One moment, it was almost as if I were outside looking in—reading the chart of a hospital patient that my preceptor wanted me to see; yet, the next moment, it was as if I were viewing things from the inside looking out—understanding, perhaps for the first time, what the words "the patient" really mean.

I elect to provide here a few details about my treatment based on what I learned from my medical records. In reference to a biopsy of a 10 by 20 cm mass in my chest, I found the following description: "Pathology came back as a malignant process. Exact tissue type unknown. The patient was then taken to the operating room where he underwent Whipple procedure for his pancreatic mass and a repeat right thoracotomy for excision of his mediastinal mass. Of significance is the fact that there was question of injury to the phrenic nerves which did compromise his postoperative course."

At first when I read this, I had difficulty comprehending that these masses had been *mine*. I wasn't sure who they belonged to, but they certainly weren't *mine*. However, I did comprehend the reference to my postoperative course being "compromised" since I do remember spending the next two weeks intubated. This was necessary because I couldn't breathe on my own due to the fact that my mediastinal mass had attached to my phrenic nerves. (I have since learned that the phrenic nerves innervate the diaphragm. If injured, they tend to leave "the patient" with an elevated diaphragm, which I have to this day.)

After about a month or so of recovery, I had to begin the real battle: chemotherapy. One day prior to beginning this phase of my treatment, I was finally given my diagnosis of non-Hodgkin's lymphoma after an ensemble of pathologists finally figured out what my cancer was. It was a huge shock that day to also learn that I would have to wear a Hickman catheter for a year in order to undergo 12 months of chemotherapy. Being that it was the middle of June and my parents had just put in a pool, having a tube coming out of my chest was not my idea of appropriate summer attire.

I thought the surgery was bad, but it pales in comparison to what chemotherapy feels like. I remember my first treatment well. My oncologists, who are all dear to me, entered the room with a tray of enormous syringes filled with colorful medications. They did their best to list the possible side effects of the medications to my family and me: "Well, this medication has been known to cause stomatitis,



Right: Teenager James Mezhir while undergoing chemotherapy for treatment of non-Hodgkin's lymphoma. ***Top left:*** James today as a second-year medical student.

HAVING THE OPPORTUNITY TO BE A MEDICAL STUDENT AFTER BEING A CANCER PATIENT IS ONE OF THE MOST INCREDIBLE LIFE EXPERIENCES IMAGINABLE. AMONG OTHER THINGS, IT SEEMS TO FINALLY LEND MEANING TO WHAT HAPPENED TO ME AS A TEENAGER.

cardiotoxicity, seizures, leukopenia, alopecia, nausea/vomiting. . ." Hearing this, I began to wonder what the hell I was thinking when I signed the consent form!

Many people have asked me what chemotherapy feels like. Depending on who's asking—a patient about to begin treatment, or a curious classmate—my answer varies. Basically, the feeling you have when you're undergoing chemotherapy can be conveyed by asking a person to imagine how he feels when he has a bad case of the flu. Then, ask him to magnify that feeling by five while simultaneously coming to the realization that it's not going to subside for 12 months. Finally, add to this the fact that there are no guarantees the drugs will work (about a 60 percent chance), and if they don't, you may have to start another regimen all over again after that.

Having the opportunity to be a medical student after being a cancer patient is one of the most incredible life experiences imaginable. Among other things, it seems to finally lend meaning to what happened to me as a teenager. It also helps me realize that there's a big difference between reading in a journal about survival rates for a disease and having to face the statistic yourself. Although I had to wait until my second year of medical school, I have finally begun to see my cancer experience through the eyes of medicine. I understand the meaning of terms like "elevated LFTs," "invading mediastinal mass" and "jaundice" as a medical professional, and also as a patient.

Now, as I begin to work with patients as a medical student, I find that I am using what I learned as a patient. Yet I am also aware of and have respect for the fact that every patient's experience is unique in many ways. Therefore, one thing I have worked to do is silence the thought "I know" that goes off in my mind when a patient remarks about postoperative pain, persistent nausea, or what it is like being intubated. While there is always the sense that I truly do understand more of what they are talking about, I also know it's important for me to learn how to listen because being a good listener, I feel, is one of the best skills a doctor can have.

Thank you for allowing me to share with you this medical student's perspective on the role of the patient in medicine. ✚

James J. Mezhir is a second-year student at the University at Buffalo School of Medicine and Biomedical Sciences.

RESEARCH

Advances at Toshiba Stroke Research Center

Prototype Camera Views Brain Stents

Researchers at the University at Buffalo's Toshiba Stroke Research Center have developed a prototype camera that can turn blurred X-ray images of brain stents made of thin wire into images clear enough to detect the condition of wire as fine as a hair.

