Pulmonary Hypertension Roundtable: Recapping 5 Years, Exploring Emerging Approaches

Vallerie V. McLaughlin, MD

Richard N. Channick, MD

Ivan M. Robbins, MD

Victor F. Tapson, MD

This discussion was moderated by Vallerie V. McLaughlin, MD, Associate Professor of Medicine and Director, Pulmonary Hypertension Program, University of Michigan Health System, Ann Arbor, Michigan. Panel members included Richard N. Channick, MD, Associate Professor of Medicine, Pulmonary and Critical Care Division, University of California, San Diego Medical Center, San Diego, California; Ivan M. Robbins, MD, Director of the Pulmonary Hypertension Center, Vanderbilt University, Nashville, Tennessee; and Victor F. Tapson, MD, Professor of Medicine, Division of Pulmonary and Critical Care Medicine, Duke University Medical Center, Durham, North Carolina.

Dr McLaughlin: The past 5 years have been remarkable in terms of advances in pulmonary hypertension, and with the fifth anniversary of the journal coming up, let's start with the journal's first editor, Dr Tapson. Vic, what do you think have been some of the most remarkable recent advances in pulmonary hypertension?

Dr. Tapson: Val, over the past 10 or 12 years, basic research and clinical trials have led to FDA approval of five drugs to treat pulmonary arterial hypertension, and more are coming. Four of these five drugs have been approved in the last 5 years. The Pulmonary Hypertension Association has done remarkable work, and the national meeting has blossomed into a tremendous venue. These are exciting times, considering we once had essentially nothing for these patients

Dr McLaughlin: Ivan, would you like to comment on some of the accomplishments over the past 5 years?

Dr Robbins: It's been a truly remarkable collection of journal articles, with the most up-to-date information on pulmonary hypertension treatment and diagnosis. I don't think you can find anything like this anywhere else. It has been an incredible journal for people who want to learn about pulmonary hypertension.

Dr McLaughlin: Rich, in terms of the therapies now available, in the last 5 years we have seen the approval of at least three agents. When we started the journal all we had was epoprostenol (Flolan). What do you think about the current therapies?

Dr Channick: There's been a remarkable evolution and it's been great to be involved in it. Five years ago there was very little we could use outside of epoprostenol. Having multiple options that clearly are effective and good data showing marked improvement in not just how patients are feeling but in how long they are living is very rewarding. More options also create new challenges and questions that we can talk about as we get more therapies on board.

Dr Robbins: In patients not doing well with monotherapy with oral agents, inhaled iloprost and combination therapy have given us alternatives other than having to start long-term intravenous therapy, with the associated complications and problems we all have encountered with epoprostenol. We certainly have a lot of patients receiving combination therapy now, with either an endothelin receptor antagonist or a PDE5 (phosphodiesterase-5) inhibitor and iloprost, and we've had some good success with this. So it has given us a lot more options in terms of monotherapy and combination therapy.

Dr McLaughlin: Rich, what do you think?

Dr Channick: I certainly agree. Most of us, however, still feel that intravenous epoprostenol is the benchmark against which all new therapies, including other prostacyclins, should be com-

pared. In a sense the development of other prostacyclins is an effort to provide at least comparable or nearly comparable efficacy to epoprostenol in an easier formulation.

Dr McLaughlin: Rich, do you think anything currently available provides efficacy nearly comparable to that of intravenous epoprostenol?

Dr Channick: In my experience nothing has the efficacy in terms of degree of benefit as well as rapidity of benefit that intravenous epoprostenol does. I don't think we have seen an equivalent drug yet.

Dr McLaughlin: I would agree with that.

Dr Robbins: I would too.

Dr McLaughlin: If some of these other prostacyclins might be friendlier in terms of patient administration but are not quite as efficacious as intravenous epoprostenol, where do they fall in your armamentarium? Give me some idea as to where you might use any of these therapies as opposed to epoprostenol, the gold-standard prostacyclin.

