2005 ASHG PRESIDENTIAL ADDRESS
If Only We Spoke the Same Language—We Would Have So Much to Discuss*

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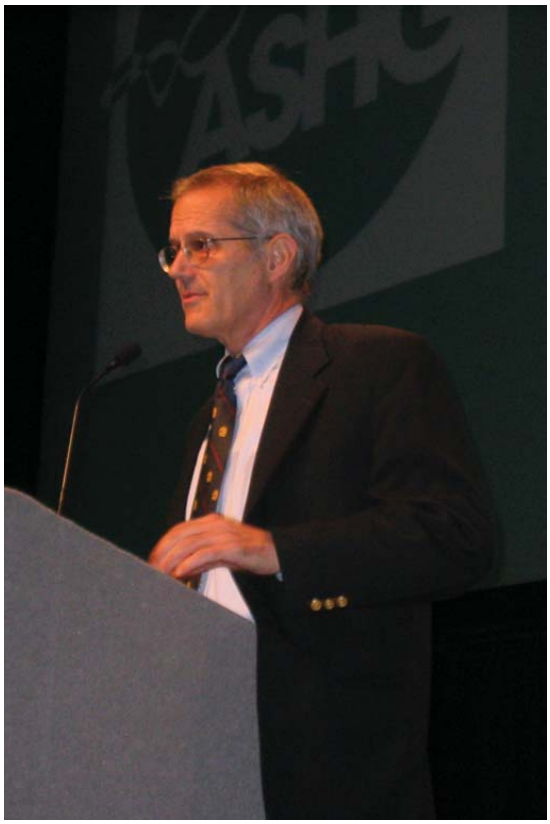

Peter H. Byers

Good afternoon. I am Peter Byers, president of The American Society of Human Genetics. Welcome to the 55th Annual Meeting of our Society. I extend a special welcome to those of you who have taken time away from rebuilding your lives, your homes, and your workplaces in New Orleans to join us at this wonderful meeting, even in the face of such adversity.

Next year, for those from New Orleans, the trip to the meeting will be a much shorter one. The directors of the Society conferred with representatives from the Convention Bureau, and we are planning to have the meeting in New Orleans in October. It is our conviction that this is the right thing to do to help rebuild the city. All elements of the meeting areas will be fully in operation by the end of March 2006. The current planned date for the ASHG meeting is October 10–14, 2006, but it may be moved back 2 weeks to the 24th–28th to avoid overlap with the Neurosciences meeting, which has moved to Atlanta for the 14th–18th period. We will have an additional discussion at the business meeting that begins at 11:30 AM on Friday, to provide you with details.

I would like to start with a story. I was in China recently, with a dozen members of the Society, at the Watson Center for Genomic Studies in Hangzhou. We taught in a course on Genetics and Genomics in Medicine. Our last official activity was an open genetics clinic on Saturday morning, which, to raise interest, had been discussed the day before in the regional newspapers and television. We expected only a few visitors, but our five teams were overwhelmed by more than 50 patients. Marilyn Li from Tulane and I shared a clinic room. Our last patient was a 63-year-old man with mild hypertension, looking forward to a long life. After telling us about his conviction that beekeeping and flowers in the bedroom every day contributed to his and his wife's good health, he turned to me with a twinkle in his eye and said—through Marilyn—that he had enjoyed the visit and thought that, if only we spoke the same language, we would have so much to discuss. This simple statement mirrors our profession. If you look to your left and to your right, you will probably see people with whom you have never spoken and who are from a different part of our field. If only we spoke the same language.

Human genetics is a complex and diversified field. Clinicians, investigators who deal with human subjects (and who may themselves be clinicians), statistical geneticists, genetic epidemiologists, subjects, advocacy organizations, the families themselves, industry, research institutions, funding agencies, and others constitute our field. We all see the world of genetics differently—we

Received November 1, 2005; accepted for publication November 29, 2005; electronically published February 1, 2006.

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* Previously presented at the annual meeting of The American Society of Human Genetics, in Salt Lake City, on October 26, 2005.

Am. J. Hum. Genet. 2006;78:368–372. 0002-9297/2006/7803-0004$15.00

see different threats, we see different opportunities, and we speak of those in different languages.

I would like to take the new few minutes to talk about three areas in which we, as individuals and as a Society, can breach those language and conceptual barriers to make differences—first, ways to bolster education in science and genetics, from the primary level through doctoral and post-doctoral levels in medicine and other fields; second, the alleviation of the growing concerns with human research, access of subjects to programs and of investigators to subjects; and third, identification of means to assure that the commercialization of genetic testing does not fragment training and access to important clinical data.

