

**IMPROVING AMERICA'S HEALTH:
EXAMINING FEDERAL RESEARCH
EFFORTS FOR PULMONARY
HYPERTENSION AND CHRONIC PAIN**

HEARING
BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDRED NINTH CONGRESS
FIRST SESSION

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THURSDAY, DECEMBER 8, 2005

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH,

Washington, DC.

The subcommittee met, pursuant to notice, at 10:08 a.m., in room 2123 of the Rayburn House Office Building, Hon. Nathan Deal [chairman] presiding.

Members present: Representatives Bilirakis, Shimkus, Pitts, Ferguson, Rogers, Myrick, Burgess, Pallone, Green, Capps, Deal, Lantos, and Brady.

Staff present: Jeanne Haggerty, Professional Staff Member; Brandon Clark, Policy Coordinator; Chad Grant, Legislative Clerk; John Ford, Minority Counsel; Jessica McNiece, Minority Research Assistant; and Alec Gerlach, Minority Staff Assistant.

MR. DEAL. The chair recognizes himself for an opening statement.

I want to, first of all, welcome all of our witnesses here today. And for those who are in attendance to this hearing, thank you for your presence as well.

I think this is a significant hearing. We have a panel of expert witnesses appearing before us, some of whom are the victims of the diseases that we are going to be talking about, and others who are certainly experts in their own right with regard to seeking relief and cures for those diseases. We are also going to examine what the National Institutes of Health has to say in their studies and in their actions to try to improve conditions and improve patient outcomes in these two areas.

We look forward to hearing their testimony, and we are grateful to all of you for your participation in today's hearing.

As our witnesses will attest, I am sure, if given the choice no one would choose to live with either chronic pain or pulmonary hypertension, which are the two subjects that we are looking at today. I believe that these two conditions highlight the need for further advancement in scientific research at agencies like the National Institutes of Health. That is why I have joined with Chairman Barton, the Chairman of our full committee, in developing legislation that will help eliminate

inefficiencies in the organizational structure of the NIH in order to help increase research investments and outcomes.

I believe that is why we must realign budget items, create a new and more transparent reporting system, and expand the authority of the NIH Director to manage the research portfolio of this very important agency. I believe that by improving the outcomes in scientific recovery, we can vastly improve the lives of people like two of our witnesses today, Charity and Captain Pruden.

And I will introduce our witness panel in just a few minutes after the conclusion of other opening statements, but at this time, I would like to ask of the committee unanimous consent that two of our members who are not members of this subcommittee or our full committee be allowed to join us here on the dais and to make brief opening statements at the conclusion of the opening statements of other members of this subcommittee, and that would be our good friends, the Honorable Tom Lantos, and our other good friend, the Honorable Kevin Brady. Without objection, it is so ordered. You gentlemen may come to the front.

[The prepared statement of Hon. Nathan Deal follows:]

PREPARED STATEMENT OF THE HON. NATHAN DEAL, CHAIRMAN, SUBCOMMITTEE ON
HEALTH

The Committee will come to order, and the Chair recognizes himself for an opening statement.

We have an expert panel of witnesses appearing before us today that will help us better understand chronic pain and pulmonary hypertension and examine what the National Institutes of Health and others are doing to study these conditions and improve patient outcomes. We look forward to hearing your testimony, and we are grateful for your participation in today's hearing.

Today's panel includes the following six experts: Dr. Joel Saper, Founder and Director of the Michigan Head Pain and Neurological Institute; Captain John Pruden, United States Army; Mr. Jake Vander Zanden, Vice President and General Manager of Medtronic Global Pain Management; Dr. Mark Gladwin, Chief of the Vascular Medicine Branch of the National Heart Lung and Blood Institute of the National Institutes of Health; Carl Hicks, Vice President of Advocacy for the Pulmonary Hypertension Association; and, Ms. Charity Sunshine Tillemann-Dick, accomplished vocal performer, advocate for those who share her experience of living with pulmonary hypertension, and granddaughter of the Honorable Tom Lantos of California.

As our witnesses will attest, if given the choice, no one would choose to live with chronic pain or pulmonary hypertension, and I believe that these two conditions highlight the need for further advancement in scientific research at agencies like the National Institutes of Health. That is why I have joined with Chairman Barton in developing legislation that will help eliminate inefficiencies in the organizational structure of the NIH in order to help increase research investments and outcomes. I believe that is why we must realign budget items, create a new, more transparent reporting system, and expand the authority of the NIH Director to manage the research portfolio of this very important agency. I believe that by improving the outcomes of scientific discovery we can vastly improve the lives of people like Charity and Captain Pruden.

Again, I welcome our witnesses and thank them for their participation. I now recognize my friend from Ohio, Mr. Brown, for five minutes for his opening statement.

MR. DEAL. I will now recognize my colleague for the purpose of his opening statement, Mr. Pallone.

MR. PALLONE. Thank you, Mr. Chairman.

I would ask unanimous consent to include in the record a statement of our Ranking Member, Congressman Sherrod Brown.

MR. DEAL. Without objection.

[The prepared statement of Hon. Sherrod Brown follows:]

PREPARED STATEMENT OF THE HON. SHERROD BROWN, A REPRESENTATIVE IN CONGRESS
FROM THE STATE OF OHIO

Thank you Mr. Chairman and thank you to the witnesses for joining us today.

We are here today to discuss ways to improve research and care for very two serious health issues: pain care and pulmonary hypertension.

No one wants to see a family member in pain, or to experience it themselves. Yet we tend not to conceptualize pain as a health phenomenon on its own. It's always a symptom of something else.

Unfortunately, for the 75 million Americans suffering from acute or chronic pain each year, this is not just a secondary condition. Pain is something that they live with day in and day out; something that can truly shape their physical, mental and social well-being.

Not only is this a burden on the individual and their family, but it leads to lost productivity in the workforce, with billions of work days, and therefore dollars, lost.

There's no one-size-fits-treatment here since everyone experiences pain differently. And unfortunately, our knowledge of appropriate pain management is seriously underdeveloped.

We need to raise awareness about the importance of treating pain and providing palliative care, and we need to invest in better understanding its dimensions and finding appropriate diagnostic tools and treatments.

The National Pain Care Policy Act of 2005 would recognize improving pain and palliative care as a national priority. The Act would assemble a White House conference on the issue, create a specialized center within the National Institutes of Health, support a national awareness campaign to educate providers and consumers about the availability of pain treatment options and patients' rights, as well as ensure that our military personnel and veterans receive prompt and adequate pain care.

We are also here to talk about pulmonary hypertension, a serious health care disorder afflicting an estimated one hundred thousand Americans, predominantly women. Pulmonary hypertension results from a dangerous increase in blood pressure in the lungs. Depending on the severity, this can ultimately lead to heart failure and death.

Unfortunately, because the most common signs and symptoms—including fatigue and shortness of breath—are associated with a number of conditions, pulmonary hypertension is often misdiagnosed. By the time patients receive an accurate diagnosis, it may be too late for them to receive the transplants that could save their lives.

The Pulmonary Hypertension Research Act would establish a series of pulmonary hypertension centers focused on research, diagnosis and treatment of this serious ailment. As part of this initiative, training programs would be established for health care professionals to promote earlier diagnosis and thereby make a real step to improve patient outcomes.

The bill will also create an information clearinghouse for providers and the public to facilitate greater knowledge and understanding of the disease.

These are important health care issues and they are very deserving of our focus this morning. I commend the chairman for bringing these pieces of legislation to the Committee's attention and I look forward to hearing from our witnesses.

Thank you, Mr. Chairman.

MR. PALLONE. Mr. Chairman, today, thanks to the benefits of government-funded research, we incredibly increased our knowledge about a number of diseases, including HIV-AIDS, Alzheimer's, osteoporosis, heart disease, and other chronic and debilitating diseases, and these advancements have enabled us to better prevent, treat, and cure many ailments that were once thought to be incurable.

Over the past 100 years, government-funded research has led to a number of scientific and medical advances. The development of vaccines and the use and the common practice of medicine has helped reduce the incidents and in some cases stamp out diseases such as small pox, hepatitis B virus, measles, and polio. New treatments have been developed to treat cancer, heart disease, and mental illness. Additionally, we have been able to improve the quality of life in millions of Americans inflicted with these chronic and often painful conditions.

Yet there is so much more work to be done. Today's hearing focuses on Federal research activities, or more importantly, the lack thereof, on two specific conditions: chronic pain management, and pulmonary hypertension. Mr. Chairman, pulmonary hypertension is a serious disease where blood pressure in the lungs rises to dangerously high levels. Over time, the increased pressure damages both the large and small pulmonary arteries in the lungs and can result in heart failure. Many people who suffer from PH are diagnosed only after the disease has entered advanced stages, far too late to provide for any effective treatment or care.

While researchers have made strides at understanding how this rare disease functions and impacts people, we still don't know enough. Additional medical research is clearly needed. Here, not enough information exists about chronic pain. Just like pulmonary hypertension, until recently, it has received relatively scant attention from medical researchers. But here is what we do know. Chronic pain disables more people in America than cancer or heart disease. It costs the U.S. economy more than \$90 billion per year in medical costs, disability payments, and productivity, as well as the emotional toll this condition takes on patients and their loved ones. Yet there is relatively little research done on this condition.

I would like to commend my colleagues who have helped to raise the awareness about these conditions by introducing legislation.

Representative Mike Rogers, a Republican from Michigan, has offered legislation regarding chronic pain that would declare adequate pain research education and treatment as national public health priorities. Also, Representative Kevin Brady of Texas and Tom Lantos of California have introduced H.R. 3005, the Pulmonary Hypertension Research Act of 2005, of which I am a co-sponsor. This bill would provide for much-needed research and help raise awareness about pulmonary hypertension.

I would also like to commend our panel of witnesses for the work that they are doing to help raise awareness about these conditions. I understand that Congressman Lantos' granddaughter is with us today as a witness. I would like to welcome her to the committee, as well as all of our other witnesses, and we look forward to hearing your testimony.

I thank you again for calling today's hearing, Mr. Chairman. I think that we can all agree that much of the medical and scientific advances we have made over the past century would not have been possible if it were not for the government support. But again, significant challenges remain that will require continued Federal commitment. Research into pulmonary hypertension and chronic pain are just the tip of the iceberg. Our Nation is faced with a number of health-related problems that will require substantial investment in medical research, including an aging population who undoubtedly continue to suffer from age-related diseases, traditional killers like HIV-AIDS and cancer, as well as new and emerging threats like avian influenza and other infectious diseases.

While I know that most of us here today agree that the commitment to Federal research must continue, advances in medical research may suffer because our Nation is currently overextended. Increasing amounts of money for the war in Iraq combined with tax cuts to the wealthy have significantly drained the Treasury, as indicated by the large Federal deficits we have been running. As a result, domestic priorities have suffered. If we are going to be serious about continuing the progress we have made in the past 100 years, then we need to put our money where our mouth is. It is not fair to continue to make empty promises to those who depend on government-funded research for the cures and treatments they so desperately need.

I yield back, Mr. Chairman.

MR. DEAL. I thank the gentleman.

I recognize our distinguished colleague, Mr. Bilirakis, for an opening statement.

MR. BILIRAKIS. Thank you, Mr. Chairman. And I, too, thank you for calling this hearing.

As former chairman of this subcommittee, I understand the competing demands, Mr. Chairman, with which you are faced and appreciate your willingness to devote time to these important issues.

The two topics which are the focus of this hearing are lesser known but nonetheless debilitating conditions, which affect millions of Americans each year and carry with them enormous personal and economic costs.

I first became aware of pulmonary hypertension when our colleague from California, Congressman Lantos, approached me several months ago and told me that his granddaughter, who we will hear from shortly, is suffering from this disease, which primarily affects young women. Tens of thousands of Americans share compelling stories like hers. They are all looking to us to help them beat this cruel disease.

This disease, which, as I understand it, is a blood vessel disorder in the lungs, which causes the pressure in the heart's pulmonary artery to rise, is very often life-threatening and can significantly shorten the life expectancy of those who have it. It is often misdiagnosed because its early symptoms are consistent with many other common conditions. The delayed diagnosis of pulmonary hypertension means fewer and more severe options for those it afflicts, which makes research into its prevention and treatment particularly, Mr. Chairman, important.

I share with nearly 250 of our colleagues in co-sponsoring H.R. 3005, the Pulmonary Hypertension Research Act. It is bipartisan legislation to expand, intensify, and coordinate Federal research efforts in pulmonary hypertension. I believe it is critically important to ensure that Federal research efforts in this area are as protected as possible to best help those suffering from this disease and support those seeking its cure.

I also am pleased that we are exploring the issue of chronic pain and pain management research. While there are no definitive statistics of how many Americans suffer from chronic pain and to what extent it impacts our society, there is little doubt that chronic pain is a serious public health problem that deserves our attention. I met last year with comedian and entertainer Jerry Lewis, who told me he had suffered from chronic pain for more than 30 years before receiving neurostimulation, which we will hear about later. He recounted how he had tried pain medications, physical therapy, and other traditional and non-traditional treatments to alleviate his hip and back pain. He described the sense of despair and hopelessness that chronic pain sufferers live with each day of their lives. We let it up to those who live with this type of pain to encourage Federal efforts in this area, and I also commend our colleague from Michigan, Mr. Rogers, for introducing legislation that seeks to raise public awareness about chronic pain and establish a national pain care policy.

Mr. Chairman, along with you and others, I look forward to hearing the testimony of today's witnesses and working with each other, the members of this committee, in a bipartisan basis, underlining bipartisan, to maximize Federal research efforts for pulmonary hypertension and chronic pain.

And again, I thank you, Mr. Chairman.

MR. DEAL. I thank the gentleman.

I am pleased to recognize our colleague, Ms. Capps, for an opening statement.

MS. CAPP. Thank you, Mr. Chairman, for calling together this important hearing. I am going to waive my opening statement, but I do want to welcome each of our witnesses coming to testify today, and would hope that this committee take appropriate action commensurate with the expertise that we are about to hear.

I yield back.

MR. DEAL. I thank the lady.

Dr. Burgess is recognized for an opening statement.

MR. BURGESS. Thank you, Mr. Chairman.

And in the interest of time, I wanted to hear from our panel. I will waive my opening statement as well.

MR. DEAL. I thank the gentleman.

Mr. Green is recognized for an opening statement.

MR. GREEN. Thank you, Mr. Chairman.

And I would like to welcome my good friend and colleague, Kevin Brady, to our Energy and Commerce hearing, and also Tom Lantos, who is a good friend, and of course, his granddaughter and Tom's wife are here.

Mr. Chairman, I waive my opening statement, but I appreciate you calling this hearing on the issue of chronic pain management and also on the issue of pulmonary hypertension.

Thank you.

MR. DEAL. Thank you.

I recognize Mr. Ferguson for an opening statement.

MR. FERGUSON. Thank you, Mr. Chairman.

I will also submit my statement for the record, but I do want to welcome our panelists. I certainly welcome Mr. Lantos' granddaughter, and I welcome Mr. Lantos and Mr. Brady to join us for this important hearing today.

Thank you.

[The prepared statement of Hon. Mike Ferguson follows:]

PREPARED STATEMENT OF THE HON. MIKE FERGUSON, A REPRESENTATIVE IN CONGRESS
FROM THE STATE OF NEW JERSEY

Mr. Chairman, thank you for holding this important hearing that will delve into two afflictions that are a cause of concern for many people in our country.

It is important that we have hearings like this to shine light on the problems of people who suffer from these ailments.

More importantly, we will discuss solutions and what we can do to initiate action and find cures.

Today, we are concentrating on those who suffer from chronic pain and people who have pulmonary hypertension.

Chronic pain is pain that persists and is different than the normal pain reaction that is experienced with an injury. Chronic pain sometimes continues for days, weeks and months.

Cancer pain is form of chronic pain – so is arthritis. Back or neck injury can cause chronic pain – or some even suffer chronic pain without an injury or evidence of body damage.

There are ways to treat chronic pain – including medication, acupuncture, local electrical stimulation and brain stimulation – and even surgery.

But it is important that more is done to make sure that people receive the treatment they need to help cope with chronic pain.

Pulmonary hypertension is an illness that leads to high blood pressure in the arteries that supply the lungs. The blood vessels that supply the lungs constrict and thicken, making it harder to supply the lungs with needed blood.

It is a serious illness, and treatment is available. I look forward to hearing from the witnesses, including Congressman Lantos' granddaughter to tell us about the problem and how we can help.

Thank you again, Mr. Chairman, for having this hearing on these diseases that affect so many people. I look forward to hearing from our panelists. I yield back my time.

MR. DEAL. I thank the gentleman.

I recognize Mr. Rogers, who is one of the leaders in the issue of chronic pain, and I recognize him for his opening statement.

MR. ROGERS. Thank you, Mr. Chairman.

I will make an opening statement.

I do want to thank you from the bottom of my heart for bringing this forward. We worked with Mr. Bilirakis last year, and he has done a great amount to help bring attention to this issue. Your effort to not only talk about it in the NIH hearings but this hearing alone, I think, sends a pretty clear message that we finally have gotten pain care and chronic pain relief on the radar screen. Millions of Americans thank you for that, Mr. Chairman.

And I also want to welcome Dr. Joel Saper, a friend who I have known in this endeavor for almost 10 years, I think, who has brought a lot of relief to a lot of suffering people and has given them hope. So, Doctor, thank you for your efforts. Thanks for being here today. I certainly appreciate it.

And with that, Mr. Chairman, I will yield back.

MR. DEAL. I thank the gentleman.

Ms. Myrick, you are recognized for an opening statement.

MS. MYRICK. Well, I just welcome everybody.

Thank you.

MR. DEAL. Thank you.

Mr. Lantos, we are pleased to have you with us today, and we will recognize you for an opening statement.

MR. LANTOS. Thank you very much, Mr. Chairman.

I want to express my deepest appreciation to you and to members of the committee for holding this hearing. In the quarter-century I have served in this body, this is the most important hearing from my personal point of view, and I am profoundly appreciative of your cooperation.

I am immensely proud that my granddaughter, Charity, has courageously decided to share her story with us today.