The development marks the first use of this technology, called a high-resolution region-of-interest micro-angiographic digital detector, for viewing stents placed inside blood vessels in the brain. The stents can prevent stroke by shoring up weak spots in arteries or blocking off aneurysms.

The UB prototype provides images that are significantly clearer than can be produced by any current system, and may allow the viewing of even the tiniest blood vessels in the circulation system, according to Stephen Rudin, PhD, principal investigator and UB professor of radiology, neurosurgery and physics. Rudin heads a radiation physics group within the center whose efforts to develop a clinical prototype of the device are being funded by a three-year, $1.2 million grant from the National Institute of Neurological Disorders and Stroke.

Intravascular interventions use the body's circulation system as a tunnel to the brain. To complete these procedures, neurosurgeons or neuroradiologists thread micro-thin instruments through the large artery in the groin until they reach the damaged area, an approach that avoids the need to open the skull.

Having clear X-ray images of the vessels and instruments is critical to reaching the repair site without damaging vessels along the way. "Even with the most advanced imaging equipment available at present, we weren't seeing features we knew existed," Rudin says. "We expect this detector prototype to help us locate the stent optimally in the vessel, visualize its integrity in place and reposition it if necessary. If you can't see exactly what condition the stent is in when it's deployed, it's not possible to change the deployment.

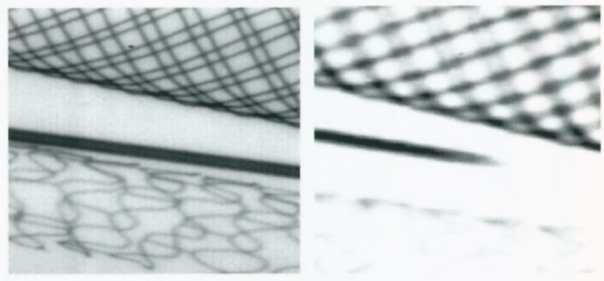
"The detector technology is similar to that being introduced now in mammography," he says. "In mammography, the site being viewed is static. We are developing the technology so it can be used in rapid-sequence imaging at that very high resolution."

Rudin says this enhanced imaging capability should allow viewing of vessels as small as 50 to 200 microns, including those called perforators, which are located at the very end of the circulation system of the brain and cannot be seen at all with conventional imaging equipment.

"Without this new capability, we would have difficulty treating aneurysms that are near these vessels because we cannot see well enough to avoid damaging the very small healthy perforators."

Additional members of the research team are Ajay Wakhloo, MD, and Daniel Bednarek, PhD, both associate professors in the UB School of Medicine and Biomedical Sciences, and Chang-Ying J. Yang and William E. Granger, doctoral candidates. ✚

—LOIS BAKER



Blurry image of stents on the right was taken using conventional X-ray image intensifier technology; clear image on the left was taken using the high-resolution region-of-interest microangiographic digital detector being developed at UB. Each photograph shows two stents separated by a 26-gauge needle. The stent above the needle is a self-expanding Wallstent with 80 micron stainless steel wire; the stent below the needle is a balloon expandable MultiLink stent with 50 micron wire.

New Technique to Treat AVMs More Effectively

A new technique for determining the rate of blood flow, developed by researchers at the University at Buffalo Toshiba Stroke Research Center, will enable neurosurgeons, using digital radiographic imaging, to characterize and treat arteriovenous malformations (AVMs) more effectively.

The technique—which has not been used elsewhere for this condition—is called dual contrast injection and has been used on 21 patients at the center with no complications, according to lead researcher William Granger, a UB physiology and biophysics doctoral candidate.

An AVM is a tangle of fragile vessels in the brain or spinal chord that forms between an artery, which carries oxygen-rich blood to the brain, and a vein, which drains oxygen-depleted blood back to the lungs for replenishment. It creates a short circuit between the two circulation systems, shunting blood directly from the artery into the vein, effectively bypassing the brain. An AVM can leak or rupture if it isn't treated. The condition, thought to be congenital, is diagnosed most frequently in young adults, Granger says.

One way of treating AVMs—and the method of choice of neurosurgeons at the UB Toshiba Stroke Research Center—is to seal off the entrances to the blood vessels nourishing the AVM, called feeding pedicules, with a glue-like substance. With the feeding pedicules sealed off, circulation resumes its normal path, full oxygenation of the brain is restored and the threat of bleeding or stroke is eliminated.

For this technique to work maximally, neurosurgeons must be able to gauge the exact rate of blood flow through the AVM so they can determine the transit time of the glue from the injection point to the site to be blocked. They then can formulate the gluing agent so it hardens at the proper point as it is carried along by the blood flow. This ensures that blood flow is blocked to the AVM without occluding the main artery or vein.

