Research: New Horizons at Eisenhower

Philip Shaver, MD

Currently, there is a clear trend toward community-based research. In 1991, 80 percent of industry funds for clinical research were spent in academic settings. By 1998, that number had dropped to only 40 percent. Much of the shift in spending is due to the growth of networks, contractor research organizations, and site management, all of which have enabled community organizations to join together in multi-center trials. Recently, Healthy Living magazine gathered Eisenhower Medical Center Board Certified physicians Lester Padilla, MD, Cardiology and Co-Chairman of Eisenhower's Institutional Review Board (IRB); Lawrence Cone, MD, Infectious Disease and a senior physician with decades of research experience; and Andrew Rubin, MD, Cardiology/Electrophysiology and director of research at Desert Cardiology Center, to discuss medical research at Eisenhower. Philip Shaver, MD, Cardiology, moderated the session.

DR. SHAVER: There is an obvious difference between research, including basic and clinical research, and regular medical care — particularly where randomized control trials are concerned. In treating patients one-on-one, the aim is to make them better. But trials are scientific tools designed to evaluate a treatment's potential for the future. Lester, as Co- Chairman of the Institutional Review Board (IRB) at Eisenhower, can you first explain to us the role of the IRB?

DR. PADILLA: An IRB is a committee of physicians, statisticians, researchers, community advocates and others whose aim is to ensure that a clinical trial is ethical and that the rights of study participants are protected. All clinical trials in the United States must be approved by an IRB before they begin.

DR. SHAVER: Would you say that the diversity of individuals who make up an IRB has a lot to do with its effectiveness in overseeing protocols?

DR. PADILLA: Absolutely. Our IRB includes several physicians, including some with a strong interest in research. But non-physicians, scientifically trained members, and lay people from the community also are included. Our IRB includes clergy, a local banker, and a realtor. This strong mix of individuals is key to ensuring that the IRB functions to minimize the risk of a study while maximizing its benefits.

DR. SHAVER: What is your process for assessing the risk-benefit ratio to patients when someone brings you a protocol?

DR. PADILLA: The IRB serves an important role in assuring, under federal law, that research adheres to certain guidelines that were essentially laid out back in 1974 with the Belmont Report. It is part of the education of IRB members and all active researchers to review the history of human research.

DR. SHAVER: Clearly, patients must realize that participating in a research study may not help them personally. But doctors should not expose patients to risks if there is no prospect of possible benefits. The researcher has an ethical responsibility to act in the best interest of subjects. When someone trusts you, you really must respect that.

assets/news/story/cfhlimages/200706/padilla.jpg DR. RUBIN: Yes. And one thing we ought to make clear for patients suffering from cancer and other serious illnesses: participating in a study does not mean you're going to be deprived of an effective therapy.

DR. CONE: You receive the current standard of care.

DR. SHAVER: For instance, someone with cancer in a clinical trial will not receive a placebo or sugar pill. The patient will get what is currently the standard of medical practice or the new research drug protocol.

DR. RUBIN: Placebos are only used when there's no established gold standard for therapy. If there is a proven available therapy, a new drug will not be compared to a placebo.

DR. SHAVER: We must always keep in mind that the goal of research is to increase knowledge of human ailments and better understand medical problems and disease to improve future patient care. Patients who volunteer for research should do this based upon their needs and values, not based upon a desire to please their doctor.

DR. RUBIN: In my mind, the patients should be congratulated for the successes we have seen. One great example of the benefits of research occurred 18 years ago with studies involving the use of beta blockers to treat heart failure. Previously, we all thought beta blockers caused heart failure. But a researcher theorized that beta blockers might prove beneficial to these patients. Studies over 15 years showed that beta blockers are vitally important in prolonging the survival of congestive heart failure patients.

assets/news/story/cfhlimages/200706/cone.jpg DR. SHAVER: Here's another example. An estimated 70,000 Americans received Laetrile, believing it would cure cancer, through the 1970s. Eventually, around 1980, the National Institutes of Health (NIH) did a trial that showed no benefit to it at all. Until that, I don't think you could talk people out of using this medication. Larry, would you like to comment on the difference between a patient undergoing regular medical care and one who's undergoing research, where he may or may not get the medication he thinks he is getting?

DR. CONE: New drugs come out and it's difficult to know how effective they are compared to a traditional regime. For example, traditional treatment of, say, early lung cancer, would probably be chemotherapy combined with radiation therapy. Recently it's been shown that one can have "targeted" therapy, using medication to shut off the blood supply that feeds a tumor. So, you augment the traditional chemotherapy with the experimental one. In this case, the study proved that the concept was viable, and indeed, people who received the traditional chemotherapy plus the substance called bevacizumab or Avastin® survived longer. Now, you can't initially give everybody the bevacizumab, but once the study has matured, it's certainly available to those who need it. In the area of oncology, these controlled studies have worked out very well to improve the survival rate. "Eisenhower was identified as a candidate to participate with university centers across the country and Canada. Out of the 200 centers, Eisenhower was seventh in the number of patients enrolled."

DR. SHAVER: Andy, I know that you have been involved in trials, especially the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) trial — I believe you were a major contributor.

DR. RUBIN: We had previously collaborated with Loma Linda for a different NIH study, so when the AFFIRM trial on atrial fibrillation began, Eisenhower was identified as a candidate to participate with university centers across the country and Canada. Out of the 200 centers, Eisenhower was seventh in the number of patients enrolled. It allowed Eisenhower to be recognized on a much more widespread basis for cardiac research, and we are now involved in 14 active cardiac research studies.

DR. SHAVER: I think you made an important point that they found out Eisenhower had integrity and that opened the door to other trials. Larry, what do you see in the future for research at Eisenhower?

DR. CONE: I believe Eisenhower will continue to do good clinical research, particularly in the areas of cardiology, medical oncology and infectious diseases. We are evaluating many drugs and many diseases. I would hope to expand that effort —we have more than 400 board certified physicians here at Eisenhower. "I think the community here in the Coachella Valley is fortunate to have a progressive medical center and administration that supports research."

DR. SHAVER: In my opinion, incorporating hospitals such as ours into such research likely increases the pool of research subjects. Additionally, large medical centers provide community-based physicians and their patients with easy access to cutting-edge treatments. Finally, they involve office-based clinicians in research previously limited to academia, government and industry.

DR. RUBIN: Indeed. I think the community here in the Coachella Valley is fortunate to have a progressive medical center and administration that supports research. Without that support, patients would not have the opportunity to get cutting edge oncological and cardiac therapies that are otherwise available only at university hospitals. I think it's a great benefit for the patient directly, whether it's for a device or a drug.

Resources: www.clinicaltrial.gov and www.nlm.nih.gov/medlineplus/clinicaltrials.html

THE PHASES OF MEDICAL RESEARCH STUDIES

Medical research progresses in different phases, with the first task being to rule out harmful side effects.

Phase I is conducted on healthy volunteers to examine how a drug should be administered and to determine the appropriate dosage of the drug and how well a drug is absorbed and handled by the body's major organs.

A Phase II trial involves a very small group of patients who suffer from the disease in question. It is still focused on the safety of the drug, but researchers also look for indications of the drug's efficacy.

If the drug looks promising, the next step is to move on to the much broader (and expensive) Phase III, which involves randomized, controlled placebo double blind studies matching the drug against the existing "gold standard" drug for a particular disorder.

Phase IV occurs after the drug is on the market to keep the new drug under surveillance for long-term harmful side effects, which if manifested, means the drug will be removed from the market. Photos: Andreas Koessler

http://www.clinicaltrial.gov and www.nlm.nih.gov/medlineplus/clinicaltrials.html