As you will hear, Mr. Chairman, pulmonary hypertension is an illness that has had a devastating impact on tens of thousands of American families, including our own. I want to thank the Pulmonary Hypertension Association and their Vice President for Advocacy, my good friend Colonel Carl Hicks, for his presentation. Their advocacy on behalf of the pulmonary hypertension community is making a tremendous difference in the lives of thousands of people.

Mr. Chairman, pulmonary hypertension has historically been a fatal diagnosis for patients. This is no longer true. I am so delighted to report to you that we are turning the corner in the fight against this condition. With the discovery of the first gene associated with PH in 2000, the development of a range of new treatment options, and the growing awareness of this disease, there is tremendous hope for the future. According to the scientific experts I have spoken with, we are at a turning point in our understanding of this condition. The opportunities for major progress are truly remarkable.

In an effort to capitalize on these opportunities, my dear friend, Congressman Kevin Brady, and I have introduced H.R. 3005, the Pulmonary Hypertension Research Act. This important legislation will expand pulmonary hypertension research activities at the National Heart, Lung, and Blood Institute of the National Institutes of Health. I am immensely grateful that over 240 of our colleagues on a totally non-partisan basis have seen fit to co-sponsor our legislation, and I am deeply grateful to both the Republican and the Democratic leadership of the House for supporting us.

As you know, Mr. Chairman, a companion bill has been introduced in the Senate by Senators John Cornyn and Barbara Mikulski and the growing number of senators that are supporting this legislation.

I would like to take this opportunity to express my gratitude to the leadership of the NIH and for their efforts in the fight against pulmonary hypertension. Dr. Leah Zarhouni and Dr. Betzenager have been tremendous partners, and we look forward to working with them to bring an answer to this condition.

There is some scientific justification for an expansion of research in this area, and I am personally committed to ensuring that we take the next step in the fight against the condition so that Charity and hundreds of thousands of other patients will enjoy a long and healthy life.

Thank you, Mr. Chairman.

MR. DEAL. I thank the gentleman.

Mr. Brady, you are recognized for an opening statement.

MR. BRADY. Thank you, Mr. Chairman.

I want to thank Chairman Deal and the members of the Health Subcommittee for your thoughtful concern about the growing health challenges of pulmonary hypertension and chronic pain. Last month was pulmonary hypertension awareness month, so, Mr. Chairman, your timing could not be better.

I want to also thank the panelists, like Tom, for appearing. The National Heart, Lung, and Blood Institute has been especially involved in PH under the leadership of its Director, Dr. Nabel, and I appreciate Dr. Gladwin being here today.

The Pulmonary Hypertension Association, whose membership has just exploded in numbers in recent years, is a valuable and tireless advocate for this disease, and I appreciate you, Mr. Hicks, for being here today. And Charity Sunshine Tillemann-Dick is the beautiful and very talented granddaughter of our highly-respected colleague, Mr. Lantos, who is the lead Democrat on the H.R. 3005, the Pulmonary Hypertension Research Act. More importantly, Tom and his granddaughter have really put a rocket booster of awareness and push behind this effort to find a cure for this disease. And Tom, I appreciate you so much for your leadership on this issue and Charity for all of your role in this.

Pulmonary hypertension is a complex disease, as Mr. Pallone said. It is considered a rare disease, but as Congressman Green's fellow Houstonian, the President of the University of Texas Health Science Center recently said at a meeting with the Texas Medical Center, "This is becoming not so rare at all among adults." Historically, it affects women of childbearing age, but now this disease is impacting Americans of all ages and all races, more than 100,000 today and growing larger each year. And patients with other illnesses, such as lupus, HIV, sickle cell anemia, and scleroderma are particularly vulnerable to PH. For now, it is an incurable disease, but we have the power to change that.

I decided to do just that when one of my closest friends noticed that his 5-year-old daughter, Emily Stibbs, could not keep up with others on her bike during a parade. She would have to rest each morning as she came down the stairs at breakfast time. After several tries, she was eventually diagnosed with primary pulmonary hypertension. Shortly after, I attended the funeral of a young 17-year-old girl in our community in The Woodlands. Her teenage friends told us at the service how she had spent the last year of her life working with the Make A Wish Foundation to ensure that she left a legacy. I don't think 17-year-olds ought to have to worry about leaving a legacy.

So the good news is, as Tom said, we are making progress thanks to the supportive leadership of Chairman Bilirakis and Chairman Deal of this committee, Federal research in pulmonary hypertension to the NIH has nearly tripled since 1997 to \$30 million. Now \$30 million doesn't seem like a lot, admittedly, but combined with the private research and the fundraising efforts by the PH Association community, it is already having an impact. The number of new treatments for PH are growing. The first was only brought on line in 1997. Today we have five available and five more in trials. That is important, because for patients, the trick is to stretch out each phase of the disease's progression.

Best of all, the survivor rate after diagnosis has now doubled from about 2 to 3 years to 5 years. Now that may not seem like great strides to you, but it is precious hope for many. Some patients may even be able to manage their disorder for 15 to 20 years or longer. And unlike some diseases, we don't have a celebrity spokesman, because ours don't live long enough to be a celebrity spokesman, so we have to reach out through patients and to you for this support.

And how can Congress keep this progress going?

Well, for the past 5 to 6 years, the Congress, our office, the National Heart, Lung, and Blood Institute, and the Pulmonary Hypertension Association has formed a working partnership that established medical infrastructure to attack this disease. We have targeted research carefully and wisely, recruited new investigators and scientists. We are educating the medical community and reaching out to medical researchers in related fields.

And I will conclude by telling you I can report to this committee that very careful infrastructure is now in place to make that large push a tour de cure for this disease. And on behalf of Congressman Lantos and myself, I urge you to continue this effective partnership and to support the Pulmonary Hypertension Research Act. This measure establishes Centers of Excellence within the NIH to increase basic and clinical research to \$50 million each in the next 5 years. Each day, we are

offering more and more hope to PH patients. Our goal is to one day offer a cure.

Thank you, Mr. Chairman.

[The prepared statement of Hon. Kevin Brady follows:]

PREPARED STATEMENT OF HON. KEVIN BRADY, A REPRESENTATIVE IN CONGRESS FROM
THE STATE OF TEXAS

OPENING

I wish to thank Chairman Deal and members of the Health Subcommittee for your thoughtful concern about the growing health challenges of pulmonary hypertension and chronic pain. This is Pulmonary Hypertension Awareness Month, so the timing is perfect.

I also want to thank the panelists for appearing:

- The National Heart, Lung, and Blood Institute has been especially involved in PH under the leadership of its Director, Dr. Elizabeth Nabel. (Dr. Mark Gladwin is appearing today)
- The Pulmonary Hypertension Association, whose membership has exploded in numbers in recent years, is proving a valuable and tireless advocate for this disease. (Carl Hicks, VP of PHA).
- And Charity Sunshine Tillemann-Dick is the beautiful and talented granddaughter of our highly respected colleague, Congressman Tom Lantos – the lead Democrat on HR 3005, the Pulmonary Hypertension Research Act.

Pulmonary Hypertension is a complex health problem – continuous high blood pressure in the pulmonary artery in the lungs that results in an enlarged heart and eventually losing the ability to pump. It's considered a rare disease, but as Dr. James Willerson, president of the University of Texas Health Science Center recently stated at a meeting at the Texas Medical Center, this is becoming not so rare at all among adults.

Historically affecting women of child bearing age, this disease now attacks Americans of all ages and all races in growing numbers - more than 100,000 today and growing larger. Patients with other illnesses, such as Lupus, HIV, sickle cell anemia and scleroderma have particular vulnerability to PH.

For now it is an incurable disease. But we have the power to change that.

I decided to do just that when one of my closest friends noticed at a parade his five year-old daughter – Emily Stibbs – could not keep up on her bicycle with the other kids, and had to rest each time she simply walked down the stairs at their home. She was, after several tries, eventually diagnosed with Primary Pulmonary Hypertension.

Shortly after I attended the funeral of a young 17 year old girl in our community – Kristen Cote – whose teenage friends recounted during the service how she spent the last year of her life helping the local Make-A-Wish Foundation because she wanted to leave a legacy for her life. Seventeen year olds just shouldn't be spending their days concerned about leaving a legacy.

PROGRESS

The good news is that we're making progress.

Federal research in Pulmonary Hypertension through the National Institutes of Health has nearly tripled since 1997 to \$30 million. That's not much, admittedly, but combined with private research and fundraising efforts by the PH patient community, it's already having an impact.

The number of new treatments for PH are growing. The first, FLOLAN, was introduced in 1996. Now there are five FDA-approved treatments and five more in trials. That's important because for patients the trick is to stretch out each phase of the disease's progression.

Best of all, the survival rate after diagnosis has now doubled from 2-3 years for most PH patients to 5 years. That may not seem like great strides to you, but it's precious hope for many. Some patients may even be able to manage the disorder for 15-20 years or longer.

HOW CAN CONGRESS KEEP THIS PROGRESS GOING?

For the past five-six years our office, the National Heart, Lung and Blood Institute and the Pulmonary Hypertension Association have created a working partnership to establish a medical infrastructure to attack this disease: targeting research carefully and wisely, recruiting new investigators and scientists, educating the medical community and reaching out to medical researchers in related fields.

I can report to you the infrastructure is now in place to push toward a cure for this disease.

On behalf of Congressman Lantos and myself, I urge you to continue this effective partnership and to support The Pulmonary Hypertension Research Act, HR 3005, which has 240 bi-partisan sponsors. The measure establishes Centers of Excellence within NIH to increase basic and clinical research by \$50 million each of the next five years, train new investigators, collect better data and generate more accurate and timely physician diagnosis.

Each day we are offering more and more hope to PH patients. Our goal is to one day offer a cure.

Thank you.

MR. DEAL. Thank you.

Mr. Shimkus, would you care to make an opening statement?

MR. SHIMKUS. Not after my roommate just talked. I'm done.

[Additional statements submitted for the record follow:]

PREPARED STATEMENT OF HON. JOE BARTON, CHAIRMAN, COMMITTEE ON ENERGY AND COMMERCE

Thank you, Chairman Deal, for holding this hearing today. This hearing addresses two serious conditions. Both pulmonary hypertension and chronic pain are debilitating and in some cases fatal conditions. I am pleased that the Committee is examining these important issues and learning about what current research is being done and how our efforts to address these problems could be improved.

Chronic pain and pulmonary hypertension are terrible disorders that affect millions of people. I commend my friends on the Committee, Mr. Rogers and Mr. Norwood, for all of their work on chronic care management. I'd also like to welcome my colleagues Mr. Lantos and Mr. Brady here today. While they are not Members of the Energy and Commerce Committee, both have been extremely active with regard to pulmonary hypertension.

I believe that today's hearing will further stress the importance of something that I am deeply committed to, and that is the reauthorization of the National Institutes of Health. Members of this Committee know that one of my top priorities is making improvements at our public health agencies, and particularly at the NIH. Although NIH's research portfolio is largely dedicated to basic research that transcends disease specific research, applying this research so that it directly benefits patients suffering from specific disease like pulmonary hypertension or chronic pain, is critical. I believe that improving the organization and structure of NIH could maximize our investments in public health.

Once again, I appreciate all of the time the witnesses have taken to make this an informative hearing. Thank you for helping us to raise awareness about chronic pain and

pulmonary hypertension so that more Americans recognize the symptoms of these conditions and can begin treatments early.

PREPARED STATEMENT OF HON. BARBARA CUBIN, A REPRESENTATIVE IN CONGRESS FROM
THE STATE OF WYOMING

Thank you Chairman, for calling today's hearing. I'd also like to thank the witnesses who have agreed to join us here today, as well as Representative Lantos, who is accompanying his Granddaughter. Today, we will have the opportunity to gain a better understanding of two very devastating and unfortunate medical conditions. We will also discuss how Federal research dollars can be most effectively used to research both chronic pain and pulmonary hypertension.

Over 100 million Americans today are living with some form of chronic pain, and approximately 100,000 suffer from primary pulmonary hypertension. These conditions are frequently very difficult to diagnose, and the prognosis is often bleak. Like any chronic disease, the long term treatment to mitigate the effects of these conditions can be prohibitively expensive. For example, it is estimated that pulmonary hypertension patients pay as much as \$100,000 a year for medications. However, the costs associated with chronic illness extend far beyond anything that can be measured in monetary value. I have personally seen the heartbreaking struggle to cope with the daily impacts of chronic pain, and I would not wish this hardship on any family. The challenge to adapt one's lifestyle in a manner that compensates for pain management can be overwhelming, frustrating, and depressing. I hope today's hearing will reveal insight on current research endeavors that may help patients better manage chronic pain.

I am aware several institutes and centers at the National Institutes of Health are engaged in ongoing research regarding management of different types of chronic pain. I expect today's hearing to shed light on these continuing efforts, as well as emphasize the importance of sharing information to prevent duplicative research. In addition, I will also be interested to hear what technological advances private industry has made to help patients better manage chronic pain. Living with chronic pain can be more devastating than a catastrophic health crisis, but I do believe medical technology can be utilized to help patients continue to enjoy life.

Once again, I thank the Chairman for calling this hearing, and I reserve the balance of my time.

PREPARED STATEMENT OF HON. CHARLIE NORWOOD, A REPRESENTATIVE IN CONGRESS
FROM THE STATE OF GEORGIA

Thank you Mr. Chairman,

We don't do a good enough job to alleviate pain. We do not understand chronic pain, and we have barely scratched the surface of how chronic pain impacts Americans. There is a significant problem of under-treatment of pain and our medical professionals lack proper training in pain management. The federal government's approach has been often misguided.

Millions of Americans, often needlessly, suffer from acute and chronic pain. 45% of Americans will seek care for persistent pain at some point in their lives and 70% of cancer patients in the U.S. suffer from chronic pain.

Pain has a tremendous cost in terms of health care services, lost productivity and personal suffering.

For many of these patients, drug therapy is an important part of treatment. Thankfully, effective prescription medications are available. While not all pain medications are controlled substances, many are.

I am proud to be a cosponsor of Mr. Roger's legislation (H.R. 1020) to expand the study and treatment of pain. However, if we don't address prescription drug abuse, no bill expanding access is going to make a lick of difference. No doctor will want anything to do with providing these services.

We need a comprehensive strategy that removes bad actors while increasing our understanding of pain. Mr. Roger's bill plays a part, and NASPER – legislation I authored encouraging state prescription abuse monitoring programs – was a good first step.

A compelling need also exists for abuse-resistance drugs. In addition, I plan on reintroducing legislation that's going to address some other issues.

For example we need to reign in Internet pharmacies. Right now, I could go on the Internet and buy a controlled substance just by pointing and clicking two things: "*I need this drug, and I'm not lying.*"

The addiction community tells me these sites represent one of the easiest ways of getting access to controlled substances, and that fact should worry us all.

Also, I want to know when a drug leaves a manufacturer, where does it go? If a secondary wholesaler buys counterfeit drugs and sells them to a retailer, how do we know? What is the best means to dispose of an unused controlled substance?

My legislation is going to try to answer some of those questions.

Above all, we need to address these issues so that the true victims of prescription drug abuse—patients suffering from chronic pain—will be able to reap the benefits of the medical research aimed at alleviating their suffering. I look forward to the testimony of our witnesses.

MR. DEAL. Wise man.

We do, indeed, have a distinguished panel, and I am pleased to introduce them at this time.

First of all, Dr. Joel Saper, who is the Founder and Director of the Michigan Head Pain and Neurological Institute, Captain John Pruden of the United States Army, Mr. Jake Vander Zanden, Vice President and General Manager of Medtronic Global Pain Management, Dr. Mark Gladwin, Chief of the Vascular Medicine Branch of the National Heart, Lung, and Blood Institute of the National Institutes of Health, Mr. Carl Hicks, Vice President of Advocacy for the Pulmonary Hypertension Association, and Ms. Charity Sunshine Tillemann-Dick, accomplished vocal performer, advocate for those who share her experience of living with pulmonary hypertension, and of course, as already has been stated, the granddaughter of our friend, the honorable Tom Lantos of California.

Welcome. And Dr. Saper, we will start with you.

I would remind everyone that we already have made your written statements a part of the record, and if you would just summarize those statements for us, we would appreciate it.

Dr. Saper. Let us make sure the microphone is on. There you go.

**STATEMENTS OF JOEL SAPER, FOUNDER AND DIRECTOR,
MICHIGAN HEAD PAIN AND NEUROLOGICAL
INSTITUTE; JOHN PRUDEN, UNITED STATES ARMY;**

JAKE VANDER ZANDEN, VICE PRESIDENT AND GENERAL MANAGER, MEDTRONIC GLOBAL PAIN MANAGEMENT; MARK GLADWIN, CHIEF, VASCULAR MEDICINE BRANCH, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH; CARL HICKS, VICE PRESIDENT, ADVOCACY, PULMONARY HYPERTENSION ASSOCIATION; AND CHARITY SUNSHINE TILLEMANN-DICK

MR. SAPER. Thank you, Mr. Chairman.

I am the Director of the Michigan Head Pain and Neurological Institute and Chairman of the Pain Care Coalition, and I am also current past President officer of the American Headache Society, the American Pain Society, and the American Academy of Pain Medicine, among others. I am a board-certified neurologist and a pain specialist and clinical associate professor of neurology.

I have devoted my entire 35-year professional career to research, teaching, and clinical practice to improving the lives of people who suffer from severe pain.

Mr. Chairman, the problem of pain in this country is an enormous size. As Mr. Pallone already noted, pain is the most common reason people seek medical help. Over 100 million Americans suffer from continuous and frequent pain, and chronic pain is the leading cause of disability. Reduced productivity due to pain to employers' costs between \$60 and \$120 billion annually, and the total cost of pain to the healthcare system and the broader economy cannot even be calculated, but it is larger than any other health condition, such as heart disease, hypertension, or diabetes. Chronic back pain alone is estimated to cost over \$25 billion to national healthcare tabulations.

Most illnesses lead to pain, and chronic pain leads to many other illnesses. From the acute pain of trauma or surgery or sickle cell disease, severe burns, cancer, heart disease, AIDS, diabetes, MS, migraine, and so many more, pain cuts indiscriminately across demographic lines and across the populations of this subcommittee that so wants to serve the elderly, the disabled, and the medically indigent.