Current techniques for determining rate of blood flow use two approaches, both involving injecting a contrast medium into the AVM through a tiny catheter threaded through the large artery in the groin until it reaches the damaged area. The contrast medium is tracked via digital X-ray imaging.

GRANGER'S IDEA WAS TO ADMINISTER BOTH CONTRAST MEDIA SIMULTANEOUSLY. DUAL-CONTRAST INJECTION ALLOWS NEUROSURGEONS OR NEURORADIOLOGISTS TO GAUGE BOTH DISTANCE AND TIME WITH ONE INTERVENTION.

One approach involves injecting a soluble contrast medium, which is effective in showing the internal contours of the vessel and its twists and turns, enabling neurosurgeons to determine distance through the AVM. But because the contrast medium dissolves and diffuses into the blood stream, it does not produce a clear, leading edge necessary to track how fast the flow is moving.

An alternate approach uses a nonsoluble contrast medium: small droplets of a poppy seed oil-based agent containing radioactive iodine. These droplets provide the necessary leading edge to provide precise information on speed of the flow. But because the contrast medium doesn't dissolve and fill the vessel, tracking the oil droplets alone provides no information on the path, or distance, the drop has traveled, which is necessary for determining the rate of flow.

Granger's idea was to administer both contrast media simultaneously. Dual-contrast injection allows neurosurgeons or neuroradiologists to gauge both distance and time with one intervention. He says the technique never has been used elsewhere for determining the rate of blood flow in AVMs.

"The two methods together allow more exact means of determining rate of flow," Granger says. "We can determine the exact time for the glue to reach the arteriovenous junction. Our method is more accurate in determining flow velocity than either single soluble or nonsoluble injections alone."

Additional members of the research group are Afshin A. Divani, doctoral candidate in mechanical and aerospace engineering; Stephen Rudin, PhD, professor of radiology and physics; Ajay K. Wakhloo, MD, associate professor of neurosurgery; Baruch B. Lieber, PhD, associate professor of mechanical and aerospace engineering; Daniel R. Bednarek, PhD, associate professor of radiology and physics; and Lee R. Guterman, PhD, MD, all of UB. Their work was funded by a grant from Toshiba American Medical Systems. ✚

— LOIS BAKER

BY LINDA J. CORDER, PHD, CFRE

A Word from the Director of Development

CONGRATULATIONS AND THANKS to those who supported the School of Medicine and Biomedical Sciences at such an outstanding level last year. In so doing, they became members of the "Class of 1998" James Platt White Society.

Since its founding in 1986, the society has grown from a small group of dedicated medical school alumni to an organization of over 200 alumni and friends who are generous investors in the future of medical education, residency training and biomedical research and graduate studies. A volunteer executive committee (comprised of active society members) works with the development staff to increase philanthropy to the school and to plan recognition events for members. Publishing this annual list of the school's most generous philanthropists gives Dr. Wright, the executive committee, and those of us who work daily on behalf of the school, an opportunity to show our appreciation.

The James Platt White Society provides two types of recognition—annual and lifetime. A gift within any year confers an annual membership for the following year. When cumulative contributions reach $50,000, honorary lifetime membership is granted. There are also a few "special" members who received "term memberships" for a specified time frame. Although no new "special memberships" have been granted since 1992, we honor those earlier commitments. Most "special memberships" will expire at the close of 1999.

A year ago, the society made the transition to a calendar year-recognition cycle. During the "14-month year" of 1997, membership passed the 200 mark. Another increase was shown in 1998, as the "Honor Roll" list grew to 216 contributing members.

Individuals and couples who support the school at an outstanding level are seen as its closest friends. They receive additional information, invitations to certain school and university events, as well as special recognition in the society. Best of all, this group keeps expanding. It is a welcoming and inclusive organization, since the more "best friends" the school has, the more outstanding it becomes.

The society welcomed one new founder this year, Mr. John Goodwin Jr, who established a scholarship in memory of his wife, Mrs. Irene Pinney Goodwin. Mr. Goodwin graduated from Harvard, Class of 1927, and was a businessman in Western New York. His family's physician was a graduate of UB's school of medicine, and Mr. Goodwin told me how impressed he was with this young person, especially during his wife's last two illnesses. Irene, he said, placed high value on both education for women and healthy living. As a result, Mr. Goodwin decided to make her memorial gift to our school, rather than her college. We never know where our influences will fall. The endowment will provide scholarships to young women studying to become physicians, and the first award will be given in the 1999–2000 academic year.

Several individuals and couples are in the society for the first time. Those marked with an asterisk (*) are Gold members, "graduates of the last decade," whose gifts during 1998 totaled between $500 and $999. The lower "entry level" for younger graduates was instituted in 1996 to encourage newer alumni to take their place in this society.

