Chapter One: Introduction to Clinical Trials

George Garmany, MD: When companies develop medications, drugs for treatment, they need to do scientific tests to show that the medicine does what it’s supposed to do and does not have unacceptable side effects. They do this through a multiple-tiered system called clinical trials.

Paul O’Connor, MD: It’s not primarily work in a lab or working with a test tube; it’s a study with real people using agents and looking at whether or not they can be helpful.

P.K. Coyle, MD: There are specified-- pre-specified outcomes, and obviously there are different stages to clinical trials depending on the questions being answered. But that’s how actually we develop new therapies for diseases.

Paul O’Connor, MD: What we’re looking for in these newer treatments is greater efficacy, drugs that reduce relapses much better than what we currently have.

P.K. Coyle, MD: When you talk about a clinical trial and the inclusion/exclusion criteria you use-- typically you want it pristine pure, so it’s not real-life to a certain extent. You want your optimized patient who doesn’t have any comorbidity whatsoever because you don’t want the comorbidity screwing up your results. So people that have significant hypertension, diabetes, they’re going to be excluded from clinical trials.
Ruth Mahnken, RN: Some of the inclusion criteria is the type of MS you have, how long you’ve had the disease, your age.

George Garmany, MD: A common consideration, especially among young women, is pregnancy. If a young woman wishes to start a family, she’s probably not right for a trial.

Tammy Skaramagas, CCRP: Most people that are interested in the clinical trials, they definitely--the reason they’re interested is because they want to participate.

Peg Sharp: Oftentimes a patient that does not qualify for one study may indeed qualify for something else.

Elizabeth Sarbutt: When I come across a patient who may not be eligible for a certain trial that they’ve expressed interest in, I always take down their name and number, and I have a separate file just for patients who are interested in research.

P.K. Coyle, MD: There may be strict criteria that will limit who will have access to trials. It won’t seem to make any sense, but obviously once the final results are in and the drug is established, the expectation would be that the use is going to be much, much broader.

John Corboy, MD: It’s a complicated process, but it really boils down to a bunch of very simple procedures. Because these are considered scientific research protocols, it’s only appropriate that patients understand everything that we know about that could happen, as well as maybe the things we don’t know about that could happen, so they can give meaningful and informed consent.

Ruth Mahnken, RN: It depends on the protocol, but there is a lengthy list of requirements for what they call a screening visit. They’re seen by the physician, they usually get a physical, they get a neurological exam, they sometimes have to have an MRI, an EKG, and sometimes there are other tests depending on the protocol.

John Corboy, MD: Assuming that someone cleared through all the screening procedures, they would then have what’s referred to as a randomization visit. At the randomization visit they would be placed into one of several different categories to receive drug A, B, C, or potentially placebo and maybe different
doses of the different drugs. And typically for a blinded study they would not know what they would be receiving, although there are studies which are not randomized.

Typical outcome measures that we use during many of our MS clinical research trials would include the so-called EDSS, or Extended Disability Status Scale, which is an amplified neurological exam.

In addition, we also do something called an MSFC, or Multiple Sclerosis Functional Composite, and that is multiple, different tests including a 25-foot timed walk. It’s also a nine-hole pegboard test, which is moving pegs from one board to another and using both hands. And then also something called a PASAT, or a Paced Auditory Serial Addition Test, in which case you serially add numbers together and you answer questions about the numbers.

**Ruth Mahnken, RN:** This is monitored throughout the study. It’s something that the study looks at to see if there’s any effect on what these scores are and the timing of them, because some people do deteriorate during studies or they get better. So they track that trend.

**Chapter Two: Challenges**

**Patricia O’Looney, PhD:** The challenge in multiple sclerosis is that it’s a heterogeneous population, meaning that the characteristics of MS is unpredictable and highly variable, meaning that no two people with MS are exactly alike.

