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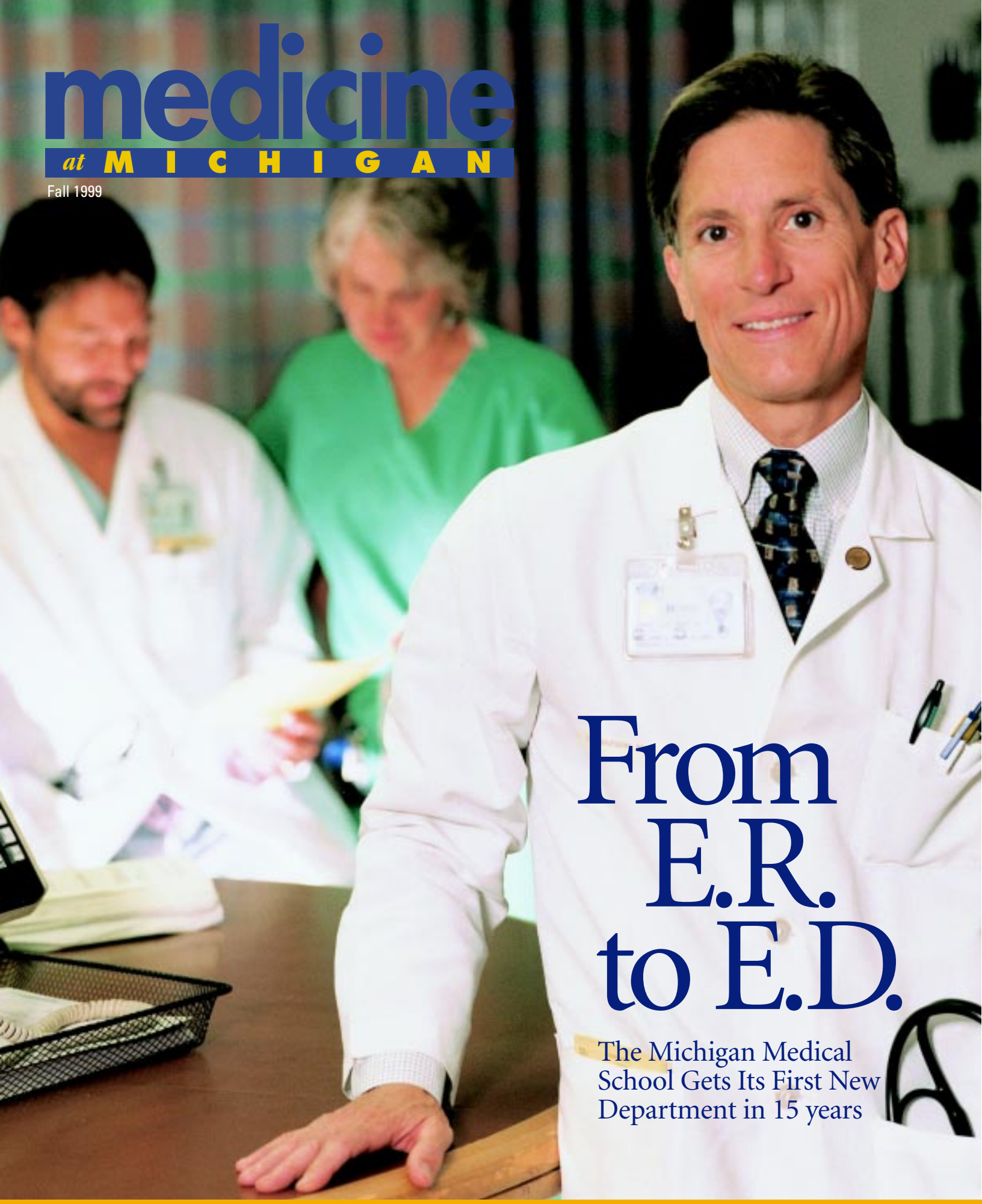

From E.R. to E.D.

