

International Conference Scientific Sessions: Past, Present, and Future

Following PHA's 9th International Pulmonary Hypertension Conference and Scientific Sessions, Karen Fagan, MD, guest editor of this issue of *Advances*, convened a call with Nicholas Hill, MD, Chief of the Division of Pulmonary, Critical Care, and Sleep Medicine at Tufts Medical Center, Boston, and Hunter Champion, MD, PhD, associate professor of medicine in the Division of Pulmonology, Allergy and Critical Care, the Vascular Medicine Institute, and the Cardiovascular Institute at the University of Pittsburgh, to discuss their perceptions of this and past meetings and the contributions they make to progress in basic and clinical science in the care of patients with pulmonary hypertension.

Dr Fagan: I'll open by welcoming everyone to this roundtable discussion. Today we're going to be talking about the Scientific Sessions that were held in conjunction with PHA's International Conference in June 2010 in Garden Grove, California. We'll also talk a little bit about the role of the Scientific Sessions and possibly the role of the research programs at the PHA as we push toward the search for better treatments and ultimately a cure for pulmonary hypertension. We all were selected to participate in this roundtable because we participated in some way, shape, or form through the PHA in the International Conferences, both the current one and also ones in the past. So I want to thank everyone for joining and welcome you to this roundtable.

One of the things that I value the most about the Scientific Sessions is that the meeting can sometimes be so overwhelming with all of us participating in the professional- and patient-led sessions and the Scientific Sessions are a really important time for the medical and scientific community to get together and to talk a little bit about what's happened over the last couple of years in the advancement of research, both basic science and clinical. And I think it's a unique opportunity that we don't get at other meetings, where we are all pulled in so many different directions. I don't know if you all have any thoughts about the importance of the Scientific Sessions in that context.

Dr Hill: I agree. I think as time has gone by the PHA meeting has drawn more and more of the pulmonary hypertension physician community along with many patients, which is one of the things that makes this meeting unique and so attractive to the physicians, nurses, and other caregivers. I see the Scientific Sessions as frosting on the cake, because I do really value the interactions with the patients. The Scientific Sessions give us an opportunity to network and to share new ideas in a setting that has many fewer distractions than most of our bigger meetings. Take the American Thoracic Society (ATS) annual meeting, which has great content, but there is so much going on simultaneously that I think we all feel frustrated that we only see a small portion of it. Whereas at the PHA meeting,

the focus is on this one Scientific Session and you know you can consume and try to digest virtually all of it. It's fun and educational and that's why I keep going back.

Dr Fagan: How about you, Hunter?

Dr Champion: I agree. I also really enjoy interacting with the patients and the nurses and other ancillary caregivers more than anything. Sometimes other meetings get bogged down solely in the basic science. I really enjoy PHA where we have an opportunity to integrate the basic and clinical science in the Scientific Sessions with practical patient care in the patient and caregiver sessions.

Dr Fagan: I particularly just enjoy the fact that you can have the Scientific Session, a full day devoted to really hearing about incredibly high quality, interesting pulmonary hypertension-related science, and then you walk into the foyer and you get to see some of your patients and their families. It causes me to take a breath and think, "Wow, this is really important that we keep pushing forward." From my perspective it really brings the message of the need for translational science much more closely together than I think other meetings that we go to. It shows very clearly that the science really does have an impact on real people.

Dr Champion: I agree.

Dr Fagan: This year we started off Thursday evening with a few talks about some of the larger, more collaborative projects that are in pulmonary hypertension. We heard from Drs. Paul Hassoun and Kurt Stenmark who are finishing the Specialized Centers of Clinically Oriented Research (SCCOR) programs in pulmonary vascular disease which were awarded several years ago. They were able to get us updates about their programs and some of the great successes that they've had. In addition, we also heard from Vallerie McLaughlin, MD, who talked about the Cardiovascular Medical Research and Education Fund (CMREF) and the tissue networks, tissue and cell banking networks, and how



Karen A. Fagan, MD



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Hunter Champion, MD, PhD

that initiative is going forward. So Hunter, you participated in the SCCOR projects at Hopkins, what impact do you think that the SCCOR projects had on pulmonary vascular research?

Dr Champion: Our SCCOR program has focused on scleroderma and connective tissue disease, a condition that has been poorly understood. This is particularly important as we recognize the fact that scleroderma affects the heart and kidney in addition to the lung. Recognizing the effect on these organ systems and the effect that can have on the pulmonary circulation is helpful with not just idiopathic pulmonary hypertension. We are finding that a significant number of our patients had non-systolic heart failure (heart failure with preserved ejection fraction, diastolic dysfunction) associated with their disease. I biopsied the right ventricle in approximately 25 patients and we gathered meaningful information as to how the heart responds to the increased workload that is placed on it by the lungs. In addition, we should be able to relate peripheral circulating mononuclear cell gene expression assays with actual tissue assays such that we won't need to do heart biopsies in the future.