Pain can kill. It can kill the spirit, vitality, and the will to live. Pain also alters the immune system and changes the brain. It makes its victims more vulnerable to other diseases. Moreover, loss of income, careers, quality of personal and family life and the joy of living are trumped by the daily and persistent agony of pain and the desperation and isolation that comes with it. The lives of those afflicted and their families are placed on the brink if not defeated altogether.

And despite great scientific strides in the past decade, improved treatment facilities and techniques, the availability of powerful medicines, and credentialed specialists, we are far from accomplishing a satisfactory impact on this enormous worldwide problem. Too many people suffer daily severe pain. We have no panaceas. We need more knowledge and more tools.

I understand that the subcommittee's primary interest today is in assessing the adequacy of Federal research on chronic pain. It is discouraging to report that halfway through the congressionally-declared decade of pain control in research, that the research commitment to pain is woefully inadequate and hardly proportional to the burden pain places on this society. An exhaustive study of NIH pain research concluded that NIH devotes a scant 1 percent of its research budget to projects with a primary focus on pain. There is little indication that NIH considers pain research to be a higher priority today than it was 10 years ago.

Nor does the data suggest a concerted effort to prioritize what little the NIH does invest in pain or to coordinate that investment across the institutes. Immediate means for expanded research in pain include, among many others, basic research to both fully understand the complex mechanisms of pain perception and how pain changes the brain; better understanding of the linkages between brain mechanisms and emotions; gender differences between males and females with respect to response to treatment and how pain affects them, basic and clinical research into how acute pain becomes chronic pain; a better understanding of the long-term risks and benefits of our treatments; and, of course, new and breakthrough treatments and therapies are badly needed.

Mr. Chairman, I could go on, but I know time does not permit, and we will make this data and other research priorities available to you and your staff.

Pain, as a public health problem, demands a comprehensive Federal response promoting research, education, and access to care. For this reason, the Pain Care Coalition and dozens of other professional and patient advocates strongly support H.R. 1020, the National Pain Care Policy Act, introduced by Congressman Rogers. It is the only comprehensive pain bill pending in the current Congress, and indeed, it is the only comprehensive pain bill ever introduced in Congress. And I urge you to hold further hearings in this subcommittee to explore problems with education and access to care, which are of equal importance to those in research, which we are discussing today.

Mr. Chairman, in a comprehensive pain bill, there are several short-term measures that could make a difference. These include requiring more coordination across institutes, Federal reporting of what NIH already spends, and more extramural participation in the priority-setting

process. These steps could be taken now at very little cost, and I urge you to consider them.

In closing, Mr. Chairman, I want to share a personal brief perspective. Our center in Ann Arbor is a national referral center for patients with intractable and severe pain. Many of those sent to us are children, and most of our patients are adults in their working years who cannot work. The majority comes to our center on large dosages of narcotic medications, and despite these, the pain is worsened, and so have the desperation and the side effects. They have exhausted their insurance, they have no insurance, or what insurance they have won't cover pain care. Most can not function normally or even go to school or even care for their families. We are able to help many of these, but too many are not able to be helped. Lives become hopeless, people give up, and you know that story from Michigan.

Mr. Chairman, thank you again for bringing these issues forward to the committee and to the House. My colleagues and I in the Pain Care Coalition look forward to working with you and Congressman Rogers and others. Working together, I know we can make a difference for the millions who suffer in pain today and every day of their lives.

Thank you.

[The prepared statement of Joel Saper follows:]

PREPARED STATEMENT OF JOEL SAPER, FOUNDER AND DIRECTOR,
MICHIGAN HEAD PAIN AND NEUROLOGICAL INSTITUTE

Mr. Chairman and Members of the Subcommittee, thank you for the opportunity to appear before you today. I welcome this hearing, and I applaud your leadership and that of Congressman Rogers, in bringing national attention to pain as a major public health problem in this country.

I am Joel Saper, Founder and Director of the Michigan Head Pain and Neurological Institute in Ann Arbor, Michigan, and Chair of the Pain Care Coalition. I am also a current or past president/officer or director of the American Headache Society, the American Pain Society and the American Academy of Pain Medicine, among others. I am a board-certified neurologist and pain specialist, and Clinical Associate Professor of Neurology, and I have devoted my entire professional life (35 years), through research, teaching, and clinical practice, to improving the lives of people who suffer from pain.

The Problem

Mr. Chairman, the problem of pain in this country is of enormous size:

- Pain is the most common reason people seek medical help.
- Over 100 million Americans suffer from continuous or frequent pain.
- Chronic pain is a leading cause of disability, both temporary and permanent.
- Reduced productivity due to pain costs employers somewhere between \$60 and \$100 Billion annually.
- The total cost of pain to the health care system and the broader economy cannot be currently calculated but is larger than any other health care condition, such as heart disease, hypertension, or diabetes. A single example--chronic back

pain—is estimated to add over \$25 Billion annually to national health care costs.

- Most illnesses lead to pain, and chronic pain leads to many other illnesses. From the acute pain of trauma or surgery or sickle cell disease or severe burns to the chronic pain of cancer, heart disease, AIDS, MS, arthritis, bone disease, diabetes, colitis, back and neck disorders, migraine, fibromyalgia, RSD, TMJ, and on and on and on, pain cuts indiscriminately across demographic lines, and across the populations that this Subcommittee does so much to serve—the elderly, the disabled, and the medically indigent.
- Pain can kill: it can kill the spirit, vitality, and the will to live. Pain also alters the immune system and makes its victims more vulnerable to other diseases. Moreover, loss of income, careers, quality of personal and family life, and the joy of living are trumped by the daily and persistent agony of pain and the desperation and isolation that come with it. The lives of those afflicted and their families are placed on the brink, if not defeated altogether.
- And despite great scientific strides in the past decade, improved treatment facilities and techniques, the availability of powerful medications, and credentialed specialists, we are far from accomplishing a satisfactory impact on this enormous world-wide health problem. Too many people suffer daily, severe pain. We have no panaceas. We need more knowledge and more tools

The Federal Research Commitment

I understand that the Subcommittee's primary interest today is in assessing the adequacy of federal research on chronic pain. It is discouraging to report that, half way through the Congressionally-declared Decade of Pain Control and Research, that research commitment is woefully inadequate, and hardly proportional to the burden pain imposes on the population. An exhaustive study of NIH pain research, based on FY 2003 grant awards, concluded that NIH devotes a scant 1% of its research budget to projects with a primary focus on pain. Broadening the inquiry to include grants that have some, perhaps only marginal, relationship to pain, only adds another 1 and 1/2% of the pie. While longitudinal data is not readily available, there is little indication that NIH considers pain research to be a higher priority, in any sense of the word, today than it was ten years ago.

Nor does the data suggest a concerted effort to prioritize what little the NIH does invest in pain, or to coordinate that investment across Institutes, Centers and programs. If back pain costs the health system \$26 Billion annually, is an investment in all forms of musculoskeletal pain research of less than \$50 Million—one fifth of one percent--reasonable? If cancer pain gets another \$50 Million, why does cardiac pain get less than \$2 Million, or headache less than \$20 Million? To put the latter figure in perspective, it represents less than one dollar a year for each and every migraine sufferer in this country. And if cancer pain does get \$50 Million, why is a third of that funded through channels other than the National Cancer Institute? Or, if some Institutes devote 80% or more of their pain research effort to basic research, why do others spend 90% or more on clinical research at the expense of basic research?

Immediate needs for expanded research in pain include, among many others, the following broad areas:

- Basic research to more fully understand complex mechanisms of pain perception and development in the brain;
- Better understanding of the linkages between brain mechanisms and emotions that effect the perception and severity of pain;
- Basic and clinical research into how acute pain (e.g. post operative or trauma pain) becomes chronic pain, and how to prevent it; and

- Better understanding of the long term risks of current therapies on brain function and long term pain prevention.

Mr. Chairman, I could go on but time does not permit, and we will make this data and other research priorities available to you and your staffs so that you may draw your own conclusions from it. Let me instead suggest some possible solutions.

Recommendations

The enormity of pain as a public health problem demands a comprehensive federal response promoting research, education and access to care. For this reason, the Pain Care Coalition and dozens of other professional and patient advocates strongly support HR 1020, the National Pain Care Policy Act, introduced by Cong. Rogers. It is the only comprehensive pain bill pending in the current Congress. Indeed, it is the only comprehensive pain bill ever introduced in the Congress, and I urge you to hold further hearings in this Subcommittee to explore problems of education and access which are equal in importance to those of research which we are discussing today.

Short of a comprehensive and long term response to the major public health problem which pain represents, there are a number of short term measures in the area of research alone which the Subcommittee should consider.

First, I understand that both Congressional and NIH leadership are seeking more effective “trans Institute” coordination of research activities. Chronic pain research would be a natural candidate for such an initiative. With funding spread across three principal Institutes, and a dozen more with smaller concentrations, the benefits of enhanced coordination and cross fertilization could be significant. NIH’s existing “Pain Consortium,” which now exists mostly in theory, could, with modest funding and staff, become a powerful tool for assessing and setting priorities across the various offices with a stake in pain research.

Second, better information could be a powerful tool for better prioritization of research dollars. The data I described a few moments ago were gleaned from NIH records by private researchers. NIH itself should be required to explain to this Committee and other interested legislators what it does on pain each year, why it focuses where it does, and what is being accomplished. This would help the NIH Director set priorities in his annual budget requests, and help legislators assess whether those requests reflect an adequate allocation of research dollars to the needs of patients in pain.

Third, extra-mural participation is critical to identifying the most pressing research needs in the pain field. Currently, perhaps because pain has no single home at NIH, there is no structured opportunity for either basic scientists or clinicians in the pain field to work with NIH leadership to establish a broad pain research agenda. With the Decade of Pain Control and Research half over, now would seem an opportune time to bring people together to take stock of what has been accomplished, and what remains to be done.

Fourth, NIH needs to invest in infrastructure development in the pain field. Other significant disease categories have either intra-mural or extra-mural centers of clinical and research excellence, and in many cases both, that advance research over years and sometimes decades. This capacity is seriously lacking in pain research.

These are modest suggestions. They will not produce dramatic research breakthroughs, nor bring immediate relief to the millions of chronic pain patients in this country. But they also won’t bust any budgets in a time of fierce competition for research dollars. Nor will they complicate the NIH organizational chart at a time when many of you seek to simplify it. I commend them to your consideration, and would be pleased to explore them in more detail with you.

In closing, Mr. Chairman, I want to share a personal perspective. Our center in Ann Arbor is a national referral center for patients with intractable and severe pain problems. Many of those sent to us are children, and most patients are in their working years. The majority come to our center on large dosages of narcotic medications, and despite these,

the pain has worsened, and so has the desperation and side effects. Most cannot work or go to school or even care for their families. Despite the challenges, we are able to help many of these people, but many are not helpable. Lives become hopeless.

Mr. Chairman, thank you again for bringing these issues forward to this Committee and in the House. My colleagues and I in the Pain Care Coalition look forward to working with you, Congressman Rogers, and others. Working together, I know we can make a difference for millions who suffer in pain today and every day of their lives.

MR. DEAL. Thank you, Dr. Saper.
Captain Pruden.

CAPTAIN PRUDEN. Mr. Chairman, members of the subcommittee, I thank you for your time today.

I have kind of a perspective on pain. I was, 2 years ago, wounded in Baghdad by an IB. I took 173 pieces of shrapnel and one bullet. Over the course of the next 2 years, I underwent 20 operations. I had numerous pain care specialists working with me. This is actually my first trip out of the wheelchair today, and it is exciting to be up and around. It is a little bit painful, but things are going pretty well.

Before I joined the military, I was working for EMS. I worked as an EMT. I had had some experience with pain, but nothing quite prepared me for the experiences I had being wounded and coping with this severe chronic pain, and witnessing my surgeons and the men and women to my left and right in uniform, who were also wounded, trying to cope with this chronic severe pain. Partially due to this chronic pain, this past summer, I decided to have my leg amputated after trying to deal with it for 2 years. It was a tough decision. I think it was the right one. Pain really changes your life. It is a debilitating thing. I found myself adjusting my schedule, changing what I was doing day in and day out to try to facilitate my pain. I would look at a given activity and think, "How much is this going to cost me in pain? How long am I going to have to recover after this? And how much medication am I going to have to take to cope with this? Is it worth it?"

Telling you about the uncontrolled pain and how difficult that is, you know, I will talk about some of the things that happened with Mike here. I had some really good pain management care through narcotics, through Oxycontin. I have been on that drug for 28 months. Actually, I have recently weaned myself off of that. After the amputation, my pain level has decreased, and I have been able to get off that medication entirely, but I can't state strongly enough what a benefit that was to me, and how it allowed me to get on with my life. There is a great fear out there of narcotics, and it seems like the medical community is oftentimes hesitant to prescribe needed narcotics for pain because of fear of legal implications or prosecution by Federal or State officials.

One thing over the past few years, also, is my soldiers are back in Iraq right now for the next year and we have already lost some soldiers and have brought several back, unfortunately, severely wounded. I have been working with them week in and week out. And there are a lot of gaps in their pain care. I have a little bit of a medical background. I was an officer, and through my assertiveness and them pushing some buttons, I was able to get the care that I needed getting to the right people, but unfortunately, there is a big gap between the hospital and adequate palliative care. Unfortunately, they fall through the cracks too often and don't ask for help due to several factors, as you know, the stigmas associated with taking narcotics for pain care, you try and be tough and not ask for help if we need. It's amazing how many guys just live with the pain and suck it up and try to drive on.

Looking at some of the gaps in treatment and care that I have witnessed, it seems important to me to have physicians who understand all of the different medications and treatments that are available for pain management, and more importantly to have good links with the experts, with the palliative care experts and the anesthesiologists so that there is not that gap, that disconnect.

And then finally, you know, there really is a lot to understand, and I went through about 12 different physicians and anesthesiologists over the past couple of years. I tried over half a dozen different pain medications. Oxycontin was the one that worked best for me, but I saw some other guys that it didn't work for. There are some pain conditions that there is nothing out there to treat right now. It seems like the H.R. 1020 would take positive steps in the direction of facilitating research to address these issues and then try to help millions of people suffering from chronic pain nationwide.

Thank you.

[The prepared statement of Captain Jonathan D. Pruden follows:]

PREPARED STATEMENT OF CAPTAIN JOHN PRUDEN, UNITED STATES
ARMY

On 01JUL03 I was severely injured in an IED attack near the UN headquarters in Eastern Baghdad, Iraq. I was there with the Third Infantry Division on the initial movement up from Kuwait. I had some previous experience with pain from severely breaking my right leg in college playing flag football requiring three operations. I also worked as an EMT for almost three years where I encountered a great deal of acute pain due to disease and physical trauma. None of these experiences prepared me for what it is like to live with chronic pain.

After taking 173 pieces of shrapnel and one bullet I quickly became hypovolemic, due to tremendous blood loss from both legs, and a large hole in my back. Tourniquets were placed on both my legs as I started to go into shock. After a couple of surgeries at a CSH in Iraq to stabilize me, I was MEDEVACed to Landstuhl in Germany, and after a couple more surgeries I made it to Walter Reed. Over the next two years I had numerous

surgeries to try to put me back together. After a total of 18 surgeries at six different Army hospitals I elected to have my right leg amputated this past summer.

The decision to amputate was not an easy one but it was, in hindsight, right one. One of the primary reasons I decided to amputate my leg was the chronic pain it caused and the acute pain I experienced each day at Physical Therapy as I attempted to bear weight on it. For two years I coped with, often times, debilitating pain.

Pain is a powerful thing. It changes everything. Your whole life is altered to accommodate it. In military hospitals all around the nation I witnessed strong young Infantrymen, Medics, and Snipers buckle under its crushing weight. Exhausted emotionally and physically they cried out in pain. I recall many long painful, sleepless nights at in hospitals and at home. When the pain was at its worst I would have done almost anything to rid myself of it but all I could do was call a nurse and hope they could ease the pain a little with another dose of Morphine. After a surgery or a tough Physical Therapy session all I could focus on was the pain. I really enjoy reading but my chronic everyday pain when uncontrolled was such that I couldn't focus to read. I found myself changing my activities and my schedule to accommodate my pain. I would often look at potential activities with an eye to how much pain it would cost me and subsequently how much medication and rest I would need to recover from it. Each day I would anxiously await the time I could take my medications, not so much because of a physical dependence, but because of a real need to control my pain.

In the same breath as I describe the challenges of uncontrolled pain I'll tell you how, for the most part, my pain was effectively managed with Oxycontin. During my extensive hospital stays I had dozens of physicians, specialists, and anesthesiologists. Through them I tried at least half a dozen pain control medications, and Oxycontin was consistently the best for managing my pain without the roller coaster effect and with minimal side effects.

Narcotics such as Oxycontin conjure up images of drug abuse, crime, and addiction for many people. While concerns over the illegal or improper use of narcotics are certainly legitimate. The line between the two should be very clear. Physicians should have unambiguous guidelines about what is legal. The fear of federal or state prosecution, unfortunately, makes many physicians hesitant to prescribe opioids even when they may be the best pain control tool for certain individuals.

Many physicians and patients fear that the physical dependence sometimes caused by narcotics will lead to addiction and drug abuse. This is seldom the case and is extremely rare among patients using Oxycontin for palliative care. After 28 months using Oxycontin I was able to stop with no real problem through a gradual reduction. I can't state strongly enough the profoundly positive effect Oxycontin had on my life.

It is understandable that some patients would have misconceptions about the realities of pain medication use but physicians should have a comprehensive understanding of available medications and pain care techniques. More importantly they should know the pain management resources available to their patients and have a close working relationship with pain management specialists.

To often, I witnessed a disconnect between physicians and palliative care experts. With my medical background, rank, and a little assertiveness I ensured that I saw the anesthesiologists who could best address my pain. Unfortunately, some of the wounded soldiers I've been working with do not get the pain care they need because they are afraid to ask for it, are ashamed to ask for drugs to control their pain due to social stigmas associated with the abuse of pain medications, or are simply trying to be tough. The fear of addiction and the associated stigma of drug use ironically may lead to more profoundly addictive behavior. One of my old soldiers was wounded and returned from Iraq this past summer. As we were talking he bragged how he was not using his pain meds, but unfortunately it turns out he was self medicating with alcohol to cope with the pain.

