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*As a way to integrate the presentations at PHA's June scientific sessions with clinical practice, Guest Editor **Karen Fagan, MD**, convened a group of attendees to discuss their experience in Orlando. The discussants included **Todd Bull, MD**, Associate Professor, Medical Director, Anschutz Intensive Care Unit, University of Colorado, Aurora, Colorado;*

Anna Hemnes, MD, Assistant Director, Center for Adult Pulmonary Vascular Disease, Vanderbilt University, Nashville, Tennessee; **C. Gregory Elliott, MD**, Professor of Medicine, University of Utah and Medical Director, Pulmonary Hypertension Center, Intermountain Medical Center, Murray, Utah; **Vinicio A. de Jesus Perez, MD**, Assistant Professor in Medicine and Staff Physician, Wall Center Adult PH Clinic, Stanford University Medical Center, Palo Alto, California; and **Paul B. Yu, MD, PhD**, Brigham and Women's Hospital, Boston, Massachusetts.

Dr Fagan:

Thank you for joining us. Welcome to this roundtable. The focus of this discussion is to allow us to talk a little about the recent international conference, but specifically, the scientific sessions. New this year is also to talk about the research room, both from the current research room, and also some perspective on biomedical research performed as part of the meeting. What I'd first like to do is to congratulate Todd and the rest of the members of the committee on really a lovely program. I think that it really allowed us to focus in a lot of different, creative ideas as it relates to pulmonary hypertension and future directions. And so Todd, I know that you worked with your committee and came up with this year's theme. Do you want to describe that theme to the rest of us again?

Dr Bull:

Thanks, Karen. Our theme for the 10th PHA International Conference Scientific Sessions was the genetics of pulmonary hypertension. I also want to extend my thanks to those that helped put this together, and I'll briefly throw the names out there. It was Aaron Waxman, Anna Hemnes, Charlie Burger, Troy Stevens, and James White. We kicked around a bunch of different ideas from the standpoint of pulmonary hypertension. And our first decision was that we wanted to come up with a theme, to try to focus our discussions around a central topic. With the time that had passed since the discovery of the BMPR2 mutations in 2000, and all the new directions this research has taken since that time, all the evolving data in the area of genetics, genomics, epigenetics, and pulmonary hypertension, we decided that the genetics of pulmonary hypertension would be a great area to explore. Underlying this idea is the realization that at some level all diseases are genetic in their development, genetic in their progression. Our ability to understand the interaction of the individual's genes with the environment will drive new developments in terms of therapies and some of the ultimate developments in terms of therapies down the road. For example, why do some HIV patients develop PH while others do not? Similarly, why do some scleroderma patients get PH and some patients liver disease? And so, it was with that idea that we decided on an underlying or overlying theme for the conference. We then set about finding the speakers that we thought could really show us not just where we've been (which is what Dr. Newman focused on in his talk), but where we are going, which is what the rest of the speakers ended up discussing.

Dr Fagan:

Well, I think that you put together a lovely program. Anna, do you want to talk about what it was like to participate on the committee and some of the thought process that you and the committee contributed to?

Dr Hemnes:

I thought it was a great committee to be a part of. There was a lot of discussion about what the best research was and how we could make it accessible to people who were attending the conference, and how to increase our knowledge about where genetics was bringing us in pulmonary hypertension. I really enjoyed working with the other committee members in thinking about how to put the best conference that we could together. And probably one of the most enjoyable things was reviewing the abstracts and seeing some of the science that is going on around the country and internationally. There were several abstracts that I recall being from international groups, which really demonstrated the draw of the conference. So that was a particularly enjoyable part of the committee.

Dr Fagan:

Well, I think that this was a record setting year for numbers of abstracts presented, as well, is that correct, Todd?

Dr Bull:

I'll have to check back to see our final count, but we had a record number—well over 100 in total. We had hit really above our target number going into it. And really some great, great abstracts. So I would agree with Anna that it was fun. We had great abstracts on genetics, genomics, and epigenetics, but also great abstracts on many other topic areas important to PH. A number of abstracts were selected for presentation during the scientific session that were not “genetic,” but were great abstracts and deserved to be oral presentations.