If the patient is sick enough why not go to intravenous epoprostenol? Having said that, I know there are centers that have a lot of experience with intravenous treprostinil therapy. Treprostinil is clearly an efficacious compound, but the subcutaneous form in my opinion is really limited by the site-pain side effect. – *Dr Channick*

Dr Channick: That's a very good question, but hard to answer given limited data to tell us which alternative combinations to use and in which particular patients. My own approach is this: Treatment in most of our patients is started with an oral therapy, typically bosentan. We then use additional nonintravenous prostanoids as add-on therapy. In the sicker patients we go to intravenous epoprostenol up front. We also have a number of patients receiving two oral drugs, sildenafil and bosentan, plus an inhaled prostanoid, but I think the initial treatment decision is typically whether we start oral therapy versus intravenous therapy up front.

Dr McLaughlin: Aren't there still some patients who come to you relatively advanced in whom you start intravenous therapy as first-line therapy and generally is it intravenous epoprostenol?

Dr Channick: Clearly there are patients who require intravenous epoprostenol right up front. There are fewer of these patients as a result, I believe, of aggressive early therapy with oral and inhaled therapy. However, we don't want to lose sight of the fact that there are still patients who are sick enough who warrant intravenous therapy up front, and when we do use intravenous therapy it is typically epoprostenol. We've had some experience, albeit not a great deal, with intravenous treprostinil, with some benefit, but our "go-to gun" is still intravenous epoprostenol.

Dr McLaughlin: Is there any particular factor that leads you toward intravenous epoprostenol versus intravenous treprostinil?

Dr Robbins: At our center we have used only intravenous epoprostenol. If patients are sick enough for intravenous therapy, we have a lot of experience with epoprostenol. If you're going to go for intravenous therapy these days, until I see data that really show efficacy, we're starting intravenous epoprostenol. The other thing is that there's a huge cost difference between intravenous epoprostenol and intravenous treprostinil.

Dr McLaughlin: Particularly when you take into account the dose of treprostinil required to obtain similar therapeutic effect.

Dr Robbins: There are patients in whom you would want a little more time in case there's a pump malfunction or the Hickman comes out, where they may have somewhat limited support or live a great distance from a medical center.

Dr. Tapson: The advantages of intravenous treprostinil include the longer half life and the lack of need for ice packs. We have a number of patients taking this drug, but also tend to start therapy for our sickest patients with intravenous epoprostenol.

Dr McLaughlin: In some patients there may be a particularly important safety window in terms of having a drug that has a longer half life, like treprostinil compared with epoprostenol, perhaps for those who live in very rural areas. I didn't hear anyone mention subcutaneous treprostinil. Is there a role for that?

Dr Robbins: Not very much at our center. I know there are some physicians who have patients who have done well with this therapy, but every one of our patients has had either pain or discomfort at the needle site. Also, when we've transitioned a number of patients to inhaled iloprost in combination with an oral therapy, even the patients who were tolerating subcutaneous treprostinil well, once they stopped receiving it, they said, "Wow, I didn't realize I had this sort of underlying discomfort." So I don't see a big role for it, but there are centers that use a lot of it and do well with it.

Dr Channick: I agree with that. We've had a few patients undergoing treprostinil therapy. I agree with Ivan—finding the ideal patient for it is something I am still wrestling with. If the patient is sick enough why not go to intravenous epoprostenol? Having said that, I know there are centers that have a lot of experience with intravenous treprostinil therapy. Treprostinil is clearly an efficacious compound, but the subcutaneous form in my opinion is really limited by the site-pain side effect.

Dr McLaughlin: It is certainly an effective therapy for a niche population—those patients who perhaps want to avoid an intravenous line for a variety of reasons, including infection, and who have probably not done well with inhaled therapy or

who are very active and, for example, work and cannot take an inhaled therapy six times per day. So we have a small population that has done very well with subcutaneous treprostinil, but it is for a very select subgroup of patients.