The prevalent attitudes towards the use of narcotics for palliative care need to be changed. When I was contacted to testify here today I was reluctant. I was feared showing my soldiers how much I pain effected my life, how badly I needed Oxycontin just to get by, and was embarrassed to be seen whining to Congressmen about my pain. But as I thought about it I realized how important it is that you all understand some of the difficulties encountered by those living with pain in the hope that through this legislation you can address some of the profound shortfalls in palliative care.

The main reason I'm here is because I saw, firsthand, soldiers who slipped in to the void that often exists between the front door of the hospital and the adequate treatment of chronic pain. I've witnessed the strong fear of certain pain medications among both doctors and patients that sometimes results in inadequate pain care. I've also experienced the lack of understanding in the medical community about what causes pain and how we can best treat it. This bill does a great deal to address these very real and widespread issues. In the time allotted I could not share all stories of soldiers coping with pain nor all of my own struggles but I hope this testimony will in some small way help you all understand the debilitating effects of pain and move you toward action to address the needs of millions who are living in pain.

MR. DEAL. I must say, Captain Pruden, you truly honor us with your presence here today. We all respect and admire your courage, your dedication to our country, and we commend you for what you continue to do to help your fellow soldiers who have been wounded. We salute you. Thank you for being here with us.

CAPTAIN PRUDEN. Thank you. Thank you, sir.

MR. DEAL. Mr. Vander Zanden, it is a hard act to follow, but welcome.

MR. VANDER ZANDEN. Thank you.

Members of the committee, Chairman Deal, on behalf of Medtronic and the millions of patients like Captain Pruden we serve who suffer chronic diseases like chronic pain and pulmonary hypertension, I thank you for the opportunity to be here today.

In my role, I am Vice President and General Manager of Medtronic's Global Pain Management Division, and Medtronic is headquartered in Minnesota. We are the leading medical technology company providing lifelong solutions for people with chronic diseases.

As a company, we are investing over \$1 billion in research and development just this year alone. Medtronic shares the subcommittee's commitment to increasing the understanding of these conditions and continually improving the therapies available to patients. We would like to share with you some of the ideas and the therapies that Medtronic currently has available in the areas of chronic pain and pulmonary hypertension, and provide you a glimpse into a few of the innovative treatments we have on the horizon.

As you have heard this morning, chronic pain is an epidemic in this country. Approximately 25 percent of the American population suffers from chronic pain. That is actually one out of every four people. Every

year, 40 million physician visits are related to pain management. The economic impact is staggering: 515 million workdays and nearly \$50 billion in economic costs on an annual basis, and an astounding \$100 billion in medical expenses are incurred due to chronic pain. These figures don't begin to tell the countless stories of suffering, depression, isolation, even suicide that are often experienced by chronic pain sufferers and the tremendous impact this has on their families and their loved ones.

Unfortunately, chronic pain is not easy to treat. The reality is that many patients simply gave up in their search for relief, and instead resolve to living their lives suffering in persistent pain, as you have heard Captain Pruden say. It is exactly these patients that Medtronic serves with our pain therapies. Medtronic has successfully treated hundreds of thousands of people who suffer from chronic pain with our neurostimulation and drug delivery therapies. These are clinically-proven and minimally-invasive options for those who have lost hope and they could find relief and live life to the fullest again. Neurostimulation is a type of implantable pain therapy, and it actually stimulates the spinal cord with a mild electrical impulse that actually blocks the signals from reaching the brain, essentially replacing the pain signals with a mild tingling sensation. The Medtronic neurostimulator is small. It is about the size of a stopwatch. It is surgically placed under the skin where it sends impulses to the spinal cord through one or more specially insulated wires, basically called leads, and these are also surgically placed. And I do believe you have got some pictures in front of you in your packet that outline some of our devices.

Based on the needs of the individual patients, the physician can customize the pain relief to maximize the effectiveness of the treatment based on every individual's need. The device is used to treat individuals suffering from pain as a result of failed back surgeries, complex regional pain syndrome, as well as degenerative disk diseases and painful neuropathies. More than 150,000 people world-wide have received Medtronic neurostimulation devices for pain, including the famous comedian that you heard about earlier this morning, Jerry Lewis, who some of you have met, perhaps most recently when he visited Capitol Hill in support of H.R. 1020, the National Pain Care Policy Act.

In addition to our neurostimulation system, Medtronic also manufactures the world's only implantable, programmable drug infusion systems. These systems, commonly referred to as drug pumps, consist of a pump placed under the skin of the abdomen and a catheter that is then placed into the intraspinal space surrounding the spinal column to deliver tiny doses of liquid morphine directly to where the product is needed.

The systems like the spinal cord simulation include a remote control or patient programmer, and this is preprogrammed by the physician so that the patient can have the appropriate dose of medication to avoid error or abuse. I will also point out that because our drug pumps deliver medication directly into the intraspinal space, it doesn't pass the blood-brain barrier, which is especially important. Studies suggest that the dose required to manage this chronic pain can be as small as one-hundredth of the amount of oral medication required to do the same thing. As a result, the overall side effects to the patient are also generally significantly reduced.

We believe that our new technologies are providing better, more cost-effective medical outcomes, and the example is our neurostimulator called Restorer, benefits patients living with the most severe types of pain who might otherwise limit the use of their neurostimulator to conserve the actual battery power that is available with a lower power model. By being able to recharge it, they don't need to hold onto that power and save it for when they really need it.

We are also expanding the conditions for where this type of implanted electricity-delivering therapy can be used. We hope that this therapy can provide relief to the more than 28 million Americans who suffer chronic migraines and can't be treated with standard migraine treatments.

While technologies continue to advance, without patient access to these therapies, the undertreatment of pain will continue to be one of the country's top public health problems. In order to address these problems, Medtronic is actively engaged with the patient and provider community to support the National Pain Care Policy Act introduced by Congressman Rogers. I am grateful for his leadership in raising this issue, and this is an important public health concern.

One of the disturbing barriers addressed in this bill is simply the lack of understanding of the array of clinically-effective therapies that are available. An astounding 40 percent of people with chronic pain do go to the doctor and then stop because they haven't been able to find effective options. Further, many general practitioners are not fully aware of the treatment options that are available for them. With enhanced education, perhaps we will see more internists and general practitioners recognize chronic pain and have knowledge or an available referral pattern and treatment options available. While this isn't a simple solution, this is a complex disease, raising the visibility of the problem and starting the national dialogue on how to ensure that chronic pain sufferers get the care that they need is a good first step in addressing the issue.

Another area that needs additional Federal focus is pulmonary hypertension, a rare, debilitating, and ultimately fatal disease of the

lungs. You will hear more about this disease from the distinguished witnesses on the panel. Medtronic MiniMed, our diabetes business located in North Ridge, California, offers a delivery system for the administration of Remodulin, a drug used to treat pulmonary hypertension that dilates affected blood vessels in the lung tissue and increases blood flow and improving the overall oxygen exchange. Patients receive this drug through the use of Medtronic's medication delivery pump that delivers the drug under the skin, similar to our insulin pump used to treat type I diabetes. Given the nature of the drug, for many years, this has been the best way to deliver the drug. And virtually, the pump is about the size of a pager. It is totally portable. It delivers smaller doses. It is readily absorbed, and there are fewer side effects, which is very, very convenient for the patients.

We are grateful of the subcommittee's interest in both pulmonary hypertension and chronic pain. We thank you for the opportunity to discuss some of the therapies Medtronic has available to these suffering patients, and we welcome the opportunity to work with the subcommittee to increase understanding of these diseases and ensure that patients have timely access to life-saving and life-enhancing technologies.

Thank you.

[The prepared statement of Jake Vander Zanden follows:]

PREPARED STATEMENT OF JAKE VANDER ZANDEN, VICE PRESIDENT
AND GENERAL MANAGER, MEDTRONIC GLOBAL PAIN MANAGEMENT

Chairman Deal, Ranking Member Brown, Members of the Committee:

On behalf of Medtronic and the millions of patients we serve who suffer from chronic diseases such as chronic pain and Pulmonary Hypertension, I thank you for the opportunity to be here today. My name is Jake Vander Zanden and I am the Vice President and General Manager of Medtronic's Global Pain Management Division. Medtronic, headquartered in Minnesota, is the world's leading medical technology company that provides lifelong solutions for people with chronic disease. With deep roots in the treatment of heart disease, Medtronic now provides a wide range of cardiovascular, neurological, gastro-uro, spinal and diabetes therapies that help physicians solve the most challenging, life-limiting medical problems that exist today. In fact, every six seconds, someone's life is saved or improved by a Medtronic technology. I think our mission says it best: "Medtronic is firmly dedicated to alleviating pain, restoring health and extending life throughout the world."

As a company that is investing over \$1 billion into research and development this year alone, Medtronic shares the Subcommittee's commitment to increasing our understanding of these conditions and continually improving the therapies available to patients. Today, I would like to share with you information on some of the therapies that Medtronic currently has available in the areas of chronic pain and Pulmonary Hypertension, and provide a glimpse into a few of the innovative treatments we have on the horizon.

Chronic Pain

Chronic pain is an epidemic in this country:

- Approximately 25 percent of the American population suffers from chronic pain – that’s one in every four people
- Each year, more than 40 million physician visits are related to pain
- The economic impact is staggering - 515 workdays are lost as a result of pain with an economic cost of nearly \$50 billion
- Annually, an astounding \$100 billion in medical expenses are incurred due to chronic pain

And these figures don’t begin to tell the countless stories of suffering, depression and isolation – even suicide - experienced by chronic pain sufferers and the tremendous impact this has on a pain sufferer’s family and loved ones.

Unfortunately, chronic pain is not easy to treat. Dr. Joel Seres may have said it best when he offered, “Chronic pain infers the failure of medical care. If previous treatment had been successful the patient would not be experiencing pain.” The reality is that many patients simply give up in their search for relief and instead decide to live their lives suffering from chronic pain. It is exactly these patients that Medtronic serves with our pain therapies.

Building on proven core Medtronic technologies, like the pacemaker, used to treat chronic disease in other areas of the body, Medtronic has successfully treated hundreds of thousands of people who suffer from chronic pain with our neurostimulation and drug delivery therapies. These are clinically proven and minimally invasive options for those who had lost hope that they could find relief and live life to the fullest again. While these therapies are not for everyone, they do provide a viable option for those patients who have not otherwise been successfully treated.

Neurostimulation is a type of implantable pain therapy that stimulates the spinal cord with mild, electrical impulses that block pain signals from reaching the brain, essentially replacing the pain signals with a mild tingling sensation.

The Medtronic neurostimulator is small (about the size of a stopwatch), and is surgically placed under the skin where it sends the impulses to the spinal cord through one or more special “insulated” wires called leads, that are also surgically placed. Based on the needs of individual patients, physicians can customize the pain relief to maximize the effectiveness of the treatment. This device is used to treat individuals suffering from pain as a result of back surgeries, complex regional pain syndrome, as well as degenerative disk disease and painful neuropathies.

There are two types of fully implantable neurostimulators available, rechargeable and non-rechargeable, allowing physicians to choose the right device to best address the pain management needs of their patient. The neurostimulation systems typically consist of an implantable neurostimulator, the implantable lead and extension. Additionally, a programmer is used by physicians and patients to adjust the level of stimulation within physician prescribed limits as well as turn the system on or off.

More than 150,000 people worldwide have received Medtronic neurostimulation systems for pain, including the famed comedian, Jerry Lewis, whom some of you have met – perhaps most recently in September when he visited Capitol Hill in support of H.R. 1020, the “National Pain Care Policy Act.”

In addition to our neurostimulation system, Medtronic manufactures the world’s only implantable, programmable drug infusion systems. Over 100,000 people have been treated with these systems throughout the world. These systems, commonly referred to as “drug pumps,” consist of an implantable, programmable pump placed under the skin of the abdomen and a catheter that is placed in the intraspinal space surrounding the spinal column, to deliver liquid morphine directly to where it’s needed. The systems, like the spinal cord stimulators, include a “remote control” or patient programmer. These systems are also pre-programmed by physicians with the appropriate dose of medication.

We recently received FDA approval for the first “remote control” that allows patients to administer their own “supplemental” doses of pain medication, when they need it, through our implantable drug pumps.

I’ll also point out that because our drug pumps deliver medication directly into the intraspinal space, the dose required to manage the patient’s chronic pain is typically only a small fraction of the amount required by oral (ie, pills) or other administration. As a result, the side effects are generally significantly reduced. For example, our pumps may better enable an end-stage cancer patient to spend her final months in the company of family and friends, without the high levels of drowsiness, and other side effects that can arise from high-dosage oral pain medications.

Our spinal cord stimulation devices, as well as our “drug pumps” for chronic pain, often are implanted in patients because other options to manage their pain have failed. Instead, patients continue to have pain after repeated back surgeries, or they may have suffered other injuries or chronic conditions that leave them with persistent, debilitating pain. A significant number of patients use them to manage the severe pain associated with the progression or treatment of malignant cancer, providing them better quality of life.

Future Technologies for the Treatment of Chronic Pain

While our neurostimulation and drug delivery systems have provided relief to hundreds of thousands of those with chronic pain, there are still too many people who are suffering in silence, and who need to know about these additional medical options to adequately manage their pain.

We believe that new technologies are providing better, more cost-effective medical outcomes. For example, our neurostimulator called Restore, which was made available to patients in the U.S. this past spring, builds on our existing neurostimulation system by offering a rechargeable battery, which benefits patients living with the most severe types of pain who might otherwise limit the use of their neurostimulator to conserve or “hoard” the battery power that’s available through a lower-power model. With both the neurostimulator and the pumps, the size of the devices have become significantly smaller over the years, and the features have been enhanced to provide both the physician and patient greater control in managing pain.

We are also expanding the conditions for which this type of implantable, electricity-delivering therapy can be used. Studies are currently underway to test the feasibility of using neurostimulation to treat severe, chronic migraine patients. We are hopeful that this therapy will provide relief to the more than 28 million Americans who suffer from migraine headaches that cannot be treated with standard migraine treatments.

Future products will no doubt be smaller to improve patient comfort and satisfaction with these devices. New “sensing” technology under development could drive change in the way patient outcomes are measured, by allowing physicians to measure patient improvement as a result of our devices, more objectively than they can now.

Patients Must have Access to Available Treatments

As I previously mentioned, chronic pain is not easy to treat and I am confident that industry, clinicians and most importantly patients would greatly benefit from research that would give us a better understanding of the causes of pain and lead us to improved treatment options. Medtronic invests in many projects each year to support on-going research efforts in the field of pain.

Unfortunately, many people who are currently living with chronic pain are looking for more immediate solutions for their chronic pain. Many chronic pain sufferers have not found the relief they need due to unnecessary barriers that hinder access to new therapies. While our technologies continue to advance, without patient access to these

therapies, the under-treatment of pain will continue to be one of this country's top public health problems.

Medtronic has actively engaged with the patient and provider community to support H.R. 1020, the "National Pain Care Policy Act", introduced by Congressman Mike Rogers. This piece of legislation systematically addresses many of the factors that have led to the under-treatment of chronic pain. We are grateful to Congressman Rogers for his leadership in raising awareness of this important public health concern.

A disturbing barrier to access is simply a lack of understanding of the array of clinically effective therapies already available. Forty percent of people with chronic pain do not go to the doctor for their pain because they believe that nothing can be done to treat it. In a study conducted by the Mayday Fund, 92 percent of respondents considered pain to be a part of life and nearly 35 percent would wait until the pain becomes unbearable before taking medication.

When they do visit a physician, treatment is often inadequate for over half of all patients seeking care, forcing them to change physicians before they find relief. Societal beliefs about pain have reinforced the idea that living with pain is a sign of strength. Addressing these misconceptions by helping to elevate understanding of this disease will greatly assist chronic pain sufferers in getting the help they need.

There are also institutional barriers to effective pain treatment. For many years medical schools addressed the treatment of pain as an afterthought associated with an underlying condition. Increased understanding about the science of pain has helped to define pain as a condition that needs to be treated and taught as a distinct medical condition. Medtronic supports the initiatives contained in the Roger's bill to help ensure that all physicians have access to current information on the wide array of pain therapies available to patients today. With enhanced education, perhaps we will see more internists and general practitioners recognize chronic pain and have knowledge of available referral and treatment options.

While there isn't a simple solution to this complex disease, raising the visibility of the problem of under treatment and starting the national dialogue on how to ensure that chronic pain sufferers get the care they need is a good first step in addressing the problem. Information sharing may be one of the easiest and most cost-effective ways to begin to chip away at the barriers preventing optimal pain treatment. Research to better define the chronic pain patient population, and public awareness campaigns aimed at educating the public on the nature of this disease, would dramatically improve the treatment of pain in this country.

Pulmonary Hypertension

Pulmonary Hypertension (PH) is a rare, debilitating and ultimately fatal disease of the lungs that affects approximately one or two people per million, totaling approximately 100,000 people worldwide. Pulmonary hypertension is a rare blood vessel disorder in which the pressure in the pulmonary artery (the blood vessel that leads from the heart to the lungs) rises above normal levels and may become life threatening. Symptoms of pulmonary hypertension include shortness of breath with minimal exertion, fatigue, chest pain, dizzy spells and fainting.

The cause of Primary Pulmonary Hypertension is a mystery, but is thought to have a latent genetic component that is "activated" after a viral or bacterial infection in the blood vessels that supply the patient's lung tissue. Secondary forms of the disease, which is more frequently observed, are seen as an adverse effect of the now-banned diet pills Redux and fen-phen and as a complication of lupus and other rheumatologic disorders. How and why this combination of drugs caused the increase is not well understood, but this "new" population is primarily young women between the ages of 21 and 40.