Dr Fagan:

So Vinicio, I don't know if this was your first PHA meeting and first scientific sessions? But I do know that you were one of those abstract presenters, in addition to attending the sessions, is that correct?

Dr de Jesus:

That is correct.

Dr Fagan:

And was this your first meeting?

Dr de Jesus:

That is correct, yes.

Dr Fagan:

So I know you as a junior faculty member and someone who has already committed a career to PH research, but for a first-time attendee, what did you think about the scientific sessions in particular, but maybe you can give us your perspective about the meeting as a whole?

Dr de Jesus:

One of the things I enjoyed the most was the opportunity to learn the latest advances in the field from the leading investigators and to participate in a very stimulating exchange of ideas with my peers. I also had the tremendous privilege of discussing my research with several patients and was able to obtain their perspective on how these advances could change their quality of life and attitude toward the disease. Regarding the sessions, I was quite impressed with the breadth of scientific content, particularly with the variety of presentations on genetics and its relevance to PH. I think the way the presentations were organized was very effective, as they managed to cover the entire chronology of the field starting with the discovery of the BMPR2 gene and touching on potential new genetic markers of disease such as the microRNAs. Like Todd was saying, it is imperative to continue to explore the genetics of PH since there are still many unknowns that require our attention, such as why some patients develop the condition after being exposed to certain drugs or why some conditions can predispose to development of the disease.

Dr Bull:

A really interesting area of research was presented by James West of the Vanderbilt group about the BMPR2 mutations that we're so interested in. Almost all the work published to date on BMPR2 has examined its effect on the pulmonary vasculature; however, Dr West presented evidence that BMPR2 mutations have a "systemic effect" with implications toward metabolism. This area may eventually have implications toward RV metabolism, which is an area of evolving interest in PH. The conference was a great opportunity to look at these mutations from different angles than we have in the past. That is just one example of the great things that came out of some of these talks.

Dr Hemnes:

I think the other exciting thing was the hereditary hemorrhagic telangiectasia data and how it intersects with BMPR2 mutation. The ability to bring top-notch scientists together and talk about how their own research, in what seem like pretty disparate fields, actually intersects pretty closely was a really nice opportunity, and something that I think the conference brought to the forefront pretty well.

Dr Bull:

I definitely agree with Anna. That was a nice look into a rare disease, but then how it comes back across to what the bigger picture is here. . . .

Dr Fagan:

I thought he had a very interesting perspective. And I think one of the things that the scientific sessions originally did and continue to do is to bring in experts in areas that are related to PH, to inform us and to help us identify other avenues that need further investigation or other areas that are complementary to what we're doing that by working together, we can advance multiple fields. I think the scientific sessions have always done a really lovely job of that. Greg and Paul, you've both been a little quiet. I want to switch over a little bit to talk about the research room. And Paul, I invited you as this year's chair of the research room activities. And Greg, obviously as the founder, so to speak, of clinical research at the PHA meeting, to

kind of bring your perspective in. Paul, if you could tell us a little bit about the research room this year and the success of that, I think that all of us would like to hear about how well the program ran this year.

Dr Yu:

Thanks, Karen. This is a neat thing to be able to sort of look back at how the research room has grown, especially with Greg's perspective of having been there at the very first research room. Was it in 1994?

Dr Elliott:

Paul, that research room wasn't much, I can tell you.

Dr Fagan:

The card table, the research card table.

Dr Elliott:

But the investigators were highly motivated. And I still remember to this day, David Badesch, MD, coming with little pieces of filter paper to collect samples. I think these were for ACE genotyping that he was doing. And Jane Morse, MD, needed help with phlebotomy. So we drew the blood samples for her. I was told that one sample was from a family that helped her team at Columbia find the BMPR2 gene mutations. So, back then, we were just kind of finding our own way. And luckily, the patients and families were incredibly supportive. And I think Todd Bull, MD, coined the phrase "stick it to PH" for the blood drawing.

