NATIONAL MULTIPLE SCLEROSIS SOCIETY

Greater Illinois Chapter
525 West Monroe St. • Suite 900
Chicago, IL 60661
1-800-344-4867

Chairman: Sean Gallagher
Regional Vice President: Maureen Reeder
Editor: Jeremy Barewin
Design: Chris Collins

FEATURE STORY

DR. BARRY ARNASON REFLECTS ON HIS LIFE'S WORK IN MULTIPLE SCLEROSIS

JOHN DYSTEL PRIZE FOR MS RESEARCH RECIPIENT IS KEYNOTE SPEAKER AT 2014 RESEARCH SYMPOSIUM

BY TAREK WILEY

Piles of neatly stacked papers covered the desk and shelves of the office starting at the door and wrapping around the entirety of the room. Thick books filled the spaces between, and a microscope could be seen peeking out from behind a stack in the far corner. Looking around the office, it was hard not to be in awe of the sheer accumulation of knowledge blanketing every inch of space. Each paper contained a small piece of several decades of important MS research, arranged into piles that only the office's occupant, Dr. Barry Arnason, could truly discern.

He leaned back in his chair, staring at the wall and fiddling with the bridge of his glasses as he paused for a moment to consider his response. After a few seconds he smiled and said, "That's a good question."

He had been asked about what drew him to multiple sclerosis research, and having begun his work in 1959 as the National MS Society's first fellow, a momentary pause to reflect on a lifetime of work was understandable.

His road to MS research began with an interest in overall neurology during his medical residency at the Massachusetts General Hospital in Boston. Four months in, Arnason attended a lecture on lymphocytes — small white blood cells that direct

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Massachusetts General Hospital, Neurology, 1966.
Dr. Arnason is located front row, 2nd from left.

the body's immune system response — given by a man named Dr. Byron Walksman. At the time, Arnason knew nothing about lymphocytes, but after hearing the lecture, he decided it was a subject he wanted to explore.

"I went up to [Walksman] and said, 'I'd like to take some time off my residency and work with you,'" said Arnason. "It sort of took off from there."

Using an antibody to lymphocytes developed by Walksman, they discovered that lymphocytes were somehow involved in causing damage in a disease called Experimental Autoimmune Encephalomyelitis (EAE), which was being used as a model for MS. In an effort to learn more about lymphocyte function, they removed the thymus gland — a small organ that develops lymphocytes — from newborn rats, finding that as the animals grew up without it, they had no small lymphocytes and did not develop EAE.

After further research, it became clear that the thymus lymphocytes, which came to be known as T-cells, were implicated in MS itself. That discovery led to the development of drugs that affect T-cell function to help control or modify the immune system response in people with relapsing-remitting MS.

Arnason was also interested in the immune system cells responsible for triggering MS attacks in people with relapsing-remitting MS. It was clear at the time that there were cells within the immune system that generated an immune response, essentially turning on the disease, but Arnason was more interested in suppressor cells, the immune system cells that turn the disease off.

"We first started looking at them in the 1970s, and we found that they had a surface marker that we could identify them by," said Arnason. "They fell out of favor among immunologists who decreed that suppressor cells didn't exist, so it was impossible to get funding to pursue that line of research for over a decade. We sort of snuck some experiments in periodically over that period of time, but I'm happy to say that the role of suppressor cells in MS has once again become accepted."

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Looking back at what drew him to MS research, Arnason realized that he had been swayed by the work of Walksman because of another experience at the beginning of his medical education. Prior to his residency, while studying medicine at the University of Manitoba in Winnipeg, Canada, Arnason watched as a polio epidemic swept through the town. As people died all around him from the virus, he wondered why some became infected and others did not, unaware that the thought would help shape the course of his career.

"The polio vaccine was available the year after the epidemic that I was involved in," said Arnason. "That, I think, also influenced me in terms of a career choice … the thought that such things could be cured or prevented."

He hopes the same can be done for MS.

"Everyone always talks about a cure, but a cure is something you do after a disease develops," said Arnason. He believes that there may be another way to end MS if a cure can't be found.

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In other words, if MS can't be cured, perhaps it can be prevented.

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>
> Dr. Barry Arnason

According to Arnason, most researchers agree that MS is set in motion by a viral infection. If researchers could pinpoint that virus and develop a vaccine, MS would not develop later in life.