Dr. Tapson: Irene Lang and colleagues published their very positive experience with subcutaneous treprostinil in *Chest* this year. More than 100 patients with mostly pulmonary arterial hypertension but some with chronic thromboembolic pulmonary hypertension were followed. At 3 years there was clear improvement, but the most interesting thing to me was that only 5% of their patients had to stop the drug because of site pain. We, however, have also tended to use intravenous prostanoid therapy.

Dr Robbins: What's your experience been with inhaled iloprost? We have had some good experience with it, particularly in combination with sildenafil. We've had 3 or 4 patients who did not tolerate it at all, in terms of the side effects from the inhalation—coughing, headache, flushing—and even when we backed the dose down they didn't tolerate it.

Dr Channick: I've had a similar case, a patient who had exactly the same side effects you're describing, cough, flushing, side effects that did not allow us to use the drug. But clearly, many patients experience a clear-cut benefit. There are published data from the STEP trial showing the benefit of inhaled iloprost in addition to bosentan, fairly convincing data mirrored in our clinical experience. But it's not for everybody, and there are those who do not tolerate the therapy.

We use sildenafil as first-line therapy in some patients and bosentan in others. Certainly underlying liver disease and coronary disease affect our decision. One of the worries with sildenafil is that because its side effect profile is very good, and because physicians have some familiarity and comfort level with it, it seems to be getting overused in certain patients who either need more aggressive therapy or in whom their pulmonary hypertension is being treated as pulmonary arterial hypertension, and shouldn't be treated at all. *– Dr Tapson*

Dr. Tapson: We've had good experience in general with inhaled iloprost and have also had some success weaning patients from epoprostenol when combining iloprost with an oral drug.

Dr Robbins: I've had some patients who have opted for epoprostenol over inhaled iloprost because of having to take six treatments a day.

Dr McLaughlin: That's one issue and the other is how sick the patient is and how durable the effect. We use inhaled iloprost in patients, for example, who are receiving oral therapy and who are somewhat better but not as well as we would like them to be, somewhat like the patients entered in STEP. But there are other patients who, despite receiving oral therapy, remain relatively ill. Those late functional class III's or IV's are where I tend to go straight to intravenous epoprostenol. So with regard to the inhaled agents, in addition to inhaled iloprost, all of us are doing some research with inhaled treprostinil, which has a longer half life than is delivered via a briefer inhalation four times per day. Rich, you did some of the initial pioneering work with inhaled treprostinil. Would you like to comment on it?

Dr Channick: We did a pilot study of 12 patients that was recently published in *JACC* [2006 Oct 3;48(7):1433-7]. The study was somewhat similar to the STEP trial except that it was an open-label, phase 2 study adding inhaled treprostinil in patients who were still symptomatic despite bosentan. Hemodynamic measurements as well as exercise capacity and the functional class parameters were assessed. We found a potent effect of adding inhaled treprostinil to bosentan in terms of functional status, exercise capacity, and hemodynamic responses. As you say, Val, there is now a large phase 3 trial of that drug in progress.

Dr McLaughlin: Let's move from the prostacyclins to the endothelin receptor antagonists. Bosentan was the first one the FDA approved nearly 5 years ago and remains the only one commercially available, although there are two investigational endothelin receptor antagonists that we have all had experience with—sitaxsentan and ambrisentan. Ivan, do you want to give us your perspective on the endothelial receptor antagonists, their similarities and their differences? Is one going to emerge as the best in class, or are they all relatively similar in terms of effectiveness, with some differences in the side effect profile?

Dr Robbins: I think it is difficult to say until we have them out there in use with a large number of patients. Bosentan has obviously been out there for quite a while and the number of patients who have been exposed to the drug is around 30,000, so there is a fair bit of data with this drug. There is also the recent publication by the group in France describing their long-term use of bosentan, so we are pretty familiar with it. As you know, about 10% of patients have liver function test abnormalities that require that they change to another therapy. But relatively few have noticeable side effects. With regard to sitaxsentan, we have certainly had some patients who have done well with this drug.

