

ALS Research: One Physician's Viewpoint

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I am often asked by our patients and their families about research on ALS. Stem cell research is in the headlines, and barely a day goes by that I am not asked about the potential for treating ALS with stem cells. It sounds so promising. For example, researchers at Johns Hopkins University recently used human stem cells to partly reverse the course of an ALS-like disease in mice. I sincerely believe that many patients with ALS would sign up for stem cell trials today if they were given the opportunity, even if the chance for success was low and the probability of side effects high. However, when I talk with scientists about ALS research, it becomes clear that stem cells may or may not be the answer to treating ALS. For starters, mice are not humans, and the ALS-like disease which was treated at Hopkins is not identical to human ALS. For treating human disease, many questions remain unanswered: Where do we inject the stem cells (into the brain? the spinal cord)? Once injected, how do we get them to go to the specific regions where they are needed? If they migrate where needed, can we get them to develop into motor neurons in humans? If they develop into motor neurons, and if there is some type of toxic factor in patients with ALS which destroys motor neurons, might those same toxic factors destroy the newly-developed motor neurons which we have just given the patient? I certainly don't want to be a pessimist with regard to stem cell research. I would be delighted if stem cells are the answer to curing ALS and closing our ALS clinic, and I am truly an optimist about the ability of research to result in effective treatments for ALS, but I believe that despite all their promise, stem cells represent only one of many lines of research that should be pursued.

There is a great deal of other research being conducted on ALS which receives little fanfare. Here are a few recent examples: 1) Vascular endothelial growth factor (VEGF) may play a role in causing ALS; 2) The SOD1 gene mutation, known to be present in about 1-2% of all cases of ALS, does not produce ALS when it is present only in motor neurons, but absent in other cells; 3) Abnormalities of SMN2, a gene involved in the motor neuron disease spinal muscular atrophy (SMA), might be involved in causing ALS. As your eyes glaze over, I am sure that you share with me the view that such research does not have the immediate appeal to the emotions of stem-cell research. After all, these research studies do not point to an obvious cure, nor are they easy to understand for most individuals without a scientific background and

education. Despite this, I believe that these studies, and dozens of other “invisible” ones like these, will ultimately be the key to understanding and treating ALS. When a disease is as complex and resistant to treatment as ALS, many different avenues of research must be pursued in an attempt to develop a better understanding of the disease process and identify possible treatments.

Most likely ALS will be found to have more than one cause, and although the end result in all patients is a loss of motor neurons, there are likely to be a number of different mechanisms by which this occurs. It is just illogical for me to think that one single cause and one single process can cause a disease which presents in so many different ways and progresses at such varying speeds among affected individuals. I believe that years from now the disease we call “ALS” will be found to be a family of diseases with more than one cause, and thus more than one treatment. This would be similar to what has occurred in other fields. For example, the disease we call “limb-girdle muscular dystrophy” is now known to be a family of diseases, with many different genetic abnormalities as causes. While I would be delighted to open the newspaper one day and read that ALS had been cured, I believe it is more likely that treatments for ALS will come in a series of steps, increasingly effective over time, similar to the way treatments have come about for cancer and AIDS. I anticipate that a number of years from now, a physician who treats ALS will be able to offer an ALS patient a treatment and tell him or her that this treatment offers 50% (or 80% or 90%) chance of remission, based on the cause of their disease and the results of various studies. Only by pursuing multiple lines of research through multiple investigators will we arrive at an understanding of the causes of ALS, and thus identify possible treatments.

This is why I have committed our ALS program to developing a research arm to complement the clinical services we offer. Dr. Philip Boyer in the Department of Pathology, Dr. James Connor in the Department of Neurosciences & Anatomy, and I have collaborated to begin a Motor Neuron Disease Research Center at Hershey Medical Center. This will enable us to perform basic laboratory research on ALS. It also permits us to offer the opportunity to our patients for tissue donation of brain, spinal cord, nerve, and muscle after death for research purposes. We are working toward obtaining additional funding for this program, and I anticipate that it will expand and that we will become ever more active in seeking a better understanding of mechanisms of ALS, with the eventual goal of effective treatment.