"At the moment, the lead candidate is the virus that causes infectious mononucleosis," said Arnason.

Infectious mononucleosis — sometimes referred to as the kissing disease because of its oral transmission — is caused by the Epstein-Barr virus, which infects a large majority of the world's population, though not everyone develops the symptoms. The rate of infectious mononucleosis in MS patients is higher than that of the general population, and there is a correlation between hygiene and MS development, which shows that late exposure to infectious mono due to better hygiene may increase MS rates, giving researchers reason to believe that the virus may somehow set the stage for subsequent MS development.

"We don't have a vaccine for infectious mononucleosis," said Arnason. "Maybe if we did and we vaccinated children, we could prevent MS and wipe it off the face of the earth."

Of course, that is no easy task.

"Infectious mono has been around for a long time, so it has been very clearly adapted,"

explained Arnason. "Developing a vaccine for it could be interesting, but it's trickier than that. It's not really a fatal illness, after all, and most people don't know they have it. It doesn't really have an immediate effect, and I think that's one of the reasons why there hasn't been much enthusiasm about developing a vaccine."

When discussing the landscape for the future of MS treatment and research, Arnason expressed a concern that getting funding for certain potentially important clinical trials would require a lot of convincing.

"Clinical trials are financed by pharmaceutical companies, and these companies are not interested in doing trials on drugs that were approved 15 or 20 years ago on which patent protection has expired, because the trials cost a lot of money," he explained. "I think there are any number of drugs out there that are already approved for treatment of various things — including various problems in the nervous system — that have never really been tested in people with progressive MS, but we've never been able to persuade any drug company to sponsor a trial."

Arnason believes that individually these drugs won't make a major difference, but collectively they could lead to substantial improvement, particularly for more advanced cases of MS.

"We have to do better in terms of progressive MS than we do at the present time," said Arnason. "We have to rethink what's going on and come at it from a totally different direction. Sometimes you have to nibble, but if you can get a 15–20 percent effect with five different drugs and combine them, you may end up with a 75 percent effect. That may be one approach."

He has already seen potential in some smaller scale studies. In one such study, Albuterol, which is used to treat asthma and other lung diseases, was given to MS patients who were receiving Copaxone, one of the drugs used to treat MS. The trial consisted of 50 patients: 25 to receive the drug and 25 in the placebo group. Of those in the placebo group, eight had attacks compared to only one in the Albuterol group.

"That was a small study, but a big difference," said Arnason. "That drug is very cheap and it could be interesting to do a clinical trial, but we have to figure out how to do that without the support of pharmaceutical companies and without it costing $50 million a pop. If we can figure out how to do that in collaborative ways by testing five different drugs against one another and keeping the readout simple, we could come at a lot of drugs that might have individually modest but collectively substantial effects on progressive MS."

Arnason has made amazing contributions to the field of MS research and to basic immunology, but his contributions go beyond his individual accomplishments. He is also responsible for mentoring many others who have gone on to make their own important discoveries in MS and other related diseases.

"Over the years I've been blessed with very good fellows and students, so I have had a hand in training a certain number of people who continue to be active in MS research," said Arnason. "In fact, interestingly, two of my fellows got the Dystel Prize ahead of me."

The Dystel Prize, a $15,000 award given jointly by the National MS Society and the American

