

Good Practices in Clinical Research
Lecture 19
Dr. Robert Rubin

Clinical Research in the 21st Century: Areas for Future Research

I have the pleasure now of speculating on what the future in the 21st century is going to bring us in terms of clinical research. The way I look at this, there is a great paradox. On the one hand, there is unparalleled opportunity in clinical research, but I also think there is unprecedented challenge. Let us look at these both in some detail.

Why do I say there are unparalleled opportunities in the 21st century? The first factor that we can identify is the globalization of clinical research. There are now international trials for international approvals of drugs, vaccines, and technologies. There is a continuing search all over the world for what I call “leveraged subject populations” for accomplishing the necessary studies. What I mean by this is that a need exists for populations with a high incidence of a particular condition or genetic background or environmental conditions. Because of this, there is a recognized need and a search to do things internationally. The third is the work that is being done in international harmonization that makes it possible for research done all over the world to have merit and meaning no matter where we are on this planet.

The second area where that is very important in this regard is that suddenly we have an unprecedented number of new chemical entities that are products of the molecular biology and biotechnology revolution. These are products from natural product screening, combinatorial chemistry, rational drug design and from high through-put screening using novel molecular targets. Probably most important in the next 25 years is the information and the molecules that will come from our knowledge of molecular genetics: from the human genome project, from studies of the yeast genome, the *E. coli* genome, the *C. elegans* genome, from studies of transgenic animals and the like. Suddenly, we are getting to the basis of human disease and we can start designing antidotes for human disease.

Another area of great promise is new drug delivery systems. We can have the best molecule in the world but we have to get it where the trouble spot is and do it in a way that will optimize the efficacy of this molecule.

What is being done is very exciting in this area: implantable, programmable delivery pumps, sustained drug-releasing polymers, and in the future we will even have microrobots that can sense, identify disease and deliver local therapies, thus maximizing clinical benefit and decreasing toxicity and systemic side effects.

The other area that I think we can comment on is new measurement technologies. These will be utilized to assess the subject's pathophysiology, the pharmacokinetics of the drug, and the impact in terms of the pharmacodynamics of the drug on the individual. Remember, pharmacokinetics is what the body does to a drug; pharmacodynamics is what the drug does to the body.

Among these techniques for measurement, the area that is progressing most rapidly right now is imaging technologies. Positron emission tomography and other nuclear medicine techniques, magnetic resonance imaging, vascular and intravascular ultrasound allow us to define processes, receptor ligand interactions, and the ability to deliver drugs to a particular site. Remember that virtually all therapeutics are based on a biochemical hypothesis; that is, that if we inhibit something or bind to something, we have the chance of effecting clinical benefit. Now we have the ability to assess whether we are achieving our biochemical objective, thus, optimizing the chance of seeing therapeutic benefit. Other areas are gene expression chips so that we can see what pathways are being expressed in a patient and, therefore, are amenable for clinical intervention. Finally, we are developing new biologic markers for endpoint measurements that will greatly facilitate the evaluation of a patient as well as the evaluation of a drug effect.

The net result of these unprecedented opportunities that are coming in the 21st century is the great potential for true disease-modifying therapy for conditions that were previously untreatable.