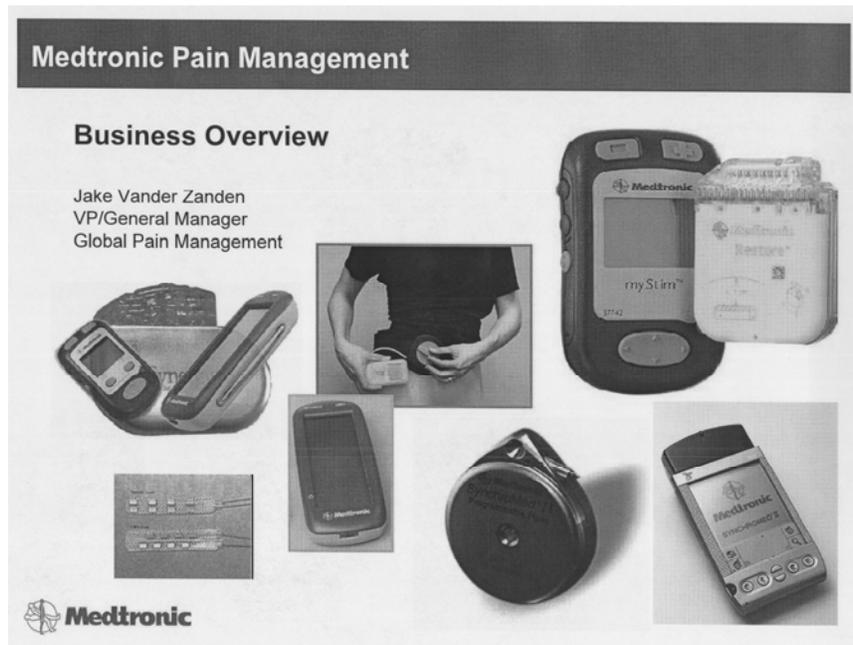
Medtronic MiniMed, our diabetes business located in Northridge California, offers a delivery system for the administration of Remodulin, a drug that dilates affected blood

vessels in the lung tissue increasing blood flow and improving oxygen exchange. Patients receive this drug through the use of Medtronic's medication delivery pump that delivers the drug under the skin and is similar to an insulin pump used to treat Type I diabetes. Many patients have found the medication pump to be a more convenient way to administer the therapy as the pump is about the size of a pager, it is totally portable, and delivers smaller doses, which is more readily absorbed and with fewer side effects.

Given the devastating nature of this disease and the need for increased research, Medtronic strongly supports H.R. 3005, the "Pulmonary Hypertension Research Act of 2005," which creates three Centers of Excellence at the National Institutes of Health dedicated to learning more about this disease as well as instituting an important public awareness campaign aimed at increasing the patient and medical community's knowledge of this disease.

Conclusion

We are grateful for the Subcommittee's interest in both Pulmonary Hypertension and chronic pain and thank you for the opportunity to discuss some of the therapies Medtronic has made available to suffering patients. While Medtronic shares the vision of finding a cure for pulmonary hypertension and chronic pain, we continue to look for ways to improve the quality of life for those afflicted with these and many other chronic conditions. We welcome the opportunity to work with this Subcommittee to increase understanding of these diseases and ensure that patients have timely access to life-saving and life-enhancing technologies.



MR. DEAL. Thank you.

Dr. Gladwin.

MR. GLADWIN. Mr. Chairman, members of the subcommittee, Mr. Brady, and Mr. Lantos, thank you very much for the opportunity to speak

to you today about research being conducted at the National Heart, Lung, and Blood Institute addressing pulmonary hypertension. I am also humbled and honored to sit with Mr. Hicks and Charity. Your testimonies are very motivating for clinical researchers, like me, taking care of other patients with pulmonary hypertension.

What I would like to do today is briefly outline the basic chronology of pulmonary hypertension and summarize our research efforts to develop new treatments and detection strategies and describe our vision for future research activities coming from the Heart, Lung, and Blood Institute.

As you have heard already, pulmonary hypertension is a disabling condition caused by the narrowing of the small arteries that serve the lung. This results in an increase in the pressure, not measured at the arm, but within the lungs. As these arteries tighten, the right heart, which pumps blood through the lung, encounters increasing resistance, as if pipes in a plumbing system are narrowed. The right heart is not equipped to deal with these high pressures, and over time, begins to fail. As the right heart fails, the ability to deliver oxygen and nutrients to the body decreases the ability to pump.

From a symptomatic standpoint, patients with pulmonary hypertension will present with rapid heart rates, dizziness, shortness of breath especially with exertion, chest pressure, tightness, fatigue, and ultimately fainting. These symptoms are so general and non-specific that the disease is often not diagnosed until the overworked right heart is close to complete failure, very late in the course of the disease.

Patients with this often progress to the point that they can't accomplish the simplest activities of daily living. My patients will complain of inability to vacuum the floor of their living room, inability to cook, inability to walk upstairs, across a room, and often inability to speak in a full sentence without taking a deep breath.

Pulmonary hypertension can be fatal, but new treatments are available that can slow its progression and improve the quality of life. The disease really exists in two forms. The first is primary or endopathic pulmonary hypertension. This is the cause of pulmonary hypertension where it is not associated with the systemic illness, and we really don't know the precipitating cause. The pathology is the same in this type of pulmonary hypertension as well as in secondary pulmonary hypertension, where that is pulmonary hypertension that is associated with a systemic disease. These systemic diseases include scleroderma, sickle cell disease, HIV infection, and a host of other conditions.

Basic transrelational and clinical studies have led to, really, the discovery of two fundamental mechanisms that lead to pulmonary hypertension. The first is the dysregulation of chemicals produced by

blood vessels that they dilate or open up the blood vessels and opposing chemicals that are constrictors that constrict the vessel. Our blood vessels normally have a very refined balance of these constrictors and dilators, and this becomes dysregulated pulmonary hypertension.

The second major mechanism is a proliferative, almost cancerous response of the smooth muscles within the blood vessels that invade and fill up the lumen or the inside of the blood vessel, and this creates a blockage of the pulmonary arteries.

With regard to the first mechanism, these chemicals are released from endothelium, which are the cells that line blood vessels. These are dilating chemicals, and then there are constrictor chemicals. The dilating chemicals include Prostacyclin, which is actually the first FDA-approved drug for pulmonary hypertension and the drug that really broke open the therapeutic side to this field. This discovery of this compound led to the Nobel Prize in Physiology Medicine that was awarded in 1982.

The second compound, something that I study personally, is nitric oxide, a gas molecule present in cigarette smoke, car exhaust, but also made by our bodies. The discovery of this molecule led to the Nobel Prize Award in 1998. This is also a very important dilating agent.

Both of these chemicals not only dilate and open up blood vessels, but they block clotting and they block abnormal growth of cells. So they maintain homeostasis of our blood vessel system. These dilators are opposed by constrictors; a principal one being a chemical called endothelin-1. This is one of the most potent constrictor molecules ever discovered. It is actually analogous to a chemical found called sarafatoxin in snake venom, so when the snake bites someone, there is a potent constriction in the tissues. So you can imagine what happens when this chemical rises in the blood of patients with pulmonary hypertension.

Over the past decade, I think we are really at the cusp of a perfect storm of basic science and clinical development of drugs. There are really, in the last 5 years, five FDA-approved drugs and another five coming for the treatment of pulmonary hypertension based on the evolving field of vascular biology and these big discoveries that led to these two Nobel Prizes.

The first part is Prostacyclin. You have heard about that. It requires a continuous infusion, an iced pump. Patients often require two pumps so there is a backup one, because you can't have that continuous infusion fail. And a recent advance, the development of another Prostacyclin analog allows infusion not to be cooled, which is an important advance for the quality of life for patients. Also very exciting, there has now been development of an inhaled form of Prostacyclin that patients can use.

And most important for patients and their quality of life, there are now two pills available. The first is Bosentan. Again, these are targeting these fundamental basic science discoveries. Bosentan blocks the endothelin receptor, that constrictor receptor. And Bosentan is taken twice a day. There a number of drugs in this class that is now being developed. The second oral drug is Viagra, of all things, or Sildenafil, which was just FDA-approved in the last month. This drug potentiates the nitric oxide dilating signal, and it turns out, really by a stroke of luck, that the lung vasculature has a high level of the enzyme that Viagra blocks, so it specifically lowers the pressure in the lungs, and this was just FDA approved.

Again, all of these classes that you hear about on Super Bowl commercials of drugs are now being developed for pulmonary hypertension. These existing medications improve the quality of life, they increase survival, but they do not and can not cure the disease, unfortunately, because they only act in that first step, the dysregulation of constrictors and dilators. The second step, we believe, is very important, and this is that this rise in pressure is being driven by a proliferation of growth, almost a cancerous growth, of the smooth muscle cells that invade into the center of the blood vessel.

If you look at the pathology of someone who has unfortunately passed away with this condition, there is no blood vessel left. There is this cancerous extension of cells into the middle of it. There is nothing left to vasodilate.

Many of the efforts targeting these diseases are being funded by the Heart, Lung, and Blood Institute. One of the exciting avenues is the use of anti-cancer drugs, or drugs derived from the coronary artery disease field that targets this abnormal growth of cells. And I would be quite interested to answer questions about this area. I think it is very exciting. It is a big promise for the future.

Many of these efforts are funded by the Heart, Lung, and Blood Institute, which supports a robust research effort in pulmonary hypertension. In fiscal year 2005, their research portfolio included more than 90 investigator-funded grants. I have a list. I would be happy to go over that with you. In this year, the funding hit \$30.8 million, which is a doubling over the last 5 years in funding.

In addition to this, we have requested grant applications for three or four pulmonary vascular disease clinical research centers, and the proposals are in now for these centers. These centers are extremely exciting, because they are going to infuse basic science, pre-clinical animal models of the disease, and require clinical research projects as well. Every one of these score grants requires that the center have state-of-the-art, new, cutting-edge science, basic science, but they have to have

two clinical projects as well. So it will add the clinical and basic scientists together.

We are also monitoring, in 2006, a multi-center trial to test whether Viagra is beneficial for patients who have pulmonary hypertension with sickle cell disease, and we will assess the best ideas, whether they come from the individual investigators with creativity who submit grant applications and we are committed to maintaining the financial flexibility to fund the most promising grant applications.

I am also proud to announce, under the dynamic leadership of Dr. Nable that we have started a new research effort right here in the intramural division of the Heart, Lung, and Blood Institute in Bethesda that I am leading in the newly-formed Vascular Medicine Branch. This is a branch entirely devoted to the study of blood vessel disease therapies.

The initiative has four major goals. The first is to develop new therapies for pulmonary hypertension. We currently are recruiting patients for five phase one and two clinical trials, and are launching two large, multi-center phase three trials for pulmonary hypertension associated with sickle cell disease. We believe the studies emanating from this will have spill-over effects, important spill-over effects for all forms of pulmonary hypertension, because the disease and the mechanism, the pathology is the same.

We have also identified a new medication in the intramural division, sodium nitrite, which can be easily nebulized with a current asthma delivery system, and this decreases pulmonary pressures in animal models of neonatal pulmonary hypertension. These are babies who develop pulmonary hypertension.

The second effort is to test whether therapy can halt blood vessel damage that occurs in patients with sickle cell disease and thalassemia. We have discovered, in a large regional study, that patients with sickle cell disease suffer a very high attack rate to pulmonary hypertension. One-third of adults by age 35 have pulmonary hypertension. It is the major cause of death. This is 20,000 Americans. Patients with pulmonary hypertension that have sickle cell disease have a 10-fold increase risk of death compared to those without.

Our third effort is to identify pre-disease in that risk populations. As you know, as is the case with diabetes with systemic high blood pressure measured at the arm, we keep lowering and lowering the target therapy, that if we can treat early disease, we have a better chance of preventing its eventual progression. We believe that there is a similar opportunity in pulmonary hypertension. And there are diseases with such a high attack rate of pulmonary hypertension that we can screen those populations.

This includes scleredema, HIV-infected patients, sickle cell patients, and thalassemia patients.

And finally, an exciting development is the implementation of phase one and two chemotherapeutic drug trials and novel small molecule drug trials that are again targeting this cancerous proliferation of the vasculature. We think such anti-proliferative therapy is going to be key for reversal of disease rather than simply improving symptoms.

Just of the script, I will say that this is a very exciting time that, as a clinician and a scientist, I had a patient in the intensive care unit more than a month ago who was a young woman with a 17-year-old son who came into the ICU in severe right heart failure. She had 60 pounds of weight gain from right heart failure, an inability to pump that blood around to the heart. She was near death in the ICU, was saying good-bye to her family members. When I started as a resident, Prostacyclin wasn't yet available beyond specialty centers. We were able to start her on three FDA-approved drugs, an infusion of Prostacyclin, Bosentan, and Sildenafil. We managed, over one week, to get 60 pounds of fluid off of her, get her out on oxygen and two pills, and she is alive and doing very well today. This is an unheard of development for an orphan disease, and a very exciting time which will require us to educate our young clinicians in knowing how to use all of these drugs as well.

So thanks to the efforts of researchers, patient advocates, the support of Congress, the American taxpayers, and advocates, pulmonary hypertension is moving from the ranks of diseases that were once considered to be untreatable to the growing list of conditions for which medical science offers a hope for a better quality of life and more years to enjoy it. Our goal is to restore the health to those who suffer from pulmonary hypertension and to prevent others from developing this dreadful disease.

And thank you for being committed to this noble cause and for allowing me to speak. And I would love to answer questions.

[The prepared statement of Mark Gladwin follows:]

PREPARED STATEMENT OF MARK GLADWIN, CHIEF, VASCULAR
MEDICINE BRANCH, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE,
NATIONAL INSTITUTES OF HEALTH

**Major points – December 8, 2005, Testimony of Dr. Mark Gladwin to the
House Energy and Commerce Subcommittee on Health**

- Over the past decade, several drugs that affect vessel dilation and constriction have received FDA approval. The first drugs available were given via injection, but three drugs recently have been approved that can be inhaled or swallowed.

- Researchers now believe that pulmonary hypertension also is caused by a cancer-like proliferation of smooth muscle cells of the pulmonary artery and hypothesize that anti-cancer drugs may have applications as therapies for pulmonary hypertension patients.
- In FY 2005, the NHLBI research portfolio included more than 90 research and training projects on pulmonary hypertension. The Institute also issued a Request for Applications for 3 or 4 pulmonary vascular disease research centers. In FY 2006, the NHLBI plans to launch a new program to test whether sildenafil therapy is beneficial for patients who have pulmonary hypertension in conjunction with sickle cell anemia.
- The NHLBI started a new research effort, the Vascular Medicine Branch, in the Division of Intramural Research. Under the leadership of Dr. Gladwin, the branch has four major goals:
 - Development of new therapies for pulmonary hypertension.
 - Testing of whether sildenafil therapy can halt blood vessel damage that causes patients who have sickle cell anemia or thalassemia to develop pulmonary hypertension.
 - Identification of “pre-disease” in high-risk patients.
 - Development of clinical trials of compounds to reverse the cancer-like proliferation of smooth muscle cells.

Testimony of Mark T. Gladwin, M.D.

Mr. Chairman and members of the Subcommittee, thank you for the opportunity to appear before you today to discuss research on pulmonary hypertension conducted by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health, an agency of the U.S. Department of Health and Human Services. Today I will briefly outline what we know about the basic biology of pulmonary hypertension, summarize our research efforts to develop new treatments and detection strategies, and describe our vision for future research activities.

Pulmonary hypertension is a disabling condition caused by a narrowing of the small arteries that carry blood through the lungs, resulting in damage to the heart. As the arteries tighten, the heart must work harder to pump blood through them. Pulmonary hypertension can manifest itself as rapid heart rate, dizziness, shortness of breath, chest pain, fatigue, and fainting—symptoms so general that the disease is often not diagnosed until the overworked heart muscle has become too weak to pump enough blood through the lungs and the patient is unable to perform even the simplest daily activities. Pulmonary hypertension can be fatal, but new treatments are available that can slow its progression and improve quality of life.

The disease exists in two forms: primary pulmonary hypertension (PPH), which arises without any clear-cut underlying illness to precipitate it, and secondary pulmonary hypertension, which is caused by another illness such as sickle cell anemia or HIV infection. Basic, translational, and clinical studies have led to the discovery of two different mechanisms common to both forms of the disease: (1) blood vessel dilation/constriction; and (2) blood vessel blockage.

The first mechanism involves some chemicals released from the lining of blood vessels (called the endothelium) that open up or dilate blood vessels and other opposing chemicals that constrict the blood vessels. Dilating chemicals include prostacyclin (the compound for which the Nobel Prize in Physiology or Medicine was awarded in 1982) and nitric oxide (the subject of the 1998 Nobel Prize in Physiology or Medicine). Both are potent biological molecules that not only open up blood vessels but also block clotting and abnormal cellular growth. They are opposed by potent constrictors such as endothelin, a chemical that is structurally very similar to sarafotoxins found in snake venom.

Over the past decade, several drugs that attenuate these vasoconstrictor chemicals have been developed and have received FDA approval. Discovery of these drugs led to a revolution in therapy and provided new hope for patients by reducing symptoms, increasing exercise capacity, and improving survival. The first of these drugs, however, has to be given through a permanent catheter placed in a vein in the neck and connected to a battery-powered iced pump. Treatment became a little easier for some patients in 2002 when the FDA approved a second, more stable drug that could be infused under the skin (thereby reducing a patient's likelihood of infection) and, because the drug did not need to be chilled, could be administered by a mini-pump that was not heavily weighed down by ice. Over the past 12 months, three additional drugs that are even easier for patients to take have been approved for treatment of pulmonary hypertension: iloprost (Ventavis®), which can be inhaled through a nebulizer, and bosentan (Tracleer®) and sildenafil (Viagra®), which are swallowed as pills. Furthermore, these recent advances have opened the door to an avalanche of new related medications with different receptor targets, different half-lives, and different side-effect profiles.

The existing medications clearly improve the quality of life and increase survival, but they do not and cannot cure the disease because they act only on the first critical mechanism of pulmonary hypertension. Researchers now believe that the devastating blood pressure increase in pulmonary vessels also is caused by an abnormal, almost cancerous (though not metastatic, i.e., not spreading to other tissues), proliferation of the smooth muscle cells of the pulmonary artery that crowds the blood vessel and eventually chokes off all blood flow. Scientists are building on advances in treatments for patients who have cancer or coronary heart disease as they search for compounds that can interfere with the cancer-like growths and thereby not only prevent disease progression but also cure the disease by reversing vessel obstruction.