The Michigan Medical School Gets Its First New Department in 15 years

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For Jeffrey Chamberlain, Fighting Muscular Dystrophy on the Genetic Level is His Life's Work

For the millions of children and adults who suffer from the disease, it may mean life itself

by Jeffrey Mortimer

For most researchers in the world of human biology, their work will always be largely invisible to all except a handful of people. Partly this is due to the complexity of biological research today; partly it is due to the sub-microscopic nature of the work.

But for Jeffrey S. Chamberlain, Ph.D., professor of human genetics, who for the past decade has headed a research team in the University of Michigan Medical School that has made several major breakthroughs in the battle to cure muscular dystrophy, invisibility has not been a problem. In his efforts to promote understanding and support for his work, he has written for *Parade* magazine and appeared on four different occasions on the Muscular Dystrophy Association's Labor Day Telethon. The Telethon, thanks to the involvement of comedian and actor Jerry Lewis, has done much over the years to familiarize the American public with the terrible effects of muscular dystrophy on both children and adults and to raise invaluable research funds for investigators like Chamberlain. The 21-and-a-half hour event was first televised in 1966 and now reaches more than 75 million viewers.

That science and visibility could go together was something Chamberlain understood from an early age. Growing up in Tucson, Arizona, where his father was an astronomer at the Kitt Peak National Observatory, he knew as family friends many of the popular astronauts and famous astronomers of the day. When Chamberlain's father was hired by NASA in the late 1960s and the family moved to Houston, Texas, it was astronaut Buzz Aldrin's house that they bought.

For Chamberlain, though, it was the mystery of cells rather than the mystery of the stars and planets, that drew his attention as an undergraduate at Rice University in Houston. The unbelievable journey from single egg to fully developed human being captured his attention in the same way that the journey of stars had captured his father's. He thought about becoming a physician. But the desire to learn more about those mysterious cells won out and ultimately he earned a Ph.D. in biochemistry from the University of Washington.

It was while doing a post-doctoral fellowship at Baylor College of Medicine that Chamberlain found a way to combine the scientist's love of discovery and the physician's love of healing: he discovered that little was known about the development of muscle cells and that whatever he learned could eventually make a difference in the lives of those with muscular dystrophy.

Insofar as there are stars in the research firmament whose luster transcends the world of laboratories and symposia, Chamberlain is one. And he is outspoken, albeit quietly. His intense determination to conquer muscular dystrophy is coupled with an equally intense frustration at those whose research fervor doesn't match his own. "If it were left to the pharmaceutical companies, there would be no hope for a cure for many of the major diseases in the world today," he says firmly. "They look for a big-time payoff within a few years."

The payoff he seeks may remain years away, but it's still closer than anyone could have imagined even two years ago. In Chamberlain's view, the progress he and his team have made can be largely attributed to the long-term perspective of the Muscular Dystrophy Association. Indeed, his admiration for the Association's modus operandi was one of the factors that lured the renowned molecular biologist into what has become his life's work. Once he became interested in muscle development in graduate school, he was surprised to discover that the Association was supporting such ground-level work.

(Above) **Chamberlain with graduate student Simone Abmayr in the lab.**

(From Left:) **Graduate students Dennis Hartigan-O'Connor, Susan Dombrowski, Scott Harper, and Laura Warner conferring with Chamberlain.**

"This was considered basic research in its purest form," he says, "so I was amazed to find out that it was heavily funded by the Muscular Dystrophy Association. The reason was that we knew almost nothing about the causes of the muscular dystrophies (there are more than 15 forms of the disease), so the organization felt it was important to learn as much as possible about normal muscle biology in the hope that it would lead to greater understanding of the muscular dystrophies. Knowing that they were supporting research that didn't have an obvious link to diseases piqued my interest. They're one of the few organizations in the world that has been willing to invest 20 or 30 years ahead of time to try to achieve a goal."

About a million people worldwide suffer from some form of muscular dystrophy; 20,000 of them are in North America, and two-thirds are children. The most common form of the disease is caused by mutations in a large, complex gene that normally produces dystrophin–a protein critical for maintenance of muscle tissue. Without dystrophin, children with muscular dystrophy gradually lose muscle tissue and eventually die by their mid-20s of heart or respiratory failure.