Dr McLaughlin: And don't forget to mention the warfarin interaction with sitaxsentan.

Dr Robbins: Yes, it is something that we are aware of. I have some concerns in that physicians in the community aren't going to be as diligent about watching out for this interaction. There are certainly many drugs that interact with warfarin, so that is something that people should be aware of, but not always. With regard to ambrisentan, there were certainly some very impressive data presented at the American Thoracic Society this year regarding a phase 3 trial in Europe, showing a mean increase in a 6-minute walk distance of about 61 meters.

Dr McLaughlin: It's a 5 mg dose.

Dr Robbins: Right, and that seems to be very well tolerated. We'll just have to see when it gets out there. Everyone is claiming that their liver function abnormalities are less and those of others are worse. This appears to be a class effect, although through different mechanisms for each endothelin receptor antagonist, but liver function will need to be monitored with this class of drugs in all patients.

Dr McLaughlin: Rich, what is your take on the different endothelin receptor antagonists?

Dr Channick: Clearly, bosentan was a breakthrough in treatment, being the first approved oral therapy for pulmonary hypertension. It is a very effective drug. Is it a cure? No, but again as we said before, we have patients who do dramatically well with the drug. I would say we really don't know where the new endothelin receptor antagonists fit in yet, and we won't until we have a lot more experience. Part of the problem is that we don't have studies comparing these agents to each other in a meaningful way.

Dr Robbins: I'd like to follow up on what you said. Let's say that we have another endothelial receptor antagonist approved here. You know none of these studies show overwhelmingly that one drug is better than the other. There hasn't been much head-to-head competition. What do you think your strategy is going to be if you have patients taking bosentan and they are not improving the way you want them to, or they are getting worse, or need intravenous epoprostenol? Would you consider another endothelial receptor antagonist or would you move to another drug?

Dr Channick: That's a great question, and I've wrestled with that myself. We haven't had that option yet but, presumably, we will. Do you go to combination therapy or substitution? Honestly, I don't have the answer to that question yet.

Dr Robbins: Well, I don't think anyone does. We are thinking about it too. It is sort of like blood pressure medications. Would you go for another calcium channel blocker or would you go to another ACE inhibitor? I don't know. I guess we'll just have to see with experience.

Dr McLaughlin: Great. So, let's move on to the phosphodiesterase inhibitors. This will be a little easier—there is only one commercially available. Vic, how has the availability of sildenafil changed your practice?

Dr. Tapson: We use sildenafil as first-line therapy in some patients and bosentan in others. Certainly underlying liver disease and coronary disease affect our decision. One of the worries with sildenafil is that because its side effect profile is very good, and because physicians have some familiarity and comfort level with it, it seems to be getting overused in certain patients who either need more aggressive therapy or in whom their pulmonary hypertension is being treated as pulmonary arterial hypertension, and shouldn't be treated at all.

Dr Robbins: Well, I don't think it has changed our practice a lot. We use quite a bit of sildenafil. We have had a number of patients with headache and flushing symptoms, which tend to get better, but we have had to discontinue treatment in a few people. In general, I think it is a well-tolerated drug. I think one has to take cost into account, and it is by far the cheapest medication available for the treatment of pulmonary arterial hypertension, and so I tend to start with that drug.

Dr McLaughlin: Do you tend to use sildenafil as a first-line drug, over an endothelin receptor antagonist as initial monotherapy?

Dr Robbins: Yes, in most cases.

Dr McLaughlin: Rich, what about you?

Dr Channick: We don't typically have that approach. And to address the issue of cost, as far as I am aware, the lowest dosage of sildenafil is the approved dosage of 20 mg tid. In my experience, and feel free to disagree, most patients seem to require more than 20 mg tid.

Dr Robbins: I think it is variable. Certainly many patients who were receiving higher doses in studies or who were getting sildenafil (Viagra) at 50 mg, a lot of them were just able to decrease to a lower dose. If a patient is not improving with 20 mg tid, then the cost goes up if you have to double the dosage. However, we have been able to work with insurance companies in a number of cases to get Viagra; then it is a similar cost for 50 mg.