Education in Science and Why

Our perception of the strength and success of human genetics as a discipline and of the contributions this discipline makes to better our understanding of us as peoples and to the betterment of our lot are not viewed by all through the warm lens that we use. To me, it is the failure of others to understand the thrill of the field and the promises that we think it brings that is so puzzling. Genetics seems, on its face, quite simple. Think about the alphabet of genetics—the four letters A, C, G, and T. Innocuous. How many words can you spell with these three consonants and one vowel? Not SEX, not GOD, not RELIGION, not POLITICS—all hot-button topics—not even WEATHER. And yet, genetics brings fear of discrimination based on genetic characteristics, is a threat because of the relationship of genetics to evolution, and these fears stand in the way of unraveling the role of genetics in medicine and the promises that genetics brings.

We need to be better at explaining genetics and its value to our public. We have a few great communicators in our midst, but most of us are uneasy in public, have not quite figured out how to get our points across, and shrink from the opportunities when they arise. We are not good advocates and don't speak the public language well. Perhaps we can start in schools.

As a Society, we have discussed ways to become engaged in science and genetics education for years, as an organization and through our members. We have established a mentor network that allows teachers around the country to contact nearby geneticists who are willing to come to the classroom, to supervise students in the laboratory if they are far enough along, and to serve as resources for those teachers. Although wonderful in concept, the execution of this tool has not always been successful. Many of us, unless we have struggled with our children's biology and chemistry textbooks in high school or helped with the ubiquitous terrarium designs in middle school, have little concept of what a student at any given level, from first grade through high school, knows about genetics, what the teaching expectations are for that grade level, or how to engage students.

Little wonder that we are, no matter our academic station, seldom called to help and, if called, rarely recalled.

We are now in the midst of a project that has the potential to change the orientation of our members to school science, a project Bob Nussbaum mentioned last year. In cooperation with our sister group, the Genetics Society of America, we (the "we" in this case being Kenna Shaw, who is not here today because she has just delivered the full sequence of her own first human genome project and is trying to figure out her son's instruction manual) have assembled the learning objectives, for all grades (1–12) in all 50 states, for biology as related to genetics. This is a phenomenal task that is nearing completion and will soon be accessible at our Society Web site so that, when you are invited to help, you can identify the curricular needs with the teacher and contribute your own expertise to meeting those learning objectives. This will remove some of the anxiety about what to talk about and how it relates to the curriculum the teacher is required to get through.

Susanne Haga, co-chair of our Information and Education Committee (who hosted a magnificent program for high school students from the region at this year's meeting), and Joe McInerney, our Excellence in Education awardee this year, have pointed out that learning in genetics need not be limited to our traditional biology courses. They do see the vertical nature of teaching with progressive involvement in biology and evolution during the transition from preschool or elementary school to high school, but also the horizontal scope of genetics as examples in mathematics classes (recurrence risks, for example), in history classes (the distribution of populations), in psychology and sociology classes (genetics and behavior), to name only a few. For us as professionals, genetics is a pervasive explanatory tool for the phenomena of the biological and social worlds around us. Teaching in schools provides opportunities to introduce these ideas to teachers and students and to transmit to them the wonder that we all discovered with mentors famous and known to us all—Barton Childs, Arno Motulsky, Victor McKusick, Charles Scriver, Jim Neel, James Crow (and you can name your own)—or those private mentors—like Lester Newman at Portland State College in Oregon, with whom I clambered up the streams on Mt. Hood looking for fly larvae from which to make chromosome preps back in the lab—and whose guiding lights still lead us.

Education in science has always been important to us as citizens, but, with rapid technological changes, the evolution in the economies of developed countries, and a rapidly changing social world, it is more vital than ever. Science teachers are a commodity in short supply in schools, and, as a consequence, the sciences as dis-

ciplines appear to suffer. All of you who have children know that they are natural scientists—until they go to school. They have "Insatiable Curiosity" and want and develop explanations for everything around them. They are busy testing hypotheses about the world, never stopping to think that they are scientists. Until they go to school. Once in school, "science" becomes a "body of knowledge" encapsulated in the courses on biology, earth sciences, chemistry, and physics, and students lose interest.