Many of those efforts are funded by the NHLBI, which supports a robust research effort in pulmonary hypertension. In Fiscal Year (FY) 2005, our research portfolio included more than 90 research and training projects on pulmonary hypertension that address the problem from multiple perspectives. In FY 2005, we also requested grant applications for 3 or 4 pulmonary vascular disease research centers. These centers will fuse basic research, studies of pre-clinical animal models, and human clinical trials to expedite development of the next generation of therapeutics. During FY 2006, we plan to launch a new program to test whether sildenafil therapy is beneficial for patients who have pulmonary hypertension in conjunction with sickle cell anemia. And because most of our best ideas come from individual investigators who submit grant applications, we are committed to maintaining the financial flexibility to fund the most promising grant applications.

We have also started a new research effort in the intramural division of the NHLBI that I am leading in the Vascular Medicine Branch. This important bench-to-bedside initiative has four major goals:

- 1) Development of new therapies for pulmonary hypertension. We currently are recruiting patients for five phase I/II trials and are launching two phase III studies this year. We have identified a new medication, nitrite, that can be nebulized easily with current asthma-delivery devices and can decrease pulmonary pressures in animal models of neonatal pulmonary hypertension¹.
- 2) Testing of whether sildenafil therapy can halt blood vessel damage that causes patients who have sickle cell anemia or thalassemia to develop

¹ Hunter CJ, Dejam A, Blood AB, Shields H, Kim-Shapiro DB, Machado RF, Tarekegn S, Mulla N, Hopper AO, Schechter AN, Power GG, Gladwin MT. Inhaled nebulized nitrite is a hypoxia-sensitive NO-dependent selective pulmonary vasodilator. Nature Medicine. October 2004; volume10, issue 10: pages 1122-1127.

pulmonary hypertension. We have discovered that patients with sickle cell disease and thalassemia are developing pulmonary hypertension at an alarming rate^{2,3}. One-third of these patients, almost 20,000 Americans, have pulmonary hypertension, which represents the greatest risk for death in this population.

3) Identification of “pre-disease” in high-risk patients. As is the case with diabetes and high blood pressure, early therapy has the potential to prevent end-organ complications. We are developing screening biomarkers and strategies for patients at high risk of developing pulmonary hypertension, such as those who have scleroderma, HIV, or sickle cell disease, so that early disease can be identified and addressed.

4) Development of phase I/II trials using chemotherapeutic medications and novel small molecules to reverse the cancerous proliferation of smooth muscle cells in the blood vessels of the lung. We believe such “anti-proliferative” therapy is the key to an ultimate cure.

Thanks to the efforts of researchers and patient advocates and the support of Congress and the American taxpayers, pulmonary hypertension is moving from the ranks of diseases that once were considered to be untreatable to the growing list of conditions for which medical science offers hope of a better quality of life and more years to enjoy it. Our goal is to restore to health those who suffer from pulmonary hypertension and to prevent others from developing this dreadful disease.

Thank you for being committed to this noble cause and for allowing me to speak with you today. I will be happy to answer any questions you may have.

Mark T. Gladwin, M.D.
Chief, Vascular Medicine Branch
National Heart Lung and Blood Institute
National Institutes of Health
U.S. Department of Health and Human Services

Mark Gladwin received his Doctor of Medicine from the University of Miami Honors Program in Medical Education in 1991. After completing his internship and chief residency at the Oregon Health Sciences University in Portland, Oregon, Dr. Gladwin joined the National Institutes of Health (NIH) in 1995 as a critical care fellow at the Clinical Center. After a one-year clinical fellowship in pulmonary medicine at the University of Washington in Seattle, he returned to the NIH Clinical Center for a research fellowship in the Critical Care Medicine Department under the mentorship of Drs. James Shelhamer, Frederick Ognibene, Alan Schechter, and Richard Cannon.

In 2005, Dr. Gladwin was appointed Chief of the new Vascular Medicine Branch in the Division of Intramural Research at NIH’s National Heart, Lung, and Blood Institute (NHLBI). As branch chief, he oversees a robust portfolio of studies to define the cellular

² Gladwin MT, Sachdev V, Jison ML, Shizukuda Y, Plehn JF, Minter K, Brown B, Coles WA, Nichols JS, Ernst I, Hunter LA, Blackwelder WC, Schechter AN, Rodgers GP, Castro O, Ognibene FP. Pulmonary hypertension as a risk factor for death in patients with sickle cell disease. New England Journal of Medicine. February 26, 2004; volume 350, issue 9: pages 886-895.

³ Morris CR, Kato GJ, Poljakovic M, Wang X, Blackwelder WC, Sachdev V, Hazen SL, Vichinsky EP, Morris SM Jr, Gladwin MT. Dysregulated arginine metabolism, hemolysis-associated pulmonary hypertension, and mortality in sickle cell disease. JAMA – Journal of the American Medical Association. July 6, 2005; volume 294, issue 1: pages 81-90.

and molecular mechanisms that underlie normal physiological function and disease processes of the lungs and their vasculature and fosters collaborations with researchers in the NIH Clinical Care Medicine Department to ensure strong and smooth interactions among laboratory and clinical investigations.

He has been involved in enrolling more than 700 patients in more than a dozen studies at the NIH Clinical Center and has co-authored 82 published peer-reviewed manuscripts addressing biochemical mechanisms involved in blood vessel relaxation and contraction. Recent efforts to develop a mechanistic, clinical, and epidemiological description of hemolysis-associated pulmonary hypertension led to the observation that pulmonary hypertension occurs in 30 percent of patients who have sickle cell disease, is a major cause of mortality in this patient population, and is strongly associated with excessive destruction of red blood cells, high levels of iron in the blood, and kidney disease. These findings, combined with his earlier mechanistic studies, are leading to clinical trials of compounds that can help patients have pulmonary hypertension in conjunction with sickle cell anemia or other disorders.

MR. DEAL. Thank you, Doctor.

Mr. Hicks.

MR. HICKS. Mr. Chairman and distinguished members of the subcommittee, thank you for convening this important hearing, and for permitting me the opportunity to testify this morning.

I, too, wish to add my sincere thanks and gratitude to Captain Pruden for his distinguished service. Thank you, Captain.

I am the Vice President for Advocacy and a volunteer of the Pulmonary Hypertension Association, and I am profoundly honored to represent the hundreds of thousands of Americans who are fighting a courageous battle against this deadly disease. In particular, Mr. Chairman, I am pleased to bring greetings to you from a PHA Georgia youth group, which is headquartered in your Congressional District in Loganville.

The Pulmonary Hypertension Association, which was founded by a handful of patients 15 years ago when there were less than 200 diagnosed patients with this disease, today, PHA is headquartered in Silver Spring, Maryland and is growing rapidly and includes over 6,000 patients, family members, and medical professional members, an additional 20,000 family members, friends and supporters, and an international network of over 120 support groups.

The impact of this disease upon so many Americans and their family members is like a nightmare you can never wake up from. For my family, it began with the words spoken not far from here at Walter Reed Army Medical Center a few years back. "Colonel Hicks," the doctor said, "Your daughter, Meaghan has less than a year to live. We can do nothing for her." Since that time, she has fought a valiant and protracted fight. And due to the hellishness of this disease, we have nearly lost her three times, twice in the past 2 months. Her blood is a pharmacy soup of many, many drugs taken in large quantities in order to survive. Among

other things, she is taking, daily, Procardia XL, Lasix, potassium, Zofran, spirodactone, Coumadin, Viagra, Tracleer, Zolof, Albuterol, Flovent, Flonase, Digoxin, Xanax, and, of course, Flolan. This drug is delivered by pump directly to her heart, as Dr. Gladwin discussed. It is delivered through her chest wall 24 hours a day. If the Flolan is interrupted for a period of time, that alone can kill her. Twice in the last month, she has had significant interruptions. She suffers chronic pain in her jaw, feet, and is frequently nauseated, and endures diarrhea daily as a side effect of these medications. She is only 24 years old.

Meaghan will never know the joy of motherhood or even marriage. Were she to marry, she would lose my insurance benefits that are keeping her alive. As you might imagine, the impact on our family has been devastating.

There are millions more affected by this in the United States alone. And although not well known and considered rare, you would be astounded to know that we have more Americans dying from this disease today in the United States than were tragically lost in combat in all conflicts we have encountered since the final year of World War II. Yes, that includes Vietnam, Korea, up through our current War on Terror. Even with a scope that horrific, I am sometimes asked why we should pay attention or focus resources on that terminal illness instead of others, of which there are clearly many. The answer is, quite simply, because we can.

Mr. Chairman, hope for our patients and their families lie in advancements made through biomedical research. And along those lines, I want to take this opportunity to express PHA's deep gratitude to two personal heroes of mine, Congressman Kevin Brady and Congressman Tom Lantos, for their leadership on our behalf. As you know, and we have heard this morning, they have introduced H.R. 3005, the Pulmonary Hypertension Research Act in the House. This landmark bill, introduced only in June, already has 240 bipartisan co-sponsors, 17 of whom are members of this very subcommittee. We owe a lot to these great champions, and we are grateful for the efforts of Congressman Lantos' beautiful and courageous granddaughter as well, Charity, to my left.

You know, this bill H.R. 3005 calls for the establishment of three Centers of Excellence on pulmonary hypertension through the NHLBI, and these centers would focus on the following: basing clinical research into the cause, diagnosis, early detection, prevention, and treatment of pulmonary hypertension; training programs designed to develop the next generation of pulmonary hypertension investigators; continuing education on pulmonary hypertension for healthcare professionals; dissemination of information to the public on pulmonary hypertension to

raise awareness; and the establishment of a pulmonary hypertension data system and clearinghouse.

Mr. Chairman, you need to realize, sir, our regard the need for additional research. On November the 11th, the Centers for Disease Control and Prevention released a long-awaited morbidity and mortality report on pulmonary hypertension. In that report, the CDC states: "More research is needed concerning the cause, prevention, and treatment of pulmonary hypertension." The science base, as Dr. Gladwin pointed out, must be further investigated to improve prevention, treatment, and case management.

On behalf of PHA, I would like to take this opportunity to thank NHLBI Director, Dr. Betsy Nable, and her colleagues for their leadership in this fight, which has clearly been outlined this morning by Dr. Gladwin. We are proud to have a partnership with this institute, and we are very grateful that Dr. Gladwin has taken the time to share his knowledge and insight with us at the hearing today. And I must say that his announcement of the three centers this morning is the most exciting news we have heard in the known history of this disease. Thank you very much. Please pass our thanks to Dr. Nable.

Moving third, PHA is very eager to work with Congress and the NHLBI to establish the Centers of Excellence on pulmonary hypertension called for in the act. The overwhelming support for this bipartisan legislation speaks to the strong interest of members in this issue, and we hope to make real progress in establishing these centers in 2006. Working together, I am confident that we can find a cure for Meaghan, Charity, and hundreds of thousands of Americans fighting for their lives against this terrible illness.

Mr. Chairman, thank you so much for this opportunity this morning.
[The prepared statement of Carl Hicks follows:]

PREPARED STATEMENT OF CARL HICKS, VICE PRESIDENT, ADVOCACY,
PULMONARY HYPERTENSION ASSOCIATION

SUMMARY OF TESTIMONY:

- 1) INTRODUCTION TO PULMONARY HYPERTENSION AND THE PULMONARY HYPERTENSION ASSOCIATION.
- 2) PERSONAL STORY OF MEAGHAN HICKS' BATTLE WITH THE DISEASE.
- 3) DISCUSSION OF H.R. 3005, THE "PULMONARY HYPERTENSION RESEARCH ACT."

Mr. Chairman, Congressman Brown and distinguished members of the subcommittee, thank you for convening this important hearing this morning and for the

opportunity to testify. I am Carl Hicks, Vice President for Advocacy with the Pulmonary Hypertension Association, and a proud parent of a pulmonary hypertension patient.

I am honored today to represent the hundreds of thousands of Americans who are fighting a courageous battle against this devastating disease. In particular Mr. Chairman, I am pleased to bring greetings to you from the PHA Georgia Youth Group, which is headquartered in your congressional district, in Loganville. This is one of PHA's outstanding support groups for young PH patients, led by a terrific volunteer named Robin Chambless.

Pulmonary hypertension is a serious and often fatal condition where the blood pressure in the lungs rises to dangerously high levels. In PH patients, the walls of the arteries that take blood from the right side of the heart to the lungs thicken and constrict. As a result, the right side of the heart has to pump harder to move blood into the lungs, causing it to enlarge and ultimately fail.

PH can occur without a known cause or be secondary to other conditions such as; collagen vascular diseases (i.e., scleroderma and lupus), blood clots, HIV, sickle cell, and liver disease. PH does not discriminate based on race, gender or age. Patients develop symptoms that include shortness of breath, fatigue, chest pain, dizziness, and fainting.

Unfortunately, these symptoms are frequently misdiagnosed, leaving patients with the false impression that they have a minor pulmonary or cardiovascular condition. By the time many patients receive an accurate diagnosis, the disease has progress to a late stage, making it impossible to receive a necessary heart or lung transplant.

While new treatments are available, unfortunately, PH is frequently misdiagnosed and often progresses to late stages by the time it is detected. Although PH is chronic and incurable with a poor survival rate, the new treatments becoming available are providing a significantly improved quality of life for patients. Recent data indicates that the length of survival is continuing to improve, with some patients able to manage the disorder for 20 years or longer.

Fifteen years ago, when three patients who were searching to end their own isolation founded the Pulmonary Hypertension Association, there were less than 200 diagnosed cases of this disease. It was virtually unknown among the general population and not well known in the medical community. They soon realized that this was unacceptable, and formally established PHA, which is headquartered in Silver Spring, Maryland.

Today, PHA includes:

- Over 6,000 patients, family members, and medical professionals.
- An international network of over 120 support groups.
- An active and growing patient telephone helpline.
- A new and fast-growing research fund. (A cooperative agreement has been signed with the National Heart, Lung, and Blood Institute to jointly create and fund five, five-year, mentored clinical research grants and PHA has awarded eleven Young Researcher Grants.)
- A host of numerous electronic and print publications, including the first medical journal devoted to pulmonary hypertension – published quarterly and distributed to all cardiologists, pulmonologists and rheumatologists in the U.S.

Mr. Chairman, I want to take this opportunity to express PHA's deep gratitude to Congressman Kevin Brady and Congressman Tom Lantos for their leadership on our behalf. As you know, they have introduced H.R. 3005, the "Pulmonary Hypertension Research Act" in the House of Representatives. This landmark bill for our community has 241 bipartisan co-sponsors, 17 of whom are members of this subcommittee. We owe a lot to these great champions, and we are particularly grateful for Congressman Lantos's beautiful and courageous granddaughter Charity, who is with us today. Charity's spirit,

determination and dedication to the fight against this disease inspires us each and every day.

I want to tell you the story of another beautiful and courageous young woman, my daughter Meaghan. The impact of this disease upon so many Americans and their family members is comparable to a nightmare you can never wake up from, right from the start. For my family, it began with the words spoken not far from here at Walter Reed Army Medical Center a few years back. "Colonel Hicks," the doctor said, "your daughter Meaghan has less than a year to live. We can do nothing for her." Since that time she has fought a valiant and protracted fight, and due to the hellishness of this disease, we have very nearly lost her 3 times, twice in the past two months. To remain alive now, she must take over 12 different pills daily, as well as flolan, an IV drug delivered by pump directly to her heart through her chest wall 24 hours a day. She'll never know the joy of motherhood or even marriage. Were she to marry she would lose my insurance benefits that are keeping her alive.

Mr. Chairman, you may be astounded to know that we have more Americans dying today from this illness, that is widely believed to ultimately be curable, than were tragically lost in combat in all conflicts that we have encountered since the final year of WWII. Yes, that includes Vietnam, Korea and all the rest, dying today, in the U.S. of this illness. Even with a scope that horrific, I am sometimes asked why we should pay attention or focus resources on that terminal illness instead of others, of which there are many. The answer is, quite simply, because we can.

Mr. Chairman, hope for our patients and their families lies in advancements made through biomedical research. According to leading scientists in the field, we are on the verge of tremendous breakthroughs in both our understanding of the disease and the development of new and advanced treatments. Our scientists are more hopeful than they have ever been regarding the future of research in PH. Ten years ago, a diagnosis of PH was essentially a death sentence, with only one approved treatment for the disease. Thanks to advancements made through both the public and private sector, patients today are living longer and better lives with a choice of five FDA approved therapies.

On behalf of PHA, I would like to take this opportunity to thank NHLBI Director Dr. Betsy Nabel and her colleagues for their leadership in the battle against this disease. We are very proud of our partnership with the Institute and we are grateful that Dr. Gladwin has taken the time to share his knowledge and insight with us at the hearing today.

Recognizing that we have made tremendous progress, we are also mindful that we are a long way from where we want to be, and that is a) the management of pulmonary hypertension as a treatable chronic disease and b) a cure for this devastating condition. That is why the "Pulmonary Hypertension Research Act" is so important to our community.

H.R. 3005 calls for the establishment of three Centers of Excellence on Pulmonary Hypertension through the National Heart, Lung and Blood Institute at the National Institutes of Health.

These Centers would focus on the following activities ...

- a) Basic and clinical research into the cause, diagnosis, early detection, prevention, and treatment of pulmonary hypertension..
- b) Training programs designed to develop the next generation of pulmonary hypertension investigators..
- c) Continuing education on pulmonary hypertension for health care professionals to help facilitate more accurate and timely diagnosis.
- d) Dissemination of information to the public on pulmonary hypertension to raise awareness of the disease.

In addition, the legislation calls on the National Heart, Lung and Blood Institute to establish a pulmonary hypertension data system and clearinghouse.

Mr. Chairman, all of these activities are essential to our efforts to take the next step in the fight against this disease. However, you don't have to rely solely on our word regarding the need for additional research. On November 11th the Centers for Disease Control and Prevention released a long awaited Morbidity and Mortality Report on pulmonary hypertension. In that report, the CDC states;

- 1) " More research is needed concerning the cause, prevention, and treatment of pulmonary hypertension. Public health initiatives should include increasing physician awareness that early detection is needed to initiate prompt, effective disease management. Additional epidemiologic initiatives also are needed to ascertain prevalence and incidence of various pulmonary hypertension disease entities." *(Page 1, MMWR Surveillance Summary – Vol. 54 No. SS-5)*
- 2) "Prevention efforts, including broad based public health efforts to increase awareness of pulmonary hypertension and to foster appropriate diagnostic evaluation and timely treatment from health care providers, should be considered. The science base for the etiology, pathogenesis, and complications of pulmonary hypertension disease entities must be further investigated to improve prevention, treatment, and case management. Additional epidemiologic activities also are needed to ascertain the prevalence and incidence of various disease entities." *(Page 7, MMWR Surveillance Summary – Vol. 54 No. SS-5)*

Moving forward, PHA would like to work with Congress and the NHBLI to facilitate the establishment of the Centers of Excellence on Pulmonary Hypertension called for in the "PH Research Act." The overwhelming support for this bipartisan legislation speaks to the strong interest of members on this issue, and we hope to make real progress in establishing these Centers in 2006. Working together, I am confident that we can find a cure for Meaghan, Charity and the hundreds of thousands of other patients pinning their hopes for a better life on biomedical research.