Dr Channick: I get concerned about making this decision about issuing sildenafil first line. There are fewer long-term efficacy data on sildenafil in terms of survival and clinical worsening. So I am not as impressed with the long-term data on sildenafil yet. In our center our general approach would be at this point bosentan first line and sildenafil as add-on therapy. We certainly have had some patients receive sildenafil first, but those are patients in whom there is a contraindication to bosentan.

Dr Robbins: Rich, what would you say your long-term monotherapy is with bosentan? In the French study at least 50% of the patients were receiving another medicine.

Dr Channick: Certainly our experience mirrors that to some degree. The majority of our patients are not receiving monotherapy because our approach is an aggressive one. The question is, however, whether monotherapy really failed in these patients. In some cases it has, but certainly not in all cases. Our threshold for adding the therapy for a patient who, let's say, is still symptomatic, doing okay but not fabulously, is fairly low.

Dr McLaughlin: Let's move on to that next step. When do we decide to add or substitute? There are relatively few data to guide us with respect to that. With very few exceptions, the

trials that we've talked about so far are initial monotherapy trials. So everyone has a slightly different approach to that, and certainly combination therapy is a very hot topic in terms of clinical trials right now. Rich, at what point do you reassess your patients? How do you reassess? How do you decide whether an additional therapy is needed? How do you decide whether you are going to add or substitute therapy?

Dr Channick: We are, of course, always watching for worsening, but routinely we'll see patients back one month after initiating treatment, to evaluate if they are tolerating the therapy, not necessarily looking for efficacy to any great degree, Then at about 3 to 4 months we'll reassess, typically noninvasively, with 6-minute walk testing and clinical assessment. I perform a follow-up right heart catheterization if there is any question that the patient is not doing very well with monotherapy, and the results of that may drive us toward another therapy. But overall, I try to make a composite assessment of whether the patient is feeling better or feeling worse.

Dr. Tapson: We see our patients every 3 months and do a pro-BNP and 6-minute walk test. We do echocardiography, primarily to look at right ventricular function, every 6 months. And we do catheterizations as needed to make therapeutic decisions. We are trying to enroll in the COMPASS study, which is in patients taking baseline sildenafil who are randomized to receive bosentan or placebo, and in the TRIUMPH study, which is the randomized inhaled treprostinil (Remodulin) study in patients taking baseline bosentan or sildenafil. We are also excited about the FREEDOM trials, which will evaluate oral treprostinil.

Dr McLaughlin: What if they're stable, maybe a little bit better, they've improved in how they're feeling but perhaps not to a functional class II? Let's say they're still functional class III. Their 6-minute walk distance is perhaps a little bit improved, but not 400 or 500 meters. What do you do with that sort of patient?

Dr Channick: That's the kind of patient, at least at our center, we're trying to enroll into a trial, specifically now with inhaled treprostinil. It is important to keep in mind that there are centers around the country that are involved in these very important clinical trials to answer questions about combination therapy. For practitioners there is the opportunity to send a patient to a pulmonary hypertension center for enrollment in a trial. That would be the ideal approach in that kind of patient.

Dr McLaughlin: I can't emphasize that enough because we are still learning about the efficacy and safety of blocking more than one pathway. And also, as Ivan has mentioned, given the costs of these drugs, the cost-effectiveness of using two or more therapies for patients with pulmonary arterial hypertension needs to be evaluated. It's very important for us to take the opportunity that we have now to enroll those sorts of patients in clinical trials of combination therapy so that we can answer those questions in an evidence-based fashion.

Dr Robbins: While you can set strict criteria, and some centers may do that, you really have to look at the individual patient. Let me give you an example. My approach or my aggressiveness would be very different between a 30-year-old woman with idiopathic pulmonary arterial hypertension and a 75-year-old patient with scleroderma. For patients like the one with scleroderma being treated with bosentan or sildenafil, if they are improved somewhat yet remain somewhat limited, I would tend to take a little more time and see how they go. For patients like the 30-year-old woman with idiopathic pulmonary arterial hypertension being treated with sildenafil or bosentan, I would consider recatheterization in 3 months if they are not doing markedly better with oral therapy.