Mort Levine, an anthropologist who taught at Reed College when I was there, said that many students come to college thinking they will major in science because it is a body of known materials that can be captured. They change disciplines when they discover that science is devoted to asking questions about what is not known. Thus, the exodus into business, law, literature, and the humanities, where known rules explain behaviors (or so they think). For us, as scientists, as geneticists, it is the ability to ask questions about what we don't know and be thrilled by the answers because we have crossed a new boundary into what is now known. I remember the sheer joy I experienced when I looked at the electrophoresis gel of proteins from a patient with a severe form of osteogenesis imperfecta (OI) and saw that the overmodification of the proteins had to be explained by a single nucleotide substitution that changed a glycine in the triple helix. There were 338 glycines in the triple helical portion and 8 potential amino acid substitutions—think of the possibilities—no wonder the clinical features of OI are so heterogeneous. And there were two genes. It took another year or so before Dan Cohn showed this was the case, but, by then, we knew that OI was a protein-folding disease and that aberrant folding was probably the underlying basis of most genetic disease.

I remember our discovery—or recognition—that recurrence of lethal OI in a family was explained by parental mosaicism. We could see it from family structure—the parent that had affected children by two different mates. Once we had the right family—a mosaic father (found for us by Bruce Blumberg)—we could look in sperm and other tissues and confirm our idea and then recognized that we had a tool by which we could, perhaps, count the number of primordial germ cells allocated to the germ line. I am sure that every one of you in this audience has had that elation of discovery—of retrieving something from the unknown. That is what we want to teach our students about—how to find answers to questions in a way that brings that thrill.

That is the beauty of being in science.

I look forward to the day when a president of the U.S. is well enough educated in science and genetics, and curious enough, to recognize that "teach the controversy" has no meaning. We need to teach the language of science so that we can all speak it.

Our educational efforts should not stop with formal schooling. Because they control the purse strings, our legislators hold the future of science, of genetics, and of science education in their hands. For most of us, neither our education in science or medicine nor our inclinations move us to work with public officials. If we look at the likely effects of the flat or declining funding for the NIH and the NSF in this country, we can predict that some of the hardest hits will come to the institutions and faculty that are just starting up the research ladder. We need to educate our legislators, our school boards, and our teachers and staff about the value of science to our communities.

Invite your legislators, your public officials, or their staff to lunch, to the lab; show them what you do—or simply go visit them. In turn, learn their language and limitations and work with them to search for ways that science education, indeed education as a whole, remains a priority. When enough of us speak the same language or our abilities to translate have improved, we will, indeed, have more to discuss.

The best advocates for human genetics and for research and teaching have been the families that have harbored the genetic disorders we study. The families and organizations they spawned have led the search for research dollars, brought effective legislation to states and the federal government that could limit deleterious effects from genetic testing, and convinced a sometimes-skeptical public that genetic studies will be beneficial, not harmful. Their help in keeping access to identified disease-related genes open should neither be underestimated nor ignored. Instead, this represents a new partnership among scientists, clinicians, and families. It is our turn as professionals to take up the banners of advocacy at all levels. As a start, we can work for the passage of the Genetic Non-Discrimination Act in the House of Representatives, to reduce the anxiety about genetic testing in the clinical setting. It is part of our responsibility to use the newly minted coinage of the human genome for the benefit of all.

Many of the family advocacy groups have joined our Society, used our extended home to engage our professional members while at this meeting and to create dynamic working relationships that pressed critical research issues and solved clinical and social problems. This year, we have provided access to our entire meeting to advocacy groups that have never had the experience, and we are helping them through the maze of new information. I welcome them and hope they will enjoy the meeting.

We have worked to get our trainees involved with the family groups. To watch the relationships develop between the members of these lay organizations and the members of our Society, particularly the young students and fellows, is to see the wonder of the human spirit meeting the marvel of science and genetics in action. To

watch the black humor of science and medicine transformed by this relationship into the white heat of commitment and advocacy is to see everything we have hoped for in forming and continuing this Society. Here, we have seen the way to learn these different languages we speak.

Institutional Review Boards and Research in Human and Medical Genetics

In the practice of medicine, an overriding concept has been "above all, do no harm" (*primum non nocere*), attributed both to Hippocrates (*The Epidemics*: "…at least do no harm") and to Galen. This concept has been institutionalized in the framework of research that involves humans in the Nuremburg Code, the elements of the Belmont Report, and detailed in the U.S. codes that govern these activities and out of which institutional review boards (IRBs) have grown. Now, every institution that conducts federally funded research has panels that review applications to do research that involves human subjects. "Involves" may be a key component. The task set before these panels was to be sure that subjects were informed of the studies to be done, to exclude coercion as a reason for participation, and to assess the potential for harm to the subject.

The statements of principle set out in the Nuremburg Code and the Belmont Report are elegant in their simplicity and objectives. During the last few decades, we have seen the application of these principles engender increasingly complex formulas that have cast investigators, potential subjects, the IRBs, the institutions, advocacy groups, and funding agencies in potential, and sometimes real, adversarial relationships.