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Dr Champion

Dr Fagan: What do you think the impact of the SCCOR program in pulmonary vascular disease research was? The grants were designed to foster collaboration and provide infrastructure to move multiple projects forward with an emphasis on translational and clinical research. Do you think that you could have made similar strides without the SCCOR program support from the NIH? Do you have any ideas for pulmonary vascular research in the future?

Dr Champion: I think that being able to put enough funding into one area in one place where you can have like-minded people working toward a similar goal but from a different vantage point was quite important in the SCCOR programs. I think that the future of the study of pulmonary hypertension will rest in setting up a PH consortium, much like what the NIH has done with heart failure. Sometimes the patient population numbers are relatively low at each site, but if you have 3-6 academic sites that work together and have similar protocols, we will have the opportunity to have further clinical drug development specifically targeted toward one particular type of pulmonary hypertension.

Dr Hill: If I could just comment and add to what Hunter has been saying. I was on the study section that selected the SCCOR sites. There were quite a number of high quality applications and it was a little frustrating not to be able to fund more than 2 of them. But I think we made the right choices, because as Hunter

said, the Hopkins SCCOR under Paul Hassoun has been very productive and has teased out some of the distinguishing characteristics between scleroderma and IPAH and also is going to give us a lot of insights about how the right ventricle fares in the face of pulmonary hypertension. So there is going to be a lot of work coming out, probably even for years after the SCCOR is finished.

Kurt Stanmark and his group in Colorado also have been doing a great job with their SCCOR and are very productive in looking at cellular and signal transduction mechanisms related to some of his models of pulmonary hypertension. Importantly, Kurt's program included an important focus on pediatrics, which is an area of growing importance and need, as well as looking at the mechanical forces in the vessel wall, such as impedance, as important determinates of patient outcomes.

So I think we can all be very pleased with how well these SCCORs have done and I think it's an important funding mechanism. I think what it does provide, as Hunter pointed out, is a lot of infrastructure at a single site that enables you to do certain kinds of studies. For looking at pathophysiology, understanding cellular and molecular mechanisms, that kind of approach works well because you can bring together a great deal of expertise at a single site and focus on specific questions.

What Hunter was suggesting going forward sounded a little bit like the PHNet that a number of us have hoped for over the years. But the feedback I get from the NIH is that because money is so tight they're not too sanguine about the likelihood of something like that being pulled together in the foreseeable future, although I think we need to keep lobbying for it. As Hunter said, it brings together the capability of studying many more patients so that you can ask different kinds of questions. Thus, both approaches have their value. Undoubtedly, the SCCOR funding mechanism has been very successful at the 2 sites that have been funded.

Dr Fagan: My initial thought was that if a nationwide (or worldwide) PHNet is not something in the near future, perhaps focusing on developing more regional approaches, providing resources for several different PH centers, both clinically and scientific, to work together to combine efforts would be useful. Clearly the benefit of a large national or international network can't be downplayed, but short of that maybe we should think more locally.

Dr Hill: Actually, I've tried to pull that off in the New England area. And it's not easy to get it funded. There is a little bit of a Catch-22 in this because if you

want to get funded, people want to see that you have something to fund. You can't just say I'm going to create this. What they want to see is that you've gone a long way in pulling it together and then they feel more confident that you've got something worth funding. But unless you have some start-up funding, it's very hard to get it off the ground. We also have barriers to creating local or regional networks. HIPAA has been a particular problem for clinical research in this country where you have to worry about how information gets transferred between different institutions, creating additional hoops you have to go through. Then every institution has its own IRB and you have to get protocols approved at every site, adding to time delays and expense and so forth. It gets to the point where to do it at multiple sites costs you more personnel time than at single sites, making it very difficult to accomplish. I think it's a great concept. I'm still working on it and I hope I can pull it off, but it's really tough.

Dr Champion: One of the things we've been trying to do between the University of Pittsburgh and 5 other centers has been to establish a consensus for diagnostic testing. Specifically, we hope to have the same protocols for exercise echocardiography and cardiac catheterization. As we amass patient data with these techniques we can come together and start putting together some publications. By demonstrating our ability to work together, these PAH centers will be poised to submit proposals when and if funding becomes available.

Dr Fagan: Well, the sun is unfortunately setting on the SCCOR programs and I think they've been a very worthy investment of the NIH and certainly for all of the investigators' time. I think that they really did what they were supposed to do, which was to move things forward at a much more rapid pace than individuals, or even that smaller, less well-funded groups of people could do on their own.