Most individual contributions were designated for the school's general fund, disbursed at the dean's discretion. A few gifts were designated to special projects, such as the Neuroanatomy Museum, or to departmental funds, which are disbursed at the discretion of the department chair for such uses as research seed money or student medical association activities.

The donors listed in this Honor Roll collectively contributed approximately $340,000 to the School of Medicine and Biomedical Sciences. We are deeply appreciative of all gifts to the school, especially those that have the potential to make a transforming difference in the quality of medical education, residency training and research in the basic sciences.

Publishing this annual list gives us an opportunity to show our appreciation.

I invite you to read through the roster of members, and to thank your friends and colleague for their outstanding support. If you are not yet in this group, please consider increasing your contributions to the school. The executive committee would like to see this honorary group continue to expand, multiplying its significant and positive impact on the academic environment of the UB School of Medicine and Biomedical Sciences. ✚

Linda J. Corder (Lyn) is the associate dean and director of development. She may be reached by phone at (716) 829-2773 or our toll-free number 1(877)826-3246. Her E-mail address is ljcorder@.buffalo.edu.

The James Platt White Society

January 1, 1998—December 31, 1998

Lifetime Members

When cumulative contributions reach $50,000 or an irrevocable deferred gift is completed for $100,000 or more, a couple or individual is granted lifetime membership in the Society. Combinations of outright and deferred gifts in appropriate proportions can also be the basis of lifetime membership. Names of Founders are repeated in an annual category in any year that they make a new gift to the School.

Founders' Circle

UB's founders, primarily physicians and attorneys, envisioned a school to train students for service to the community. The Society's Founders help to actualize that vision by providing a generous base of support for programs and activities that enrich the academic environment and enhance medical training.

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Just as a department chair leads a program, donors of leadership gifts in the range of $10,000 to $24,999 are given special recognition.

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A strong faculty is central to a great university. Likewise, central to the future of our School is the dedication of a cadre of supporters whose annual gifts range from $5,000–$9,999.

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Fellows within the School are recognized for added depth they bring to postgraduate study. Within the Society, Fellows are honored for gifts that total $2,500 to $4,999.

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One strength of an outstanding institution is the caliber of those who study there. Scholars within the James Platt White Society have made gifts to the School totaling $1000 to $2,499 during the past year. Those marked with asterick (*) are young scholars, graduate of the last decade who qualify with gifts of $500 to $999.

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Dr. Frank T. Riforgiato and Mrs. Mary-Cecina Riforgiato
Buffalo, NY

Dr. Bruce H. Robson
Geneva, OH

Dr. Jeffrey S. Ross
Lebanon Springs, NY

Mr. and Mrs. James Rosso
Buffalo, NY

Dr. Albert G. Rowe
Tonawanda, NY

Dr. Eric J. Russell
Chicago, IL

Dr. Arthur J. Schaefer and Mrs. Elizabeth Ann Schaefer
Snyder, NY

Dr. Adolphe and Mrs. Nancy Schoepflin
Tucson, AZ

Dr. James N. Schmitt
Kenmore, NY

Dr. David S. Schreiber
Westwood, MA

Dr. Joseph I. Schultz
San Pedro, CA

Dr. Fred S. Schwarz
Buffalo, NY

Mr. Mark R. Schufman
Woodside, NY

Dr. Edward Shanbrom and Mrs. Helen Shanbrom
Santa Ana, CA

Dr. Roy E. Seibel Sr. and Mrs. Ruth Seibel
Eggertsville, NY

Dr. Arthur M. Seigel and Mrs. Ellen M. Seigel
Guilford, CT

Dr. Molly R. Seidenberg
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Dr. Elizabeth G. Serrage
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Dr. John B. Sheffer
Williamsville, NY

Dr. Timothy S. Sievenpiper and Mrs. Karen S. Sievenpiper
East Aurora, NY

Dr. Roger M. Simon
Las Vegas, NV

Dr. Edward H. Simmons
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Dr. Albert Somit
Carbondale, IL

Dr. John J. Squadrito
Sarasota, FL

Dr. William C. Sternfeld
Sylvania, OH

Dr. Burton Stulberg
Buffalo, NY

ALUMNI

Dr. Michael A. Sullivan
Williamsville, NY

Dr. Michael S. Taxier
Worthington, OH

Dr. Wayne C. Templer
Corning, NY

Dr. and Mrs. James Tibbetts
Sturgeon Bay, WI

Dr. George Toufexis
Williamsville, NY

Dr. Bradley T. Truax
Lewiston, NY

Mr. James J. Trzaska
Lancaster, NY

Dr. Barbara Von Schmidt
Oakland, CA

Dr. Charles E. Wiles
Grand Island, NY

Dr. Richard D. Wasson and
Mrs. Janet Wasson
Holiday, FL

Dr. Arnold Wax
Henderson, NV

Dr. Harold J. Weinstein
Van Nuys, CA

Drs. Charlotte and Hyman Weiss
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Dr. Gary J. Wilcox
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Dr. Richard G. Williams
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Dr. John R. Wright and
Mrs. Deanna Wright
Williamsville, NY