Dr Bull:

I wish I could take credit for that, Greg. That was actually one of the patients who came up with that. And then we thought it was such a great idea, we should get it on a sticker. She's one of the organizing committee members. Again, PHA being all about patients, at its origin, patients helping drive this forward, that's a nice example of that. So we came up with the sticker, "Stick it to PH," which the people that then participated in the research room could wear sort of proudly for helping us with this work.

Dr Elliott:

It really is one place where physicians, scientists, patients, and clinicians all come together. I think the research room has always been a tangible way for the community to organize and advance our scientific knowledge. This year I was so impressed at how well organized it was and how well people were interacting with each other. In 1994 I had no idea whatsoever that we'd ever end up with anything quite as great as what you have done.

Dr Fagan:

And with that actually, Paul, I'm going to ask you to just give us a little bit of a summary about the research room. And like the abstract submissions, I understand it was a record-setting participation, not just with patients, but also with investigators. Is that correct?

Dr Yu:

Yes, that's right. We had more interest from investigators than in years past. There were 4 or 5 groups that returned from 2010 to continue their studies. They were interested in following patients with some continuity, as well as recruiting new patients. And then we had some interesting new groups join the research room effort, for a total of 9 groups. So there's been a steady progression in terms of number of groups interested in participating, as well as the patients participating themselves. We had people doing quality-of-life studies, looking at correlations between exercise function and markers of depression. We had people doing actual sorting of progenitor cells, circulating endothelial progenitor cells right there in the room. We had people doing some very interesting proteomics, some very interesting genetic studies, as they've done since the beginning of this research room. So I was impressed with the increased diversity in the types of research and the research methods that were being pursued in the room this year. We've tried to be as inclusive as possible in accommodating both numbers of groups, and types of activity. The only real constraints are that some exercise or walking studies aren't considered to be safe for this setting, but any other imaging, questionnaire, or phlebotomy study that has been proposed has usually been accommodated one way or another.

Dr Bull:

I just want to compliment Paul on getting this all organized. It's always a tricky thing making sure everyone's got their IRBs in place. That we're drawing the appropriate amount of blood from people, that the consent forms are being filled out appropriately. Then trying to organize the appropriate infrastructure in terms of centrifuges, phlebotomy equipment, etc. In 2010, we had a broken centrifuge show up. And then actually Paul, at that point, somehow managed to finagle another centrifuge at the last minute. Anyway, it is no easy task.

Dr Yu:

No, that was fun. There's a lot of troubleshooting on the day, no matter how much planning we tried to do ahead of time to make it as smooth as we could from the patient's perspective, the participants, as well as for the investigators, things always happen. And, I wish I could say this year was perfect. We still had some issues. As the scope of the effort has grown, as we've had more patients interested and had more investigators, and the potential for things to get out of hand is always there. This year the proactiveness of the PHA staff and the other people on the research room committee helped a lot. And this is to say that we still have a lot of aspects that we'd like to work on, because we think that this effort will continue to grow. We've had some nice constructive and critical feedback from the patients who participated, and some of the board members, who felt that, even though we've made strides, we could make the experience better from the patients' perspective. But from the investigators' and researchers' perspective, I think we all agree that there's nothing quite like the experience of reaching out across the table and talking to people who live with this disease, or who have family members with this disease. To me, nothing quite encapsulates the whole interface between investigators, physicians, and patients that is the philosophy of the PHA scientific sessions the way the research room does.