My approach or my aggressiveness would be very different between a 30-year-old woman with idiopathic pulmonary arterial hypertension and a 75-year-old patient with scleroderma. For patients like the one with scleroderma being treated with bosentan or sildenafil, if they are improved somewhat yet remain somewhat limited, I would tend to take a little more time and see how they go. For patients like the 30-year-old woman with idiopathic pulmonary arterial hypertension being treated with sildenafil or bosentan, I would consider recatheterization in 3 months if they are not doing markedly better with oral therapy.
– Dr Robbins

Dr. Tapson: I agree. It is key to individualize patients. The classic young idiopathic pulmonary arterial hypertension patient or young patient with scleroderma who does not have a stiff left ventricle needs to be treated as aggressively as possible.

Dr McLaughlin: Right, one needs to be more aggressive in a patient like that. We've mentioned some of the combination trials that are going on—the TRIUMPH trial, which is looking at inhaled treprostinil in patients who remain symptomatic while still taking either bosentan or sildenafil as monotherapy—but there are a number of other ongoing combination trials. The COMPASS-2 trial is looking at the addition of bosentan or placebo in patients who are receiving sildenafil monotherapy and remain symptomatic. The COMPASS-2 trial will be the first morbidity and mortality trial ever in pulmonary arterial hypertension.

Dr Robbins: It is important to find out how these drugs are working. Physicians in the community are not only using bosentan but are also using combination therapy with sildenafil, and with iloprost in some cases, and they're using these agents without data, so it is important to get as much data as we can to make some evidence-based decisions.

Dr McLaughlin: We will prepare ourselves better in the long term if we do that. I got a phone call from one of my referring physicians a couple of weeks ago who said he treated a patient with idiopathic pulmonary arterial hypertension with bosentan and the patient wasn't doing as well as he would

have liked. He tried to add iloprost and the insurance company would not pay for it because there weren't enough evidence-based data to support that. I think we have been under the radar screen in terms of insurers for a long time and now that these therapies are being used with increasing frequency many insurers are starting to develop disease-management plans that question the evidence for many decisions we are making. So there are many combination trials going on with drugs we are very familiar with that target the three pathways we've already discussed. Let's take a minute and discuss some novel therapies. The Rho kinase inhibitors are getting some attention lately and will soon be studied in pulmonary hypertension. Ivan, would you like to comment on those drugs?

Dr Robbins: Rho kinase seems to be involved with virtually every pathway applicable to pulmonary hypertension. The results in animals are pretty impressive but it really acts, from what I've seen, as a vasodilator. Whether it leads to beneficial remodeling, I don't think we know. There's been some efficacy in patients with coronary artery disease and it seems to be reasonably well tolerated. Whether it will provide any benefit over sildenafil or bosentan, I don't know.

Dr McLaughlin: Inhaled vasoactive intestinal peptide (VIP) will, it's hoped, be studied soon. Rich, do you want to comment on that?

Dr Channick: VIP appears to be an important mediator in the development of pulmonary arteriopathy so is a very attractive target for therapy. Giving the drug by the inhalation route is a great idea. As pulmonologists, we really like the concept of inhaled therapy for pulmonary vascular disease. VIP is certainly an attractive player. There are some preliminary data that look positive. Whether it will add anything, we will have to see. There is no way to extrapolate from animal data or in vitro data to what we see when it comes to patient studies. As many of us have joked, we have cured pulmonary hypertension in the mouse but are still working on the human.

Dr Robbins: If you look at VIP, its effects are almost identical to those of prostacyclin. The only data we have out there are from one small study, and the data were incredibly good, remarkable, in fact. Whether the results could be reproduced, I don't know.

Dr McLaughlin: Are there any other novel therapies that may be entering phase 2 or phase 3 clinical trials in the near future?