Mr. and Mrs. Gilbert J. Yager
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Dr. and Mrs. Gregory Young
Holland, NY

Dr. Lynda M. Young-Sorrenti
Worcester, MA

Dr. Franklin Zeplowitz and
Mrs. Piera Zeplowitz
Buffalo, NY

Dr. David C. Ziegler and
Mrs. Susan D. Ziegler
Walnut Creek, CA

SPECIAL MEMBERS

A few individuals and couples were granted multi-year memberships based on generous gifts made betweeen 1989 and 1993.

Dr. David W. Butsch
Montpelier, VT

Ms. Janet Butsch
Aurora, CO

Dr. John L. Butsch
Buffalo, NY

Dr. and Mrs. Marvin Z. Kurlan
Williamsville, NY

Dr. John Naughton
Buffalo, NY

Mrs. Marvin (Helen) Winer
Sarasota, FL

IN MEMORIAM

The following individuals left generous bequests or made arrangements for gifts from testamentary trusts.

Mrs. Virginia Barnes

Dr. Clara A. March

Dr. Mark W. Welch

Sherman Hanson

Anonymous

We have made every effort to ensure accuracy in these lists. If you have any questions or corrections, please call Mrs. Mary Glenn tollfree at 1 (877)826-3246.

1950s

EDWARD HOHENSEE, MD '54, writes: Thank you for printing my note in the winter issue of *Buffalo Physician*. However, you printed my email address incorrectly! The correct address is: edhohensee@aol.com

WILLIAM J. SULLIVAN, MD '55, writes from Los Angeles, CA: "Recently, I changed my medical practice from a solo forensic psychiatric one to a partnership structure with other forensic psychiatrists. This will permit more time off, longer vacations and greater flexibility in my working schedule. I now function as the medical director of the group."

1960s

WILLIAM K. MAJOR JR., MD '69, has been named new executive director of the Individual Practice Association of Western New York (IPA/WNY), the physician organization of Independent Health, Buffalo's largest health maintenance organization. In this position Major is responsible for the day-to-day business of the IPA/WNY, including serving as an ombudsman for physicians and working closely with Independent Health's senior management on health-care policies, programs, strategy development and other issues affecting local physicians. Major has 25 years of experience as a practicing physician and medical administrator. He is a board-certified cardio-thoracic surgeon and formerly was director of Cardio-Thoracic Associates of WNY, P.C. He has also been an associate clinical professor at UB's school of medicine since 1981.

1970s

THOMAS G. DISESSA, MD '71, writes: I recently accompanied the surgical team of the International Children's Heart Foundation to Zagreb, Croatia. While there, I performed ten interventional catheterization procedures on children two months old to 14 years. I dilated six patients with coarctation, two patients with aortic stenosis and coil closed two ductus. In January, I went to Peru for the second time and may return to Croatia in the future.

1980s

DONNICA L. MOORE, MD '86. If the trio in the photograph below look familiar, it's because you may have seen them while channel surfing Saturday or Sunday morning. In the center is Donnica L. Moore, a regular guest on the *NBC Weekend Today Show* with anchors Jack Ford and Jodi Applegate. Applegate has interviewed Moore on diverse women's health issues, including complications of pregnancy, menopause, hormone replacement therapy, aging, contraception and migraines. Moore has also recently been awarded the Woman of the Year Award in Health/Medicine from New Jersey's Somerset County Commission on the Status of Women for her role in women's health research, advocacy, education and leadership.

NIRANJAN M. KUMAR, PHD '88, writes: I have joined Wyeth-Lederle Vaccines and Pediatrics Pharmaceutical Company in Pearl River, NY. I was a visiting scientist at Merck and Company, Inc., prior to this appointment.

HOWARD CHANG, MD '89, suffered a stroke due to an AVM. He is currently unable to practice medicine. He lives with his wife and two daughters in San Diego, CA.

Pictured above are the children of Matthew J. Phillips, MD '91, and his wife, Toula. From *left to right* are James, Michael, newborn daughter Markella Aretee, and Matthew, Jr.