Dr Fagan:

I was very lucky in that we were able to bring some projects to the research room from our

institution. And we brought the graduate students who were working on these projects. And for those working on a PhD in basic medical sciences the profound interaction they had with the patients and their family members and other people willing to volunteer to provide specimens to them was great. Each and every one of them came back and reported in their respective lab meetings the profound impact that this type of interaction has on them as a scientist—and that it's no longer a theoretical situation that people find themselves in. These are real people with real faces and real names, and real stories to tell. I've personally experienced that in the meeting—even though I get that interaction clinically all the time; somehow it brings that to a much more heightened awareness. Maybe just the sheer volume of patients does that. Greg, I was wondering: again thinking back to maybe the shoebox that you sat on to collect blood samples, not as long ago as all of us would like to imagine, and speak to the progress of the meeting. I think that there have been a lot of things that relate to the theme of the meeting, including the genetics story that came out of this. And I was wondering if you, as you looked at the research room this time, what were some of the things that you were thinking about in terms of where the research room has ended up now?

Dr Elliott:

Well, I think first Paul said it correctly. I think when we started, it really was an idea. I mean, the history, as briefly as I can tell it, is that I heard that there was someone in Chicago named Judy Simpson who was planning a patient conference. And I thought, that's interesting because I'm interested in collecting DNA from patients with pulmonary hypertension. And the pace at which I can collect here in Utah is pretty slow. But maybe if I went to this meeting, I could find some patients with this rare disorder and collect more samples. So I called Judy Simpson, and Judy was incredibly cautious. She said, "Can I get back to you?" And then I'd since learned that she called Al Fishman, MD, and Lew Rubin, MD, to check and see if I was a legitimate person to talk to (laughter). And luckily, they said yes. And then it went forward from there. I had a fellow, Gary Alexander, MD, working with me at the time. Gary agreed to come with me. We packed up all our tubes and headed to Stone Mountain, Georgia. And in one weekend, we collected 40 DNA samples from patients with PPH and accessed their records to confirm the diagnosis. I said it would have taken me 8 years of work in Utah to do what I did in that one weekend. So that was the beginning. And then we came back every 2 years—I think we skipped one conference because I didn't have the resources. But we came back and added to our pool. And I just sent off to Wendy Chung a map of the United States, showing that we have DNA samples for patients from all over the country. In the meantime, investigators have come with other questions. That's been very rewarding to me. We've seen a lot of projects. And I think I've also seen people interacting and sharing their ideas there, which I think is terrific. So those are the things I've liked.

Dr Fagan:

So Anna, I know you're someone who has done basic science research and translational and clinical research, in addition to caring for patients with PH. What are some things that you think that the research room might be able to do in the future that might be good? Are there ideas that you have about other things besides questionnaires, samples, things that you think as an investigator would be something interesting to do there?

Dr Hemnes:

Gosh, there are so many things that I don't know where to start. I guess the samples are

really a particularly unique thing that are available at the PHA, because there's such a large number of patients with a rare disease together at one place. So I don't want to discredit that. But there are certainly many different kinds of research that are available. For instance, questionnaires about quality of life and pulmonary hypertension, and how drug therapy has affected quality of life for patients come to mind. I think looking at exercise capacity, using some of the newer techniques, like the Shape heart failure device may be an option. So perhaps bringing some of the ideas that people have had, that have only been able to study at their local centers, to the research room in the future may be a venue to broaden that research applicability and enhance knowledge. And, in particular, the participation of various subtypes of patients with pulmonary hypertension may allow greater comparison of different subtypes, really enhancing research in patient samples, as well as outcomes research and also quality of life, which I think also would be interesting.

Dr de Jesus:

I would like to add to that. One of the things that I think cannot be overlooked is that, in addition to the patients themselves, we may also have access to their immediate families. Affordable complete genome sequencing will soon be a reality and we will be asked to provide input on variants that could have potential roles in PH development. The genetic information obtained from family members may facilitate interpretation of a patient's genetic data and could help us elucidate the impact of some of these genetic variants in disease development.