Dr Robbins: There's imatinib (Gleevec).

Dr McLaughlin: What do you think of that?

Dr Robbins: I think there are some interesting case studies. There are also some recent reports of patients developing some heart failure who have been treated with imatinib for, what is it, chronic myeloid leukemia? We need to be careful. I think there is a small pilot study going on, so we will see what that shows. We've contemplated using it in a few patients in whom other therapies have failed, but we haven't yet. Rich, have you tried it?

Dr Channick: I have not tried it. I am waiting to see the results of those early studies. All I have seen are a couple of case reports that look favorable.

Dr. Tapson: We have not used imatinib yet, but are coming close. We need to be sure that the case report data can be backed up. This sort of salvage therapy, if effective, could lead to new approaches to induction therapy as well.

We've mentioned some of the combination trials that are going on—the TRIUMPH trial, which is looking at inhaled treprostinil in patients who remain symptomatic while still taking either bosentan or sildenafil as monotherapy—but there are a number of other ongoing combination trials. The COMPASS-2 trial is looking at the addition of bosentan or placebo in patients who are receiving sildenafil monotherapy and remain symptomatic. The COMPASS-2 trial will be the first morbidity and mortality trial ever in pulmonary arterial hypertension. *– Dr McLaughlin*

Dr Channick: Another novel thing is gene therapy. There is a trial with gene therapy going on, is that correct? In Canada?

Dr Robbins: That involves harvesting endothelial progenitor cells and transfecting them with nitric oxide synthase and then readministering them to a patient. Only patients with very advanced disease who have been refractory to many other therapies, I believe, are eligible. I'm not sure that even the first patient has been studied.

Dr McLaughlin: The last question is where and how these patients get treated. It's obviously a complex and relatively rare disease and it requires more than simply prescribing a pill. How do we ensure that patients with this disease get appropriate and comprehensive care, given the current environment?

Dr Channick: In some cases we are victims of our own success. We have done a fabulous job of educating physicians through journals like this about the disease and the diagnostic approach and treatment options. With that education, however, comes the potential of physicians getting in over their heads and managing cases where a patient would be better served by experienced staff at a pulmonary hypertension center. Of course, we can't dictate how physicians treat their patients, but part of the educational message is that there are physicians who do nothing but take care of these diseases and there's no substitute for experience. Making ourselves accessible to community physicians and making it easy to refer patients to a center is a large part of our mission.

Dr Robbins: That's a good point, to create an environment where you have a partnership with community physicians, but I don't know how you can do quality control. As all of us

stress, you can have patients referred for at least a one-time visit. But we all approach patients a little differently and there are different thresholds for treating patients that we use. There is not one way to do it. I don't know how you can enforce any standards, really.

Dr McLaughlin: Vic, Rich, Ivan, thanks again for your participation. As always, it has been great working with you. ■

Editor's Memo

(continued from page 2)

Erika Berman Rosenzweig, MD, to the team of Associate Editors. Her focus and enthusiasm for the journal are refreshing and will help guide content in 2007.

We will benefit also from new input by physicians who are joining our Editorial Board, including Kristin Highland, MD, Ioana Preston, MD, Zeenat Safdar, MD, Rajan Saggar, MD, and Francisco Soto, MD. They will be taking over from physicians whose contribution as Editorial Board members is also much appreciated: Gregory Ahearn, MD, Jacques Benisty, MD, Raymond Benza, MD, and Jeffrey Edelman, MD.

We have seen significant progress in our effort to provide more hope to patients with pulmonary hypertension and I am honored to have been able to work with my colleagues and serve as Editor-in-Chief during the last 2 years. I also look forward to continued involvement with the journal and its outstanding educational program for more than 30,000 physicians engaged in pulmonary hypertension care.

I am sure I speak for all of our physicians and PHA staff in extending our best wishes for a joyous holiday season and a healthy and happy new year.

Vallerie V. McLaughlin, MD
Editor-in-Chief