Mr. Chairman, thank you again for the opportunity to appear before you today. We appreciate your interest and your leadership on these issues. I would be pleased to respond to any questions you may have.

MR. DEAL. Thank you, Colonel Hicks. Our prayers will be with you and Meaghan, and thank you for your courageous leadership on this issue.

MR. HICKS. Thank you, sir.

MR. DEAL. We are now pleased to hear from Charity Tillemann-Dick.

MS. TILLEMANN-DICK. Good morning. Thank you, Mr. Chairman, Ranking Member Pallone, and honorable members of the subcommittee.

I also would like to thank Congressman Brady, who has stepped out for a moment. To the distinguished member from San Francisco, who happens to be my grandfather, I can only say that I feel your love so much every day. Love has a way of inspiring the best in us and making us stand a little taller and be a little better, live to our higher selves and make the world a better place to be in.

It also has the ability to inspire hope, and you and all of the members of the subcommittee know what I am here to talk to you about today. Most of us in life are in a race against ourselves, really, against those things which are based on selfish, those parts of us which are apathetic and ignorant to find hope, to find action, to live the lives that we have the potential to live.

In May of 2004, my life was changed. It became a race against time, and that is what I am here to talk to you about. My experience with pulmonary hypertension is typical. When I was young, I was an excellent sprinter, and there are videos of me playing soccer, and I would run up to the ball. I would kick it, and then I would slow to a shuffle, put my hands on my waist, and wait to catch my breath. We weren't a particularly athletic family, even though we did make an effort, so I always thought my problem was my lack of fitness, that I didn't exercise enough. So when I turned 18, I decided that I was going to change that. It was my senior year in college, and I started working out at least an hour a day, and sometimes 3 hours a day, 4 days a week. I was almost fanatic about my exercise regimen. And while in certain respects I got stronger, anytime that I would step onto a treadmill or try to run, I would quickly lose energy, and I would feel like I was going to faint. I decided that that there were just some things that I couldn't do, that everyone had their natural limitations and I wasn't going to be an athlete, and I wasn't trying to be one. So I pushed it aside and put other concerns in front of me.

The climax of my medical drama came over a 9-month period of time, which started on the campaign when I was doing disability on the street. I was crossing one of the largest intersections in Denver, and I fainted in the middle of the street one morning. Well, I had fasted the day before, and I hadn't eaten breakfast, and there were reasons for me to have fainted. There were three subsequent syncopal episodes in the coming months, and with each episode, I became more concerned that maybe something really was wrong. At the same time, my parents had had fainting episodes at similar ages at a similar time in their life, and they had hoped that that was what it was. However, as I would climb the three stories to my apartment in Budapest every day, I would have to stop numerous times, I wondered what was wrong. I knew that I wasn't neglecting my physical needs. I would wake up at 5:30 every morning to go and exercise. And I knew that there was something the matter. I went to doctors, and they suggested everything from increasing my salt intake, which I have found subsequently is not good for those of us with pulmonary hypertension. My blood pressure in my arm was very low. They would tell me to increase my caffeine intake, increase my intake of

red meats, I am a vegetarian, and I had mild anemia, and so they thought that might help.

However, regardless of the advice that I heeded from the medical professionals around me, I grew weaker.

I came back to the United States, and I was having paperwork filled out for the next year, and the year before, I walked to the same gym where I had started my almost religious crusade for fitness in my life that was less than a mile from my home. And Denver is a mile high, as you may or may not know. I walked there with my younger brother, who was beginning the Air Force Academy that summer. And as we walked, I had to stop what seemed like three or four times a block just to catch my breath. My brother looks at me quizzically because we had a lot of bonding time at the gym, and he knew something was wrong. I toned down my workout, but I still couldn't finish it. On the way back, on our slightly downhill trek home, I was so exhausted that I stopped under an oak tree, and Corban said, "Charity, please, just stay here. I will go get the car." As we were driving the short drive home, we were quiet, which is unusual in my family. He asked me if I was all right. And with 11 siblings, the last thing you want to be is an alarmist, and so I said that we would find out the next day.

As I went to the doctor the next day, at a very excellent physician named Susan Relsic-Kaiser. She first talked to me about my physical well being and health. I told her about my concerns. And she had a long checklist that she had to go down for this paperwork that I needed. At first the explanations of low blood pressure, anemia, and possibility of diabetes made sense. And plus she listened to my heart when she immediately ordered an EKG. I didn't have my contacts in. But I thought that I was imagining things. As I sat in the rather stark waiting room waiting for the doctor to return with the results, I heard her talking about me in the hallway, and I knew that I should either be very flattered or very afraid, and I was in a state of not knowing which to be. I waited there for what seemed like a very long time. When she came back and told me that I had a condition, or that I might have a condition called primary pulmonary hypertension, "But don't look it up until you have a firm diagnosis," she cautioned me.

Well, of course, the first thing I did was I told my mother, who had come to the doctor with me, about the possibility of my having this condition. When we went home, we looked it up in our medical encyclopedia. It wasn't there. So I continued to our family computer room, and I looked it up on the computer. I read through it. I was having some of the symptoms, some of the more serious symptoms, but not all of them, by any means.

However, when I read the conclusion, the prognosis was bleak, to say the least. It said most patients who suffer from primary pulmonary hypertension, or pulmonary hypertension, die within 2 to 5 years. There are few treatments, and over time, they are proven to be ineffective. This wasn't particularly uplifting news. As I waited, and as I went in for future doctor's visits, I did receive a firm diagnosis that I did have idiopathic preliminary pulmonary hypertension or primary pulmonary hypertension.

There have been incredible side effects from the drugs that I use. I started out on a medical trial, which was effective for a short time. However, by the end of last year when I went in to have a heart catheterization, I had pressures in my heart, which ordinarily are ten times the pace that any living person should have. I then went onto an intravenous medication called Flovent. I remember them telling me that jaw pain might be associated with this treatment. The first night that I was on Flovent, I remember waking up at 2:00 in the morning, my face flushed and my temperature soaring and thinking that until that moment I had never experienced pain. It was incredible, searing, burning, intense pain like I could have never imagined until having experienced it myself.

It would be easy to isolate the experiences of those of us suffering from pulmonary hypertension to the medical drama, because that is what it is, and it is a very intense medical drama. However, we lead very real lives. I go to school, and well-intentioned people often try to remove my purse when I get up to sing or when I give a presentation, when I have to inform them typically in front of a whole classroom that I am on life-saving medication that they can't take away from me. The side effects from the medications are almost unbearable.

However, we live with hope, we live on hope, and we depend on hope of a cure, of overcoming the very real threat to our lives every day, the knowledge that we might not wake up in the morning, the knowledge that our time is running out.

Today, I come before you to ask you for your help, for your support. I just went in for a series of blood tests and a lung x-ray on Tuesday, and it appears that my heart is continuing to get larger. My body, and the bodies of hundreds of thousands of Americans who are living with a literal death sentence for nothing they have done are running on hope that cannot run this for that much longer, and we will continue to lose some of the best and brightest members of this country. We will lose those who hold the future of our Nation in their hands, and you have the opportunity to make incredible contributions to our country, to our society. I am asking you for your support. Please support legislation to help us find a cure to pulmonary hypertension. It is just around the corner. The breakthroughs that are being made are victories for all of us

suffering from pulmonary hypertension. And they also are victories for all of us in helping us put aside our selfish desires and working to be better, working to stand a little taller, to be our better selves.

Ladies and gentlemen of the subcommittee, I ask you for your support. I thank you so much for being here. And thank you.

[The prepared statement of Charity Sunshine Tillemann-Dick follows:]

PREPARED STATEMENT OF CHARITY SUNSHINE TILLEMANN-DICK

Our lives are a race against ourselves – we struggle to replace fear with hope, selfishness with selflessness, ignorance with knowledge, apathy with action. And in this contest, it is the hope that the good inside us will prevail. But in May 2004, my life’s race was no longer between my higher and baser self, but against time.

My story is typical of many who have suffered or who are suffering from PH. From the time I was a little girl, I was an excellent sprinter. We have old videos of me playing soccer, running to the ball and then slowing to a shuffle, hands on my waist, catching my breath. We weren’t a particularly athletic family, so when I’d have trouble running back and forth on the basketball court or finishing allotted laps on swim team, I would blame it on a lack of physical activity in my life. So, when I was 18, I started working out – at least an hour a day, and sometimes three hours a day, four days a week. But still, when I stepped on a treadmill to run, I would quickly feel faint and stopped before something happened.

The climax of my pre-diagnosis drama came over a nine-month period of time when I experienced four syncopal – or fainting -- episodes spanning two continents. My first actual fainting spell came when I was crossing a street in Denver. I fainted in the middle of one of Denver’s largest intersections. Three subsequent episodes were similarly dramatic; I never knew how unromantic fainting into a man’s arms could be. I knew something was wrong; I just didn’t know what it was. But I went on with my life. Doctors told me to do everything from increase my salt intake to lift my blood pressure to eat red meat to cure mild anemia. My parents had both experienced fainting spells around my age, so I hoped that perhaps, nothing was wrong.

When I returned home for a visit to Denver, the Mile High City, in the spring of 2004, I had some medical paperwork that needed to be filled out for the next year. The day before my appointment, I walked to my old college less than a mile away to go to the gym with my little brother, Corban, who was entering the Air Force Academy that summer. I had to stop every 25 feet or so, when I was too exhausted to go on without a rest. Seeing how tired I was from a simple walk, I toned down my workout, which I still couldn’t complete. Finally, on our slightly downhill walk home, Corban, seeing something was obviously wrong, told me to wait under an oak tree four blocks from our home so he could run home and get the car. When he returned, I got it. “Charity, are you all right?” he asked. In a family of 11 children, the last thing anyone wants to be is an alarmist. But it was difficult to explain why at 20 years old with a clean bill of health and an exercise regiment that I kept with religious diligence for two years, I became weaker. I had to stop three to four times when climbing the stairs to my third story apartment in Budapest. So, I told Corban that I had a doctor’s appointment the next day and we’d see.

I went to the doctor’s. It was a rather extensive list they had to check off, and Dr. Susan Wells did an excellent job. She first discussed my health with me. My arm’s blood pressure was very low, so some of the explanations seemed logical for my problems. But as soon as she listened to my heart, she ordered an EKG. I wasn’t

wearing my contact lenses, but the tech's eyes seemed to pop open when the results were printed out. I hoped I was imagining. As I waited in the stark check up room, I heard the doctor talking about me and my accomplishments with someone for what seemed like a very long time. I knew that it was time to be either very flattered or very concerned. When Doctor Wells returned, she kindly informed me that there was a slight possibility that I was suffering from Primary Pulmonary Hypertension. She advised me not to look it up until the diagnosis was made. I thanked her and went on my way. Thinking about it, "primary," sounded alright. It comes first. "Pulmonary," whatever. Hypertension. That's me. I told my mother who, when we got home, looked it up in our medical encyclopedia. It wasn't there. I proceeded to our family computer room where I put it into a search engine. Some things matched up, but I certainly wasn't suffering from all of the symptoms yet. The prognosis didn't parse words. It said, "For those suffering from Pulmonary Hypertension, the prognosis is bleak. There are few effective treatments and patients typically die two to five years after diagnosis." I assure you that is an interesting prognosis for anyone to read.

In the next days and weeks, my family and my entire community grappled with how to deal with this disease, helping me to see a whole other range of societal problems. In the next months, I realized while my form of the condition, Idiopathic or Primary Pulmonary Hypertension, was very rare, that there were 100,000 Americans like me, living with a very literal death sentence. I was on a medical trial, but its benefits didn't last that long. By the end of the year, my arterial blood pressure was nine times higher than anyone who is alive should have. I took the last three weeks off of my studies at the conservatory and was given intravenous medication over the Christmas holiday. I was told that patients experienced jaw pain. At 2:00 a.m. I awoke, my face red and my temperature soaring. At that moment, I realized that until then, I had never experienced real pain. It was so intense, so searing, so unbearable that, had it not been so painful, would have been comic.

It seems simple enough to isolate PH patients' experience to the medical drama, but we have to go on living our very real lives. With those I don't know well, I deal with the social awkwardness of the really of not being able to keep up, only going somewhere with elevator access, not going out to eat, and people thinking I'm clutchy for my never putting down my purse. Occasionally people try to take it from me when I get up to sing or make a presentation. They don't realize that there is a line connecting my heart to the pump in that purse which must dispense medicine to me 24 hours a day. Patients are overlooked for promotions, and I have been overlooked for castings because directors or employers often have valid concerns about medical concerns interfering with productivity or the final production. We hope to live as normal a life as is possible, but in reality, our lives are being cut tragically short, every day. I am in relatively good health, but a chest x-ray taken Tuesday indicates that even with the very invasive treatments I am undergoing, my heart continues to get larger.

While I feel relatively good, I don't know how much more time hope can keep my body alive. Without action on your part, thousands of American lives, including mine, will be lost, fighting this battle alone. Diagnosis with a life-threatening disease is not something I would have ever asked for. But I know that with funding, we can make this disease, first, manageable, like most forms of cancer and AIDS and that soon, we will find a cure. (A situation has to be pretty desperate when anyone would hope their condition would be as manageable as AIDS or cancer!) In our race against time, every breakthrough is a victory – as we approach treatments we all get closer to winning our race against time, and with your action, we can cure Pulmonary Hypertension.

Please do everything in your power to add Pulmonary Hypertension to that list of conditions that will be at least manageable if not cured in the next few years. This bill is a starting point that will shed light on this life-threatening disease and give thousands of people the hope they need and deserve.

MR. DEAL. Thank you, Charity. You share the eloquence of your grandfather, and we thank you for your personal story.

Even though we are dealing with very serious subjects here, this is, perhaps, one of the most inspirational hearings that I think I have attended since I have been in Congress. And I thank all of you from your personal points of view from the horror stories that you share with us of the dangers that lurk, but also the hope that I think is present in some of the testimony.

And I would like to elaborate perhaps on some of the hope. And Dr. Saper, I would like to start with you.

One of the concerns that all of us have had is trying to do what is best for every disease, every serious condition in this country, using our resources most appropriately there. Dr. Zarhouni at NIH, of course, has announced his road map for the reorganization of the NIH. How do you view that proposal as it might pertain to the issue you are here for of chronic pain? Is this something that you think would be helpful in dealing with the issue of chronic pain?

MR. SAPER. To the extent, Mr. Chairman, that I understand all of the aspects of the proposal, I do not think that, at this point, it allows for the development of a separate entity devoted to pain or to initiatives that primarily address the key brain and treatment issues related to chronic pain. So to the extent that I currently understand those proposals, they don't answer the issues that we think are primarily relevant.

MR. DEAL. One of the concerns that we have heard expressed, however, is that in the absence of creating new institutes, which continues the silo effect that we have, and one of the things you eluded to is maybe the failure to share information across institute lines. I would personally view that his initiative in that regard would be helpful in dealing with this issue. I think it is going to be very difficult to create additional separate institutes, but I would hope that his road map would be an effort to be able to share resources, to share information so that those areas such as chronic pain, such as pulmonary hypertension that have not been elevated to a level of justifying, perhaps, in the overall scheme of things separate institutes that you would be able to be benefited by this new approach. That is the hope that I hold.

Colonel Hicks, would you share some opinion, if any, on that issue?

MR. HICKS. Well, Mr. Chairman, I am not very well versed in the road map, but I would hope that the road map would not be to the exclusion of what we are asking for in terms of support in the House bill.

MR. DEAL. Okay.

Dr. Gladwin, would you comment about the three organizational proposals?

MR. GLADWIN. Sure. In terms of the road map, while there are some very concrete road maps initiatives that affect specific clinical research activities, I will say that in the intramural division, the philosophy of the road map is very much permeating the establishment at all levels. So it is very frequent when we discuss research initiatives, especially clinical research initiatives. The idea of the road map is brought up to support those activities. This has had a direct affect on pulmonary hypertension for us with one example that I will give you and that is that the intramural division is typically not collaborated heavily with the extramural programs because of the separation of funding. So when we discovered in the phase one and two trial that Viagra Sildenafil was very effective for patients with sickle cell and pulmonary hypertension, we went to Dr. Nable and Dr. Alving and suggested that this would be a good target strategy. This is before the Viagra trial came out even for FDA approval for patients without sickle cell disease but with pulmonary hypertension, and the idea of the road map was called upon to suggest that we need to link the intramural division with the extramural division to synergize this NIH money. And so what has ended up happening now is there is going to be an 11-center trial. The intramural division, I am the PI in the project. I am heavily involved in the development of the science for this project. We are going to be one of the non-funded centers. We are going to be funded with intramural money. We have a commitment from Pfizer for \$1.5 million to supply drugs, even though this drug will become generic just 2 years after the completion of the trial. So the road map initiative, that vision and that philosophy, had an effect, and I do see that effect. It also just puts a continuous pressure on the basic science establishment that we need to link up basic science with clinical research. So I think as a philosophy and a principle, it is guiding us.

MR. DEAL. Good. Well, I am pleased to hear that, because I do think all of us want any breakthrough to be shared across every disease category and make sure that our money goes as far as it can, and working cooperatively, I think that is everyone's concern.

Mr. Pallone, I will recognize you for questions.

MR. PALLONE. Thank you, Mr. Chairman.

First, let me reiterate what the Chairman said and say what an inspiration so many of you have been this morning with your testimony. I really appreciate you being here, and it really has been not only thought-provoking but also gives us a lot of hope about maybe what we can do at the government level.