1990s

MATTHEW J. PHILLIPS, MD '91, writes: My wife, Toula, and I joyfully announce the birth of our daughter, Markella Aretee, born December 21, 1998. She joins her three brothers: James, age five; Michael, four; and Matthew, Jr, two; *pictured above.*

FAITH E. GRIETZER-FRANKEL, MD '91, is a pediatrician in private practice in Fairfax, VA. She recently contributed to a video on SIDS prevention, which is available nationwide through the One Step catalogue. Her husband **DOUGLAS FRANKEL, MD '91,** is in private practice in trauma/internal medicine in Maryland. He is also a physician for professional boxing. They have three sons: Maxie, Aidan and Riley, and live in Maryland, 15 minutes outside of Washington, DC.

HOWARD S. PODOLSKY, MD '91, writes: Following completion of my residency in internal medicine at The Christ Hospital/University of Cincinnati, my wife, Rabbi Elizabeth B. Hersh, and I have settled in St. Louis,

MO. In 1994, I joined the staff of Southwest Medical Center as an attending physician. Since that time, I have cultivated a largely geriatric practice in a multi-specialty group environment. I continue to function as a resident instructor as well as a mentor to medical students who are interested in pursuing a career in internal medicine. My wife is now the associate rabbi of the United Hebrew Congregation located in Chesterfield, MO. In the fall of 1998, fulfilling my quest to remain a perpetual student, I was accepted, as a Dean's Scholar, into the St. Louis University School of Law. After one semester of evening classes and early morning rounds, I have come to long for the days of merely being a resident. While I encounter the law school experience, I continue to draw on the many skills I acquired during my medical school career. As I look to the future, I hope to become involved in health-care policy while continuing my work in primary care. Rofay@aol.com

ELIZABETH CONROY, MD '92, and husband, Jeff, proudly announce the birth of their third child on February 4, 1999, a daughter, Julia Grace, 8 pounds, 3 ounces. Elizabeth is a practicing dermatologist with Buffalo Medical Group.

KETAN DAVAE, MD '96, writes: "I completed a surgical internship at Michigan, radiology residency at Tufts, vascular interventional radiology at Harvard, and musculoskeletal, Cornell."

IN MEMORIAM

HARRY BERGMAN, MD '34, surgeon and cancer researcher, died of heart failure on December 14, 1998, in Hollywood, FL, at age 87. Last spring, Bergman received an Award of Special Recognition from the Dean's Advisory Council of UB's School of Medicine and Biomedical Sciences for his life's work in urology. The award recognized that, in 1947, Bergman devised an instrument capable of obtaining an early neoplastic degeneration inside an apparent benign tumor, an accomplishment for which he received an award from the American Cancer Society in 1948. It also acknowledges Bergman's discovery of a radiological sign for cancer of the ureter, named "Bergman's Sign" in his honor by John Emmett, professor of urology at the Mayo Clinic, and first catalogued in *Dorland's Medical Dictionary* in 1981. Also noted in the award was Bergman's work as a writer and editor of many publications, including his highly respected text, *The Ureter*, which he published in 1960 and revised in 1981. Bergman moved to Florida from New York when he semi-retired in 1978. He was a professor of urology at the university of Miami's School of Medicine and worked as a clinical professor at Jackson Memorial Hospital in Miami for 10 years. At age 21, Bergman graduated at the head of his class at UB and, at the time, was the university's youngest medical school graduate. A successful practice as a urologist and surgeon in Manhattan and Bronx, NY, followed. As his practice grew, so did Bergman's reputation for doing *pro bono* work. "He was a person who had a tremendous love of people," said Albert Sirota, a friend. "He never had a negative word to say about anybody. He believed if you didn't have anything good to say about somebody, don't say anything. He was a practitioner who really cared." Bergman is survived by his wife, Mollie Holtzman Bergman, and daughter Ann Sue Matasar of Chicago, IL.


Gilbert "Ben" Tybring, MD '45

GILBERT "BEN" TYBRING, MD '45, died on February 1, 1999, of heart failure at age 79, in Madison, WI. According to his wife, Jane, he also had been diagnosed with Alzheimer's disease. Originally from Endicott, NY, Tybring graduated from the New York State College for Teachers—Albany in 1942 (now SUNY at Albany). After earning his medical degree at UB, he interned at Buffalo General Hospital for a year prior to serving in the military for two years. From 1948-1951, he was a resident in psychiatry at Buffalo State Hospital. In 1955, he moved to Madison, WI, to serve as clinical director at Mendota State Hospital, a position he held until 1962, at which time he went into private practice with the newly formed Madison Psychiatric Associates. He was a staff psychiatrist at the Dane County Mental Health Center during the 1970s and an associate clinical professor of psychiatry at the University of Wisconsin in the 1960s and early 1970s. Following his retirement in 1984, he established and edited a state newsletter, *The Wisconsin Psychiatrist*. In 1993, the newsletter won the Newsletter of the Year award from the American Psychiatric Association. In addition to his wife, Jane, he is survived by the children of his first marriage (his first wife, Jean Agnes Smith of North Tonawanda, NY, died in 1970), Gilbert Benson IV of Lakeland, FL, Nancy Morningstar of Palomar, CA, and William Mark of West Bend, WI.