Dr Bull:

Yeah, that's great, Vinicio. I think that's an important point to add up. And then one thing I want to throw out that Greg Elliott and I have talked about in the past, and that I know Paul has talked about, is that it's such an amazing opportunity, being allowed to work with the patients at the PHA, who give so much of their time, that I wonder if we can come up with even smarter ways of approaching it in terms of collaboration. One thing Greg and I had discussed once was trying to get a planning meeting of the participating investigators well before the next PHA meeting to try to figure out where our interests come together, and then come up with projects that attack this at multiple levels. For example, coordinate the efforts of the investigators doing DNA work versus those doing RNA work and those interested in circulating factors, and coordinate the efforts. One of the things that becomes very difficult with projects such as this is getting the phenotypic data after you have gotten the sample, because it involves requesting clinical data from multiple institutions from around the country. If there were some way to get this data once and share it among all the investigators, it would make these projects much easier. I think it would be something worth exploring now. In the modern age of IRBs that becomes in some ways a difficult thing to contemplate. But at the same time, could the PHA, for example, serve as the clearinghouse for the data that then lets multiple groups access it. These are the sort of things that I think could really ramp up our ability to use this incredible resource in more effective ways.

Dr Elliott:

Well, Todd, I am glad you brought that up. I was going to bring it up if you hadn't. And I've always viewed that as what I call an unrealized opportunity. I think there really is an opportunity that goes beyond the conference. And I think the conference is such an intense activity that if there were funds somewhere available to bring the investigators of the research

room together, as you said, before the meeting, and to have a little more of an organizational structure to allow for integration, then I think even more could be accomplished.

Dr Hemnes:

I would also agree with that and say that it's possible now in the electronic age that some of those interactions with patients don't even necessarily have to happen in the context of the conference. And that people who are interested in participating in research protocols may sign themselves up to some sort of database that's sponsored by the PHA ideally, or another organization, as people who are willing to be contacted for research purposes. And many blood samples, or even other types of samples, could be collected remotely, so that some of the real riches of the research room in terms of patient benefit and research knowledge could be extended beyond just this once-every-two-year opportunity. A sort of a pie-in-the-sky dream, but why not dream big?

Dr Fagan:

There's no reason to say that that couldn't happen. And indeed, there are companies out there that sell database access, where people can input data and things like that. And certainly, the PHA has been looking at those, because of the concerns raised there. In just the last couple of minutes, what I thought I might do is switch gears just a wee bit. And one of the things that I can say from my personal experience with the PHA International Conference and Scientific Sessions is the focus the meetings have made on trying to engage young physicians and young scientists in an enthusiastic career in pulmonary hypertension research. I think that one of the things that the meeting does, and again because of its uniqueness, is to really inspire those types of experiences. And I know, Vinicio, I'm going to pick on you a bit, since this was your first time at the meeting, to ask you to say a little bit about how you think that the meeting is moving you forward a bit in your interest in pulmonary hypertension.

Dr de Jesus:

The PHA international meeting was a great opportunity to meet with mentors and colleagues who were excited to share knowledge and experience with a young clinician scientist such as myself. Also, it is a great platform to interact with people who are at my stage of career development, and exchange experiences that go beyond just what we're doing in the lab to include the challenges that we face in our clinical PH practices. As far as the science, I was clearly blown away. In the end, I felt that I had a good idea of where I would like to be as the field evolves over the next decade. It is my goal to become a better scientist and to learn how to fit a mentor role in my career, as exemplified by the rest of the colleagues in the meeting, such as Greg, Karen, and Todd, among others. I certainly hope to continue my current career track and contribute as much as they have in the coming years.

Dr Fagan:

Paul, anything else to add in terms of the impact that the meetings had on you in your professional career?

Dr Yu:

Well, it's been pretty amazing actually to see the meeting grow, both in the scientific sessions, as well as the research room, over the past 3 or 4 meetings that I've been to. I was a trainee at the first 2 meetings that I went to, and I was blown away then. And I didn't anticipate that it would grow as much as it has. The scientific programs have gotten better and better, in participation, breadth of research topics, and ambition. I agree with Vinicio that the quality and the scope of the science that's presented there is just amazing. From the perspective of anybody who's interested in pulmonary vascular disease, there's pretty much something for everybody, even though there was a well-defined theme at this year's meeting. And the research room has been really fun to be a part of. Since I think I was introduced to it by Greg Elliott, I think 4 years ago, it's done many of the things that he's talked about in terms of exposed me to mentors in the field, to thought leaders in the field; it has exposed me to science and has led to really nice collaborations with people scientifically—and friendships, as well, beyond the collaboration. So I'm very grateful for a lot of that.