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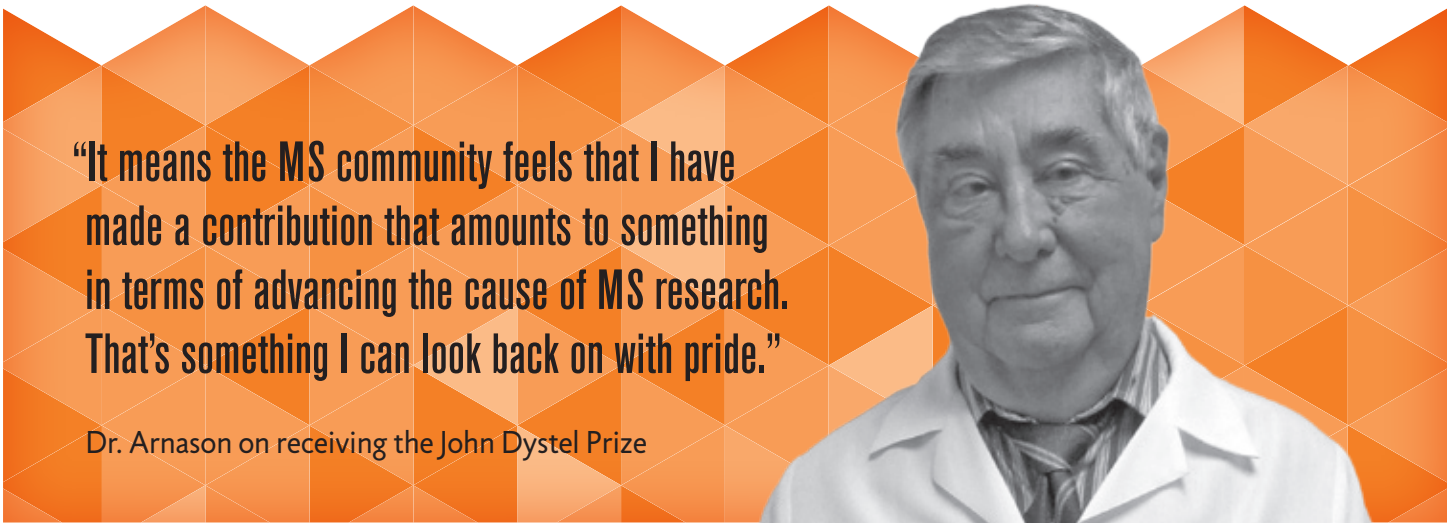

Academy of Neurology, recognizes outstanding contributions to research in the understanding, treatment or prevention of multiple sclerosis. The award is made possible through a contribution from the John Dystel Multiple Sclerosis Research Fund at the National MS Society, which was established by late Society National Board member Oscar Dystel and his late wife, Marion, in honor of their son, John Jay, an attorney whose promising career was cut short by progressive disability from MS.

This year's award was presented to Arnason in recognition of his fundamental contributions to the study of immune attacks on the brain and spinal cord in MS, which led to the development of immune-directed MS therapies.

"It means the MS community feels that I have made a contribution that amounts to something in terms of advancing the cause of MS research," said Arnason of receiving the honor. "That's something I can look back on with pride."

His previous fellows Drs. Jack Antel and Howard Weiner received the prize in 2005 and 2007.

Though he has already done so much to advance MS research, Arnason isn't ready to stop. In addition to his continued work with suppressor cells, he is currently studying the effect of high-dose steroids on long-term disease progression.

"It's standard practice to treat attacks of MS with high-dose steroids, and there is absolutely no question that when you give them high-dose steroids, the symptoms improve more quickly than they would without them," said Arnason. "At the same time, if you compare patients who have been treated with steroids to those who haven't and look at them 10–15 years later, the amount of disability between the two is exactly the same."

He wanted to discover why this mismatch exists and how we can improve steroid effectiveness in the long-term, and he did. Through his research, he discovered a population of T-cells that are resistant to steroids.

"It looks as if the reason is because they have a transporter that pumps the steroid out, so it goes in and gets kicked out," Arnason explained. "If we can succeed in showing that we can block that and make those cells sensitive to steroids, then maybe we'll have a better effect on the long-term."

Arnason has a great deal of hope about the future of MS research, and he believes that his patients do as well.

"They are more optimistic about their futures with MS now than they were when there were no treatments available," said Arnason. "The attitude has shifted rather dramatically, and there's no question in my mind that giving vigorous treatment early has a substantial effect on lessening the severity of MS in the longer term. Almost all of us now who deal with MS patients believe that they should be started on one of the immunomonitory drugs as soon as they are sure of the diagnosis — none of this waiting to see if you'll have multiple attacks or not."

Still, with all the progress made in the treatment of MS, a gap still exists, and Arnason hopes it can be filled.

"We did not foresee at all that drugs that would work in relapsing remitting MS would not work in progressive MS; we thought they were two variations of a single theme, but they aren't," said Arnason. "That begs the question: How do you deal with someone who already has MS and some disability and has developed the slowly worsening form of the disease?

"And there, it seems to me, we have to sort of do better … we have to do better." ■

Dr. Arnason will be the keynote speaker at this year's Annual Research Symposium, taking place Saturday, Oct. 18, in Rosemont, Illinois. To learn more about the event or to register online, visit **MSillinois.org.** Registeration is nearing capacity. If full, call **1.800.344.4867** to get on the waiting list.