HAROLD PESCOVITZ, MD '47, died in March 1999 at his winter home in Amberley Village, FL, at age 74. A native of New York City, Pescovitz moved to Cincinnati, OH, after he earned his medical degree at UB. In Ohio, he completed his residency and practiced general surgery at Jewish

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Hospital, after which he entered private practice in Avondale, Fairfield and North Bend. Pescovitz, whose first wife, Anita, preceded him in death, is survived by his wife of seven years, Shirley; sons Mart of Carmel, IN; Robert of Los Angeles, CA; Michael of Evendale; Charles of Symmes Township; Rick of Hyde Park; David of San Francisco, CA; and daughters Pam Tiemeyer of Farmington Hills, MI, and Maxa Pescovitz-Gider of Pembroke Pines, FL.

Support Appreciated for Summer Externship Program

The Primary Care Summer Externship is preparing for its seventh summer and would like to thank the institutions who have pledged their generous support for 1999. These include a renewed commitment from the Charles E. Culpeper Foundation, the Independent Health Foundation, and the Lake Plains Community Care Network, as well as new support from the New York State Department of Health Minority Participation in Medical Education Initiative. Each of these institutions has demonstrated a long- term commitment to primary-care education. Their support will have a direct impact on the development of physicians educated in Western New York, many of whom will be the future health-care providers for our community. ✚

FERDINAND A. PAOLINI, MD '47, died on February 16, 1999, in Erie County Medical Center after a long illness. He was 74. Paolini, who was born in L'Aquila, Italy, came to Buffalo when he was two years old. Following graduation from Canisius College and UB's medical school, he served a residency in internal medicine at the former Edward J. Meyer Memorial Hospital, now Erie County Medical Center (ECMC). He returned to the hospital after completion of service with the Army Medical Corps. Later, during the Korean War, he served as a captain at the Second Army Hospital in Fort Campbell, KY. After his Army service, Paolini began a lifelong association with the ECMC and the UB school of medicine. He was director of clinics and ambulatory care as well as president of the medical-dental staff at the hospital. He was acting medical director during the hospital's transition to a medical center and expressed concern that care for needy patients would suffer at the hands of a private institution. Paolini argued in 1978 that savings from a private program would come from programs helping "people who can't take care of themselves." In his teaching career at the medical school and as a longtime member of the school's Admissions Committee, he influenced the lives of many dentists and physicians. Paolini was known as a gifted teacher, with a flair for quoting maxims in Latin and Greek during his lectures to students, as well as passages from his favorite authors and poets—Shakespeare, Dickens and Housman. He retired from the medical school as emeritus clinical professor of medicine in 1979. He then was appointed medical director of Brothers of Mercy Nursing Home in Clarence and was instrumental in establishing the facility as a major rehabilitation center. Survivors include his wife of 48 years, the former Emily Diakun; three daughters, Anne Shaw of Minneapolis, MN, Susan Quek of New York City, NY, and Judith Walton; five sons, Michael of California, John of Chicago, IL, James, Alan and Joseph; and six grandchildren.

CLARENCE CRANDALL, MD '50, died on November 12, 1998, at his home in Melbourne, FL. He was 77. Crandall was born in Kennedy, NY. In 1942, he enlisted in the Army Air Force and served as an armament instructor for three years. Upon leaving the service, he enrolled in UB's medical school. Following graduation, he practiced medicine in Holt, MI, for four years. In 1954, he moved to the old Eau Gallie area of Melbourne, FL, where he worked until he retired in 1987. A friend of Crandall's in Melbourne said she wanted him to be remembered for what a former patient had once said of him: "He treated me when I was dirt poor as though I had all the money in the world." Survivors include his wife, Jean, of 56 years, daughters Valerie Crandall Jackson, Charlene Crandall and Dr. Melanie Crandall McMahon; son Dr. Blane Crandall, brothers, Vernon and Rodney; sister, Carol Everett; and eight grandchildren.

HERSHEL ULLMAN, MD '50. Sanford Ullman, MD '38, writes: "My brother, Hershel, died February 2, 1999, at the age of 76. He was an internist/cardiologist in Los Angeles, CA.