**Jeffrey Cohen, MD:** It appears that the people that are entering clinical trials are changing over the years. The number of relapses that they experience seems to be decreasing, and as a result it’s much harder to measure a benefit.

**P.K. Coyle, MD:** If you are encouraged to put everybody on treatment, you don’t have a large untreated population to enter trials.

**John Corboy, MD:** Multiple sclerosis is a condition that can change either rapidly or slowly, but oftentimes what we can measure takes quite a long time to measure differences between groups, either placebo versus treatment or two different treatments.
Paul O’Connor, MD: On top of that, clinical trials, because they are so lengthy and involve so many patients, they do involve a great deal of expense, and that expense has to be paid by someone. That someone is usually the pharmaceutical drug manufacturer.

P.K. Coyle, MD: I think we’re going to have to be much more clever about how we approach clinical trials in MS in the future.

Chapter Three: Different Roles in Clinical Trials

John Corboy, MD: There are many different groups involved with clinical trials, beginning with the sponsor. And it could be a governmental agency; it could be a private industry such as a pharmaceutical company or device company.

P.K. Coyle, MD: When we talk about the pieces of the puzzle and putting together clinical trials, certainly the patients who participate, the physicians, the neurologists who take part as evaluating and treating physicians, etc.

The MRI technicians, because that’s a major component of MS clinical trials, the human IRB personnel that help to get the trial put in place and go through the appropriate approvals and have to review it and make sure that no patients are being harmed ethically.

The study coordinators, often a nurse.

Tammy Skaramagas, CCRP: The nurse will do the majority of the visit. That entails anything that deals with their medical symptoms, their management of it, and then of course they relay it over to the physician.

Ruth Mahnken, RN: The role of the study coordinator in clinical trials is to make sure that all the aspects of the protocol are followed according to the rules.

And some of the rules of the study have to do with timeframes, when the patient’s screened. Then they tell us how many days it is before they could get their drug, how many days it is before they need an MRI, when they get their neurological exam.
We also make sure that the patient understands they can stop the trial at any time, go back on therapy, still be taken care of in the same setting and by the same doctors that they went to, whether they participate in the trial or not.

We like to see from 10 years ago how patients are long-term doing so much better. The face of MS is completely different in the last 10 years that I’ve seen.

Chapter Four: MS Research Goals and Progress

Patricia O’Looney, PhD: Well this has really been an incredible time for people with MS, for those of us who want to find a cure for the disease. So for the past 15 years, we now have six FDA approved therapies for relapsing forms of MS, and probably as many as 130, 150 different clinical trials that are now underway in development.

George Garmany, MD: The question of a cure for multiple sclerosis is, like so many other things, a complicated issue. Cure means different things to different people.

Paul O’Connor, MD: First, we’d like drugs that would stop the disease from progressing or worsening. So that would be the first step. A second step would be drugs to reverse the ongoing neurologic disability that patients have because of MS, and the third aim we have is actually the prevention of the disease.

George Garmany, MD: I think that in time we will achieve some of these things, but I don’t know when. I only know that by doing the appropriate science, we will speed that day.

Jon M. Temme: Here we often think that the solution to the puzzle of MS is going to come through the discovery of piece after piece that gives us more insight into what’s going on in this disease.

Jeffrey Cohen, MD: Ultimately the only way to determine whether a treatment works and is safe is through a valid clinical trial. But in addition, even if the drug turns out not to work, we frequently learn more about the disease from the trial. We learn how the disease behaves, we develop new techniques for monitoring the disease, and we also may learn something about the mechanism of the disease.
Oftentimes a treatment not working tells us that we were on the wrong track and we have to come at the disease from a different angle.

**Paul O’Connor, MD:** And this information adds to the body of knowledge in terms of how MS evolves over time. Particularly in a study where patients might be on an inactive agent such as a placebo, we gain more information about what we call the natural history of the disease.

**P.K. Coyle, MD:** I think clinical trials should really be viewed as goldmines, and they should be mined for all the possible data that we can glean from them.