Federal regulations appropriately require that IRBs not be monolithic in makeup but broadly represent the interests of the society. From the perspective of the genetics community, the application process has become increasingly burdensome as "genetics" has been singled out for special treatment. The University of Washington Human Subjects Division Web site illustrates this point:

> In response to increasing national concern about genetic testing and other genetic studies, the University of Washington Human Subjects Committees are now examining all studies which involve genetics with increased scrutiny. While genetic studies often involve minimal physical risk, they do carry significant psychological and social risks. Genetic information carries with it risks to insurability, risks to family life (for example, in incidentally generated information about paternity), and risks to life plans (for example, from discovery of previously unknown but possibly stigmatizing conditions).

Thus, while we as geneticists have tried to eliminate the idea of "genetic exceptionalism," we now find the concept institutionalized without validating data. The ethicist, who used to be descriptive, has become prescriptive, viewing the situation from the bottom of the slippery slope.

As the need for large cohorts gathered from multiple sites increases, the problems of dealing with multiple and independent IRBs at many institutions has become an industry in itself. We find ourselves unable to speak the same language.

This is the time for the advocacy groups to step in, to work with investigators and IRB staffs and members, to clarify what, for them, are the real issues, and to craft novel and creative solutions to the impasses that we see and feel. The advocacy groups have been adept at learning the language of disparate groups and providing translation and guidance in other situations. Let's see if it works here. If it doesn't, we are in for a long haul.

Commercialization of Genetic Testing and Loss of Genotype Data and Training Sites

I would like to turn to one final topic—the effects of moving genetic testing out of the academic medical centers to commercial sites. There are three elements that concern me—the separation of genotype information now located in the testing sites from the phenotype data stored at disparate institutions, the loss of academic training sites for molecular geneticists, and the culling of the only financially stable component of medical genetics. These latter two have been a favorite issue of Aubrey Milunsky for years—ones he has articulated well.

While I think the technical quality of testing in most commercial sites is very good, the interpretation of the studies may leave something to be desired. But, more importantly, the clinical information collected is often limited and, because the expertise in the clinical conditions is separated from the testing, the opportunity to interpret the effects of the mutations—that is, to perform coherent genotype/phenotype analyses—is being lost. The solution to this problem is not clear. But efforts to follow best-practice recommendations in terms of licensing of use and a commitment from testing laboratories to maintain a continued relationship with test or gene originators, so that clinical data accumulation continues and genotype-phenotype relationships are determined, should all be pursued. Advocacy groups can and should intervene in the process because, in the long run, it is their members who have much to lose.

A Personal Statement

I have—and I think many, if not most, of you think you have—the best job in medicine. I am a clinician by training and an investigator by temperament. At any given moment, my job involves me with a patient; his or her family; the nucleotides gone astray that cause their dis-

orders; treatments at the gene or physiological level; a consideration of what we know, how we know it, and what we don't know; with the role of genetics in society; teaching students and fellows; and trying to understand how to integrate genetics as a medical discipline within our university structure. Mine is a job I have trouble imagining differently, one that fulfills most of the hopes and aspirations that I have, and one that occupies me throughout the day. I am never not a geneticist. This Society has made a home for me, and I am deeply grateful to it.

Our Society is robust today, with a strong financial position and an energetic role in science and social policy—something only imagined less than a decade ago. We have created a family of genetic organizations from our nest—The American Board of Medical Genetics, The American College of Medical Genetics, The American Society of Genetic Counselors, The American Board of Genetic Counseling, The Society for Gene Therapy, The Society for Metabolic Disorders, the Human Genome Organization, The Society for Human Variation, the International Societies of Human Genetics. Under our roof, many other organizations have developed, including some of the very strong advocacy groups—the National Organization of Rare Disorders, The Genetic Alliance—that flourished under our wings, if not always our guidance.

Last Remarks

As we begin our 56th year, we are like parents whose children are out of the house and launched in successful careers, perhaps writing books about genetics and society like my own son, Michael. We have immeasurable pride in their accomplishments, recognizing what little we have done besides providing the safe harbor for their development. We measure our strength by our offspring and the ability to produce them. As a Society, as our "children" have left home, it is not that we are once again enjoying sex with noise, but that we are looking to the appearance of a new generation of genetic organizations and relationships—the genetic grandchildren of the Society.

It is my profound hope that, as they arrive, we will have common tongues—the languages of science, of genetics, of humanity, and a shared vision and hope for the future—ones that we will share with our constituencies, our colleagues, and our advocates.