The next big step will be human clinical trials, expected to begin within the next year, of a viral vector, developed in Chamberlain's lab, that proved capable of long-term delivery of the dystrophin gene to the muscles of adult mice with Duchenne-like muscular dystrophy. Duchenne is the most common type of muscular dystrophy, and the hope is that whatever will remedy the Duchenne form will also be effective against most other forms of the disease.

"We have a vector with the potential to deliver a miniature factory capable of producing normal dystrophin, but which should not lead to self-destruction of the treated muscle," says Chamberlain. "By taking a cold virus known as adenovirus and removing all the viral genes, which was critical because they can trigger a person's natural immunity, we've been able to pack a normal dystrophin gene into the virus." ➤

Jeffrey Chamberlain is the recently appointed interim director of the U-M Health System's Center for Gene Therapy. The Center was created in 1997 to link basic science, clinical investigation and technology transfer at a time of extraordinary activity and progress in gene therapy and molecular medicine. The Center's original director, Gary Nabel, was recently appointed director of the new Vaccine Research Center at the National Institutes of Health in Bethesda, Maryland.

Morton and Henrietta Sellner

Sellners Endow Professorship in Department of Human Genetics

A reception in the late spring at the Ford Amphitheatre in University Hospital honored Morton and Henrietta Sellner of Coral Springs, Florida, for their gift of $1 million in the form of an irrevocable charitable remainder trust to benefit the Department of Human Genetics and to honor the work of George J. Brewer, M.D., professor of human genetics and a specialist in the research and treatment of Wilson's Disease.

Morton Sellner worked for many years as an insurance broker in New York City and served as an adviser to the New York State Insurance Commission. The Sellners' gift, with $750,000 in matching funds from the Medical School, will eventually establish the Morton S. and Henrietta K. Sellner Professorship in Human Genetics, and a $250,000 endowed research fund to accompany it.

H. Ascher Sellner, M.D., a gynecologist in private practice in Brookfield, Connecticut, who was in Ann Arbor with his parents for the annual meeting of the Wilson's Disease Association, of which he is president, with Dean Allen Lichter. Wilson's Disease is a rare, inherited disorder of copper metabolism in which copper accumulates slowly in the liver and is then released and taken up in other parts of the body.

But, he says, "the greatest challenge is that we must find ways to get these viruses to muscles throughout the human body. And we must show that these new viral vectors can be used safely, without toxicity or side effects. We also need to know as early as possible if there are serious drawbacks to the system we're developing. If it's not safe, it's not worth spending years to perfect. If it is safe, only then can one start to ask questions about efficacy."

There are, in fact, a whole host of questions to be asked. The relative youth of gene therapy means that its investigative protocols are often quite different from those for traditional drug therapy. "For example, we don't have a single drug that can be given in pill form to a patient and it will spread throughout the body," says Chamberlain. "We have a very complicated delivery system that's in the infancy of its development. Even after we find out if it's safe and showing promise for further development, we'll want to perfect the ability of the system to produce maximal levels of the therapeutic protein, and we'll need to modify the way the system is put together in order to maximize its ability to persist for very long periods of time in the human body."

The initial trials will "be addressing some of the early questions," he says. "We'll be testing our system by single-site injections in order to ask whether we are getting a safe uptake of the virus at the site of the injection and long-term retention in the muscle. But taking this to the next level and being able to deliver these type of viruses to all the muscles of the patient is an enormous challenge. It is going to extend many years beyond the initial trials."

"Today we know muscular dystrophy can be cured," he says with the determination of a man who knows his goal and intends to reach it. "It's only a question of when."

But, just like Jerry Lewis, who has been associated with the Tucson, Arizona-based Muscular Dystrophy Association, now in its 50th year, since its earliest days, Chamberlain has made a long-term commitment. So have his sponsors, the National Institutes of Health (slightly more than half his support comes from the NIH), the Muscular Dystrophy Association and private donors. "Today we know muscular dystrophy can be cured," he says with the determination of a man who knows his goal and intends to reach it. "It's only a question of when."

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