I wanted to switch gears just a little bit and talk about the second part of the meeting, which was the day filled with talks from people who have a long-standing history in PAH, those that are new to PAH, as well as talk a little bit about the abstracts and poster sessions that were submitted.

The overall theme started with inflammation in an animal model and humans in vascular disease in general, then moved into some special topics in pulmonary hypertension, and finished with the notion of a potential therapeutic use of stem cells in pulmonary hypertension. How did the day progress for everyone at the meeting? Did you find that the talks were pretty interesting? Did we learn new things? Solidify what we did know?

Dr Hill: I do think the meeting had a nice mixture of basic science and translational work; and I do recall being engaged in every talk. Even though the theme was inflammation, it touched on a lot of different related areas so there was a nice balance. I also liked the fact that the abstracts were interspersed so that you had sort of a more in-depth, intense type of presentation, and then you had a sort of snapshot with the abstracts.

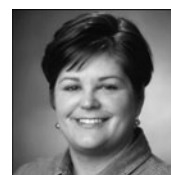
Dr Fagan: I agree. I thought that it was a nice, wide-ranging group of presentations. And what I've always appreciated about the PHA Scientific Sessions is that it's also a nice mixture of people whose voices we hear frequently who are doing great research intermixed with people who are outside of the immediate PAH community. They frequently bring to us some really powerful and important new ideas. I think that the committee was very successful in accomplishing that this year.

Dr Champion: I agree. I like the idea of linking the program to inflammation. It allowed for the integration of information that spanned HIV to glucose intolerance and the role in inflammation. I thought that it flowed very nicely. I like having an overall theme to the program.

Dr Fagan: And I thought the quality of the abstracts that were presented, both those at the podium and in the poster session, was really outstanding. It was the largest number of abstracts to date that have been submitted to the meeting. I think that the poster session was exceptionally lively and people lingered long after it was technically due to end. So I thought that it was a highly successful abstract submission and poster process as well. It's a great opportunity for young investigators, people relatively new to the field, in a smaller venue to be able to show some of their work and to get to really interact with some of the most important minds in pulmonary hypertension.

In terms of themes for future meetings, any thoughts? We can pass this on to the committee.

Dr Hill: I think there is always interest in looking at newer pathways, developments in mechanism of disease, things like that. There is also a lot of attention being paid to the role of the right ventricle. Some of us are saying, "Well, you know people die of right ventricular failure, therefore this is ultimately a disease of the right ventricle." I don't really see it that way. I think the right ventricle would be perfectly happy if we could get rid of the pulmonary vascular disease. But I do allow that if we can help the right ventricle deal with the increased afterload, which certainly has the potential of prolonging survival.



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Dr Champion: As much as I love the right ventricle, I would probably say having the theme be the heart in PH would probably not be the right direction at this time. I think that certainly could be a component of it. I think that the time is ripe for discussion of the broad subject of reverse remodeling in PH. You could then fold in topics of reversing RV hypertrophy and failure. That then would allow you to have a little bit of discussion about the interaction between the pulmonary circuit and the RV under a more global rubric.

Dr Fagan: I think that's an outstanding idea. You're right, we know better how both remodeling and reverse remodeling in cardiac tissues occur. Certainly in the left ventricle, we're a little bit ahead of the right ventricle. So that would be a good way to marry the lung circulation itself and the reverse remodeling that would need to occur in the right ventricle, as well.

One last question: Nick, I'm going to put you on the spot a little bit as the soon-to-be-president of the American Thoracic Society. You know these types of meetings have always held a very unique niche apart and separate from the American Thoracic Society's large International Conference, in large part through some of the things you spoke about: that it's more focused, you have more time to network specifically with the colleagues who are doing the types of research specifically that you're interested in, as well as in the attendance of patients and their caregivers. So the "putting you on the spot question" is, over the last few years I've noticed that there have been more sessions at the American Thoracic Society meetings that include a patient presenter, sometimes that are run by some of the patient organizations (PAR organizations) independently. Do you think that these types of meetings that bring together the health professionals, the researchers, and the patients are the wave of the future?

Dr Hill: Actually, it's interesting that you bring that up because that's going to be part of my theme for my presidency year at the ATS. One of the things that I plan to emphasize during my very brief year as president will be to try to bring patients more to the forefront and to remind us that ultimately we're there to help those suffering from disease, to prevent disease in those who don't yet have it, and to improve respiratory health generally. Thus, we need to work with the public and focus on patients. I am working with PAR to enhance these kinds of things. We are getting more patients coming to the ATS meeting. There have been more sessions, as you point out, that are somewhat like the ones that are done at the PHA where "experts" discuss certain topics in front of a largely patient audience in a question/answer format.