JOHN S. CARLETON, MD '59, died of heart failure on June 3, 1998, following a long illness. He was 70. After graduation from Harding University in 1944, Carleton entered the Navy. Following World War II, he entered the Air Force Aviation cadet program, where he trained as a pilot, later becoming a decorated fighter pilot during the Korean War. In 1952, Carleton chose to leave the Air Force and pursue a career in medicine. He entered UB, where his father, William

Deborah A. White, MD, Physician, Wife and Mother, 1961—1999

She was a physician who listened compassionately to her patients. She was a partner in a solid marriage. She and her husband, Christopher, were devoted to the three children who formed the center of their lives. How do we make sense of the tragic car accident on February 21, 1999, that claimed the lives of Deb, Chris and their youngest son, Adam?

I can't make sense of it, but I know the tragedy has affected many of us, particularly those in the Medina area, where Deb practiced. Her death has given me an opportunity to examine who she was and what her accomplishments were. She grew up on a dairy farm in Eden, NY, one of four children, two of whom still live in Eden, near her parents. She was a diligent student who worked hard to get into UB's school of medicine, graduating in 1987. She did her residency in internal medicine at Buffalo General Hospital while her husband, a cellular and molecular biologist, worked at Roswell Park Cancer Institute. In 1990, at the end of her residency and upon the birth of their first child, Andrew, Deb and Chris's lives took an unusual turn. Chris quit his job at Roswell to become the *at-home* parent and Deb joined a busy internal medicine practice with David Stahl, MD '79, in Middleport, New York. She went on to have two more children: Elizabeth, born in 1993, and Adam, in 1995. After each birth, Deb took off just a few weeks because of her commitment to her partner and practice. It was because of the support she received from her husband that she was able to "not miss a beat" with the birth of each of her children.

Being a doctor in a small community, it was only natural that her practice extended beyond internal medicine. She was in much demand for the services she could provide not only to women in the community, but to children and adolescents, as well. Whenever I called her from the Emergency Department at Medina Memorial Hospital regarding one of her patients, she was always responsive and respectful, despite the frenzy in her office. At noon, I could always find her at home with the frenzy of the family in the background. "Frenzy," though, is not a word that relates to Deb at all. She had a way of listening and *being there* that made you feel like you were the only thing on her mind. I know her patients felt this way because they tell me so when I talk with them in the Emergency Department.

I have searched for meaning in this tragedy but have found little. I am, however, comforted knowing that the surviving children, Andrew, age nine, and Elizabeth, age six, have been embraced by the wonderful extended families of both Deb and Chris. I am inspired by Mr. Preischel, Deb's father. He was able to articulate, while in the Emergency Department on the afternoon of February 21, that his daughter lived a full life. She wanted to be a doctor more than anything, and she became a remarkable physician. She wanted a family life, and she became a loving wife and attentive mother. — **Elizabeth Maher, MD '85.**

Dr. Maher is director of Emergency Services at Medina Memorial Hospital, where Dr. White was a member of the medical staff.

Wallace Carleton, and his grandfather, John Falloon Carleton, had also attended medical school. Following graduation, he received his specialist training in otolaryngology (ENT) in Houston. He then practiced medicine in affiliation with Baylor University in Texas from 1962 to 1966 and in Arizona. Throughout his career, Carleton performed much volunteer work, especially with children. He was invited to establish an ENT program and physical ward at an Air Force hospital owned by the Saudi government in Saudi Arabia from 1981 to 1984. He is survived by his wife, Alice (Sid) Carleton.

MURRAY A. MORPHY, MD '72, professor and vice chair of the UB Department of Psychiatry and senior medical officer for the Veterans Administration Western New York Healthcare System, died November 30, 1998, at his home in Snyder, NY, at age 51. Following graduation from UB, Morphy served as chief of psychiatry at Veterans Hospital and later was promoted to chief of psychiatry services for the VA Healthcare System of Western New York, as well as senior medical officer for the agency's entire health-care system of Western New York. Involved in the training of hundreds of young physicians studying to become psychiatrists, he is credited by his peers with the ability to combine scholarship with excellence in clinical care and administration. He was widely published and presented papers at conferences worldwide. Morphy was a senior examiner for the American Board of Psychiatry and Neurology and president of the National Association of VA Psychiatrists. He also served as president, secretary and treasurer of the Western New York Psychiatric Society.

Murray A. Morphy, MD '72

The Pulmonary Rehabilitation Center

Garden Gate Health Care Facility is pleased to offer a rehabilitation program specializing in the care of individuals with pulmonary and respiratory disorders.

Our Unit is coordinated under the guidance of Dr. Robert McDonald, Board Certified in Pulmonary and Critical Care. The unit is staffed by Respiratory, Physical and Occupational therapists and a team of professional support staff educated on the specifics of caring for and treating pulmonary disorders.

In addition, Dr. McDonald is a Fellow in the American College of Chest Physicians, President of the WNY Pulmonary and Critical Care Society and partner with Buffalo Cardiology & Pulmonary Associates, P.C.

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