Dr Fagan:

I'm going to pose the same question to the rest of the panel. Greg, don't think you're off the hook (laughter). Todd, do you want to go next?

Dr Bull:

Similar to Paul, I attended my first conference as a fellow and was—I remember thinking to myself—what an unusual conference. I'd never heard of patients going to the same conference as the physicians. And I came out of that conference saying to myself, what an amazing idea. Why doesn't every organization do something like this? And similar to you, Karen, I come away from it re-inspired, even though I take care of patients all the time with pulmonary hypertension, there's something unique about that conference in terms of refocusing you on why you do what you do, and what's so important about it, and why it matters so much to so many people. There's nothing else quite like it I have to say.

Dr Elliott:

I guess what I'd say first is, first, well said, both you and Paul. I think you're right, it's always—it gives back to us more than we ever—at least to me, it's given back to me more than I've ever been able to give to the community. So I really have valued the conference. Historically, it might interest you to know that that first conference at Stone Mountain was purely a patient-driven conference. And it was because Judy, I think, and perhaps others were willing to have some good physician advisors, I think, to welcome us in as scientists. I remember once they gave the green light for research, then we came a little early, and I met with a number of colleagues. I think Jim Loyd was there. And I don't remember if John was. And we talked about what we were going to do with research and basically said, if any of you want to do this, too, we've partitioned off a room. And I think that's when James stepped forward and Dave Badesch, to the best of my recall, that first room just had the 3 of us in it. But there was no scientific session.

And the first stab at a scientific session I think I was a program chair or something. And I invited Ted Lowe from the University of Utah to come talk about advances in cystic fibrosis and the genetics and some of his work with survival curves. Ted was probably the mathematical modeler. And that was sort of a seminal event. And it really had come because somebody said, why would physicians and scientists come all this way to a conference that's

purely patients? And so you can see, it really—I think it grew out of ideas that good people had. And what we've seen is, it is a lot condensed into the conference, including great scientific sessions on the front end. And then, the sessions for patients and families and caregivers and the PH community, locked arm in arm with the research room. So, it really has evolved to where it is. And it's evolved because people have had good ideas and been willing to work, do the work to see them through.

Dr Hemnes:

I would say it was only my second scientific session that I've ever been to. But both times I've been, I've been inspired by 2 things. First is the enthusiasm of the patients for what we're doing and for their interest in research. And really on a more personal level, for finding a cure for this terrible disease. And that's brought a lot of personal meaning to my own research. And the second thing that inspired me was the tremendous quality of science that's being done by our colleagues and it's inspired me to raise up my own science. So on both levels, I really love the meeting because of the unique interaction of patients and researchers and caregivers all together, it can't be found anywhere else.

Dr Bull:

The one thing that Paul remembered to do and I've neglected to do was to really thank the PHA for their outstanding work in putting this together. I mean, we obviously had work to do, but it only comes together just because they've organized it and keep us on task and then really do all the things that need to happen to make it—just to make it occur. So, Rino and his staff never cease to amaze me at how well they can put this sort of thing together and keep them rolling.

Dr Fagan:

I'm going to conclude by just again thanking all of you for participating. I know that we all have busy days and this occurs right in the middle of everyone's day. But like all of you, I share a commitment to helping the PHA advance its causes for patient advocacy, for research, for education, and ultimately to find a cure. And thank you all for participating in this. And we're looking with great enthusiasm to the next scientific sessions, which will be chaired by Anna in Indianapolis, and Eric Austin has kindly accepted the position of being the new chair of the research room. I am certain that the sessions and research room will be terrific under their leadership. Thank you all so much.

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