This is something that patients really appreciate. They learn a lot from it. And the "experts" also get a lot out of it because it helps them focus their thoughts on what's important for their patients. I'd like to see that kind of thing expand. I also think there's tremendous potential in patients and health professionals working together to achieve common goals. By that I mean we are ultimately trying to more effectively treat, and ideally cure, not only PH, but many other respiratory diseases as well. When we as professionals go to Congress to advocate for more research to try to achieve those ends, we can be effective. But if we can go to Congress in collaboration with patient groups, we're much more powerful. I think the patient voice is often heard more clearly by politicians. But if we can join our voices, we are much more powerful advocates. I also think that working collaboratively creates a feedback situation where we can learn more about patients' needs; and help to meet them more effectively. So in many regards, such as fund raising, political advocacy, communication, we achieve our missions and goals more effectively by working together.

Dr Fagan: I concur. The most powerful professional experiences that I have had have been at the PHA International Conference. In the Scientific Sessions I can kind of have my mind exercised by thinking about some of the latest and greatest things that some of the people I most respect in the laboratory are doing, be it clinical lab or basic science. And then walk out the door and to get a visual image of the impact that all of that work potentially has is an incredibly invigorating experience and reenergizing. I find that it reenergizes me to work harder in the clinic and the lab.

Dr Hill: I think one other area, and this gets maybe politically even more sensitive, is the interaction between physicians, physician organizations, and industry. As you well know, this has been under a lot of scrutiny in recent years and it's in a process of evolution. But I see this as a threat because industry has tremendous resources to apply to more effectively treat diseases and achieve cures. And if we as caregivers have restricted access to these resources, the traditional funding mechanisms like NIH and other private foundations will be unable to sustain our current rate of progress. We must work collaboratively with industry to lend our expertise and take advantage of their expertise and resources in trying to achieve common goals. I think the clamor we hear on some sides of our fence opposing any interaction between industry and physicians or physician organizations is a tremendous threat to innovation and progress. We need to interact properly with industry and manage the relationships ethically. We also need to be clear on our



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mutual objectives. But I think we would be missing out on tremendous opportunities if we discourage these interactions too much. I see patient organizations as being helpful in this regard. Because when physicians are being scrutinized by the media for their interactions with industry, it seems that there is a presumption of corruption. The press prejudices physicians with any conflict of interest. I think that patient advocates can be quite helpful in that their efforts are often received by the media and politicians in a different light and they can focus the discussion on what's important – the need to make progress in treating disease. Clearly there have been egregious examples of unethical behavior at the interface of industry and medicine in the past and these must be sanctioned, but going forward we can't throw the proverbial baby out with the bath water.

Dr Fagan: PHA, the PH community, and industry have kind of all grown up together so to speak. As PHA has grown, so have opportunities for treating these patients. Hopefully PHA can serve as a model of an organization that can interact with industry with patients in mind to move things forward.

Dr Hill: I think the PHA has done a great job. I think Rino Aldrighetti gets credit because he's managed industry relations very skillfully over the past decade. But I think organizations like the PHA have an advantage over the professional organizations, because it's a patient run organization and I think people can accept that patients with disease are needy and deserving of help from industry. But the perception in the press and in the eyes of some politicians is that the professional organizations are out just to serve their own interests. We need to work hard to make those relationships productive for all stakeholders in them and importantly restore the trust of the public in the goals of medical professionals and their interactions with industry.

Dr Champion: I think that the most important thing is that the level of interest that has been growing for pulmonary hypertension in general over the last decade has been incredibly impressive. This has spurred new research in both clinical as well as from the basic science level. I believe that we really are poised to make a significant impact in not just treating the disease but hopefully coming closer to something that would actually be curative. It certainly is going to take a lot more work from a scientific standpoint and from a funding standpoint. I think that with organizations like the PHA, ATS, the American Heart Association, and the American College of Cardiology, we should be able to do that.

Dr Hill: Echoing a little bit of what Hunter just said, we can take the perspective of thinking where the PHA started and how each new biannual meeting has been almost a quantum leap over the previous one. I think I first started going in maybe '98 or so and the meetings have gotten much bigger and more and more people are coming. There is really a critical mass there now of people bringing in all kinds of different viewpoints, expertise, and it's more exciting to go to these meetings. And I think these Scientific Sessions that we've had are just a reflection of that process. I think they've been getting better. They're up to date. They bring in a lot of information, a lot of exciting new material, and I think they will continue to do so. So I think we can be very happy with the level of success that's been achieved and I'm looking forward to the next one.

Dr Fagan: On that note, my concluding remarks will be to thank all of you for your time and your enthusiasm for the PHA, the patients, and the science. Hopefully in 2 years we'll have another quantum leap, to quote Nick, in the quality and contents of the meeting again.