I wanted to ask. I guess I will start with a question for Mr. Hicks. In your testimony, you stated, and I quote, "I am sometimes asked why we should pay attention or focus resources on that terminal illness instead of

others, of which there are many. The answer is quite simple, because we can.” Do you have any more advice for us, you know, for the committee, on how to make improvements in the research priority-setting process for chronic and other illnesses, you know, how much money we should spend, how we should prioritize this versus other illnesses?

MR. HICKS. Well, that is a very difficult question. I think that I look towards the recommendations in the legislation more than anything for direction with regard to pulmonary hypertension. As I indicated in my testimony, I am asked that question so many times, and oftentimes, I get the feeling that, well, because there are so many, it is just too difficult to decide, and so our answer to you is no. And I guess I am just coming to you as a father and as someone who has met many, many of these people who are, in fact, perishing from this illness. Every day I get an e-mail that says that Susan so-and-so has just perished. Tom Jones has just perished over here. For a while it seems, on the Board of the Directors, you know, you go to a new board meeting and someone who was on the board before is no longer there, and then you find out why they are not there. So I know it is a difficult task for you. I can only ask that you consider this one as one that is worthwhile and support the legislation.

MR. PALLONE. Thank you.

I wanted to ask Dr. Gladwin a couple of questions. The legislation on pulmonary hypertension that Congressmen Brady and Lantos have introduced calls for the establishment of three Centers of Excellence on pulmonary hypertension at NHLBI. And as you know, the institute does have the authority to establish these centers administratively. And given the strong interest in pulmonary hypertension within the scientific community and Congress, can you tell us if there are any plans at NHLBI to establish Centers of Excellence in this specific area?

MR. GLADWIN. So first of all, I am clearly a middle tier scientist and clinical investigator and not a policymaker, but there are now these requests for score centers, Centers for Clinical Research Excellence, that have been sent out, and all of those grant applications are now in. I do have personal knowledge of the structure of the score grant system, and in many ways, it meets those goals of setting up those centers. So what it is, is it will be three to four highly-funded centers that are required to have two major clinical research initiatives and very creative cutting-edge, vibrant basic science channeling into those research efforts. In addition to that, Betsy Nable has now set up our branch with an intramural division, which really creates another center, and we will have a 3-year jump on all of this, and we are working on this. So I think de facto, these vibrant centers are being set up.

The other element I would mention is being inside science and seeing how science works, it is difficult to envision that you could have a

system that is so productive based on funding independent novel ideas from independent investigators. It is very much like the business model. The NIH works like a venture capital business model. We put out small business grants. The best and brightest ideas rise in this competitive environment, and the home runs are supported with future research. And the best example that is pertinent to pulmonary hypertension is an emerging story, which excites me very much. There was an investigator, Brian Druker at Oregon Health Science University, who is a basic scientist studying tylosciene chinace inhibitors and how tylosciene chinace, a self-signaling pathway, could modify disease. He was dusting old drugs off of the shelf and came upon a drug called chliatglybac that blocked tylosciene chinace and found out that it completely put into remission chronic myelogenous leukemia, CML. Well, this seems unrelated to pulmonary hypertension, but in the last few years, it was discovered that the growth hormone is one of the mediators that drives the proliferative vast response in blood vessels, and lo and behold, this drug blocks that activation of tylosciene chinace. So there was just a publication last month in the Journal of Clinical Investigation wherein two animal models of pulmonary hypertension they not only prevented pulmonary hypertension, but after the development, they could reverse it. And there was a case report in the New England Journal of Medicine where Glybac, which is FDA-approved for chronic myelogenous leukemia, reversed pulmonary hypertension on a patient on three different drugs on a heart transplant list. So these kind of remarkable, unpredictable events rise out of a system where you get the best and brightest around them and you give them the resources to innovate. And I think this is complemented by these Centers of Excellence, which have been set up by existing leadership.

MR. PALLONE. Thank you.

My time is up, and thank you.

MR. DEAL. I am going to recognize Mr. Rogers, because I believe he has to get somewhere else rather soon.

You are recognized.

MR. ROGERS. Thank you, Mr. Chairman. I certainly appreciate it.

Charity, thank you very much. I had the great privilege to hear you sing at the U.S. Embassy in Budapest. It was one of the highlights of our trip. As a matter of fact, I think you did something in Hungarian, but I couldn't tell you what you sang, but we knew it was beautiful.

MS. TILLEMANN-DICK. Thank you.

MR. ROGERS. We appreciate it.

And just for the record, Mr. Chairman, I have to correct one thing. There are many that said you got your talents from your grandfather, but

we believe you got not only your talents and your good looks from your grandmother.

MS. TILLEMANN-DICK. I would rather look like her.

MR. ROGERS. For the record, I will vote for that.

Captain, thank you very much for your service, and thanks for your continuing counseling of the soldiers. It is immeasurable that you continue to give back to your country, and we are grateful for it.

Dr. Saper, I have a couple of questions quickly.

At some of the earlier hearings, we heard that it is more or less 13 stops for an individual pain patient seeking care before they are found a medical provider that was even willing to take them. You want to talk about losing hope, that is where depression sets in, the level of suicide that we saw jump up off the charts at that level of patient care. Can you talk about access? One of the things that H.R. 1020 talks about is access to pain care providers. Can you talk a little bit about why--

MR. SAPER. Yes. Yes, I can. Thank you, Congressman Rogers.

Pain can't be proven. We don't have a test that shows a person is in pain. And therefore, it is easily the victim of someone denying that that person hurts. There is a great deal of prejudice toward people in pain in part for that reason and the concern that they are simply looking for drugs or that they simply have another agenda. As a result, insurers and managed care organizations find it possible to deny care, to say, "Well, we don't do that." I had a patient just last week, Mr. Rogers, that required hospitalization for very severe pain and various other complications to treatment, and I personally talked to the managed care person who had to approve my recommendation to put this person in the hospital. And I was told, "We don't cover pain management." It is common. It happens all of the time. Several years ago I talked to a managed care medical director who listened to me talk about this rare disorder that the patient I was treating had and the need to place this person in the hospital. And after my lengthy discussion with this medical director, she responded that she was denying coverage against my recommendation for this patient. I asked her if she had ever taken a course in this illness or in treating pain. She said, "No," and then I asked her the question, "Do you even know what I am talking about?" She said, "No, but I am going to deny it anyway." That is what we feel is in the pain care community in trying to get coverage and provide service to people in pain.

MR. ROGERS. In addition, there is not a lot of training through the educational system on pain care. Can you talk about that briefly?

MR. SAPER. Yes. It is rare for a medical school to have a formal training program in pain. There may be a lecture here or there, but pain is a major problem, and it covers many disciplines in professional

disciplines. A year ago, H.R. 1020 addresses medical education, so access and medical education and research are the truly important pillars of your bill, and that is why we so strongly support it, Congressman.

MR. ROGERS. Thank you. Talk to me a little bit. I mean, someone said earlier we have this NIH pain consortium. Go away. That is all we need. Can you tell me why you think that is not appropriate?

MR. SAPER. Yes. I will give you the diplomatic answer.

MR. ROGERS. You don't even have to be diplomatic here.

MR. SAPER. It was started several years ago. I don't know exactly when, but it meets about two times a year. Its last minutes were put forward in 2003. It has no staff. It has no budget. It has no extramural participation. And to the extent that I know everything that goes on in that consortium, it provides no benefit. It has no effect.

MR. ROGERS. And that was the diplomatic answer?

MR. SAPER. That was the diplomatic answer.

MR. ROGERS. Doctor, thank you very much. And thanks for the work that you do.

Captain Pruden, can you tell me, what do you tell your soldiers that you are counseling? I know we are running out of time, but I tell you, I think this is important, Mr. Chairman, to have somebody who is, you know, a tough Army soldier, and thank you again for your service, to stand up and say, "Hey, listen. We have problems, too." It gives hope, I cannot tell you, to millions of Americans. I will tell you a quick story. When I introduced this bill a few years ago, we had calls from all over the country of independent folks who were just neighbors, friends, associates that had gotten together on their own to have these support groups so they didn't think they were going crazy, because they couldn't get a doctor to treat them. Their friends and family didn't understand it. And to have someone like you to stand up and say, "Hey, look. This is a problem." I hope you know it gives hope to millions.

And I just wanted to see if you could just touch on that briefly. I know my time is up, Mr. Chairman. If you will indulge me on this.

Thank you, Captain.

CAPTAIN PRUDEN. Thank you very much.

Obviously, as you are saying, this is a widespread problem. The soldiers that I am working with oftentimes feel very isolated because of their pain, but they don't want to be the whiners. They don't want to be the one asking for help when other people are seeing there is not a need. People perceive that there is not a need for this palliative care. A lot of times physicians want to focus on an underlying disease, which is very important, but they don't have an understanding of how to deal with the pain when either there is not the ability to adequately treat the underlying disease or the ability to cure the disease. I think working with these

soldiers has just really opened up my eyes as far as how much of a stigma there is out there against certain forms of pain medication and how afraid people are to talk about it. And I am just trying to provide what I can in terms of support and getting them through some of these hoops that they need to jump through to get the proper pain care management. You were talking about the 13 steps. It is not that far in the Army and the Army does a pretty decent job with it, by and large. But there are still a lot of guys who fall through the cracks between the physician and proper pain management.

MR. ROGERS. Okay. Thank you very much. Keep talking about it. You are making a difference. Thanks to the panel. Thank you, Charity, too, for sharing your story. It takes a lot of courage to be here. Thank you very much.

Mr. Chairman, thank you.

MR. DEAL. Thank you.

Mr. Bilirakis.

MR. BILIRAKIS. Thanks, Mr. Chairman.

Just to be clear, regarding these three Centers of Excellence which are required under the legislation, the Lantos Brady legislation, Mr. Hicks, are the three centers that Dr. Gladwin has discussed with us, communicated with us, and shared with us, are those satisfactory as far as you concerned? In other words, is the legislation, or at least that portion of the legislation, necessary at this point in time?

MR. HICKS. Sir, I think it would be premature for me to state that. This announcement being made this morning, a very important announcement, is really the first that we have heard of it, so we have got to look at it more. But at this point, I would like to continue with legislation until we are certain that the needs are met otherwise. But I must say, once again, that we are very, very excited with this news this morning. This is tremendous news for us.

MR. BILIRAKIS. All right.

Dr. Gladwin, what is the timeline regarding those three centers?

MR. GLADWIN. Well, I know for a fact that those grant RFA was released and the proposals have already been received. So now the study sections have met and have scored the centers, and now the priority scoring, based on priority scoring, the centers will be chosen, and a decision will be made whether it is three or four. Oftentimes, if it is very close on scoring, the money will be extended to four centers, so it could be three and it could be four. But that decision about who is being funded we look for shortly. The centers have now been asked to submit supplemental material, so these things are submitted months back. Now the centers have opportunity to submit new material, and new research

has been generated in the interim, and then the final decisions will be made. My understanding is that these will start in December of 2006.

MR. BILIRAKIS. December 2006? That is a good timeline. And probably we are well ahead that then they would be through the legislation, if the legislation waiver got through the process and whatnot, isn't that correct?

MR. GLADWIN. Yes. I also comment that our center, this branch, was started on October 1, but our activities preceded that. And this program is being grown in the intramural division, and I welcome anybody here to see what we are doing there both at the basic and the clinical side. I think that will really be another center. In addition to that, I have a list of the 90 funded investigators, and the NHLBI has funded this \$11 million trial in patients with pulmonary hypertension with sickle cell. So I think that at least the spirit is being enacted.

MR. BILIRAKIS. Okay.

Doctor, a few years ago when I chaired this committee, we took a look into NIH. We have done another one or two since then. But I remember the doctors, whoever it is, that greeted us and sort of gave us a little bit of a background telling us that our diseases are either genetic or from the result of trauma. Now that being the case, if that is, in fact, I guess, the case, you are talking about genetic as far as PH is concerned?

MR. GLADWIN. Actually, it depends how you would define genetic. But if you look at a strict mutation, a major mutation, it causes a large percentage of patients with that mutation to have a disease. There is only a very small fraction of pulmonary hypertension that is genetic versus so-called familial pulmonary hypertension. This is caused by a mutation in this BNPR. That is the one that was discovered in 2000. That is only a very small percentage of pulmonary hypertension. We don't know what the cause is in the vast majority of cases of pulmonary hypertension. It could be epigenetic, meaning that there is multiple partial polymorphisms, or changes in genes, that lead to it. It is also very possible that, as opposed to trauma, that it is environmental. There is tremendous interest in the possibility that there could be unidentified viral infections, for example, that lead to this. Research in Denver is looking at the virus that causes caposi sarcoma, for example, and there are other efforts to try to identify possible infectious etiologies. But we really don't know, and I think the development of a field of vascular biology and tools, such as functional genomics. You know, one thing we are working on is the ability to isolate, from a human, copies of few numbers of those circulating endothelial cells that have been shed, take those endothelial cells and amplify the RNA and to look genetically at what those cells are doing, as opposed to looking at something in a dish or a culture dish that is so far from the human condition. But I think

there has really been a basic science revolution focused on vascular biology to try to figure that out.

MR. BILIRAKIS. Well, should Charity's family all be tested to determine whether or not there is a possibility or probability that they would be susceptible to this disease and can possibly then catch it early on, if you will?

MR. GLADWIN. I don't think so. I am answering as a clinician here, but the percentage of patients with that mutation is very small. I think that is really more of a researcher epidemiological interest at this point. I think there are diseases, though, that are associated with a very high attack rate of pulmonary hypertension, and I am sure Charity knows. Many of her friends that she has met and certain people with PH association know patients with scleroderma. Scleroderma, which is a mixed connective tissue disease, is an autoimmune condition. In those patients, a recent study from Canada suggests that 20 percent of those patients have pulmonary hypertension of a mild nature, and that could be, for example, a targeted pre-disease. So we believe that patients with scleroderma, they should all get echocardiography to screen to see if they have pulmonary hypertension. And we are currently screening patients infected with HIV in the clinical center. We have screened 300 patients to determine what percentage may have pre-disease. In sickle cell, we have recommended universal screening across the United States, that is 70,000 adults with sickle cell, because 30 percent of pulmonary hypertension is caused by that.

So I think there are some specific diseases where we need universal screening. Unfortunately, primary idiopathic pulmonary hypertension that you have heard about occurs in two out of a million Americans, so it is difficult to have a screening strategy at this point.

MR. BILIRAKIS. Thank you.

MR. GLADWIN. I hope that answers your question.

MR. DEAL. Ms. Capps, you are recognized for questions.

MS. CAPPS. Mr. Chairman, thank you. And I want to share your comments after the testimonies were finished of you saying this has been one of the more enlightening hearings that we have had. And thank you for doing what I have always thought hearings should be about, which is to educate Members of Congress and help us order our priorities, because really, that is what we do. And we need to do two things, which I think both components of the hearing did today, which is to remove the stigma, to remove the barriers that we might have in our understanding, and that is why I am thinking most especially about the eloquent testimony on pain by the experts in background but also the technology that is available. Medtronic has a plant in my District in Toledo, California and many places around the country, I know, and you are just one example of

technology that could be opening so many more doors that spreads across the range of what we have been talking about today. But also the personal testimony. Captain Pruden, I can't thank you enough for what you are doing to help to educate, particularly your age and your cohorts who you are surrounded with. The stigmas to pain, and I would like to give you a chance to expand upon that, any of you, because pain is a part of what you described, Charity, so eloquently and painfully to hear, as well. And I have a daughter with cancer, and the stigmas against giving pain medication, the fear of some law enforcement, that it will become addictive, that it will go out into the black market, all of the things that will happen that make us freeze in terms of doing the right thing to support both research and also the kind of palliative care that hospice is good at understanding but so often is disconnected even from mainstream medical care. So, Captain, you gave your testimony, but maybe go into it a tiny bit more about what you ran into and what you think about now being where you are with this.

CAPTAIN PRUDEN. Sure. I have one example to give of the sort of stigma that is prevalent. I had a soldier who returned very badly wounded, and he is sort of on both sides of the stigma, both from his side and from--

MS. CAPPS. Being macho and being tough?

CAPTAIN PRUDEN. Right. I talked to him, and I was asking him how he was doing and how he was walking, how he was, you know, coping, how his physical therapy was going. And he said, "Well, sir, I am doing good. You know. I am in a great deal of pain, but I am not taking that pain medication."

MS. CAPPS. Yeah.

CAPTAIN PRUDEN. You know, "I can suck it up and I can make it happen." And he was very proud of that, but then as I was around him more and talked to him more, I realized that he was self-medicating with alcohol, trying to cope with the pain, but didn't want to be associated with taking these opiates and narcotics. And the other side of that is this gentleman was completely dedicated to returning to Iraq to be with his soldiers. He lost several men over there, and his goal is to get better and get back, and he is undergoing some surgeries to remove some shrapnel before he could return. Time and again, you keep hitting these walls with the social workers and different people. He wasn't getting the pain medication that he needed, and a lot of times they would treat him like he was pretending, that he was acting like he needed pain medication when he didn't, and the fact was, he was very motivated to get off the pain medication and get back to his job. But he was extremely frustrated with the physicians and some of the individuals who acted like he didn't need as much pain medication. He needed to just, you know, go on about his

business. That was one example. And you know, my understanding is that proper use of narcotics and opiates for pain medication has a very low rate of addiction when they are properly used and supervised.

MS. CAPPS. Do you want to add to that, Dr. Saper?

MR. SAPER. Yes, thank you.

I think that I would agree with the Captain's remarks. The pain patient is stigmatized, and so are those of us who treat pain patients.

MS. CAPPS. Yes.

MR. SAPER. So there are two sides to that issue. Most patients who are provided narcotics or opiates do not abuse their medicine and do not misuse them in any way and do not divert them. We do know that that can be a problem. And we deal with that problem not by denying access to those treatments or access to stimulator neuromodulation but by training doctors to monitor what they provide their patients. We do that in all care systems by teaching doctors how to use opiates are one tool in a broad range of services that we can provide for headache and general pain patients, and we have to have coverage for those services, the neuromodulation, the expensive medicines, and of course the professional services that are required. And I think that H.R. 1020 helps by, one, establishing the credibility of the pain problem by the stamp of Congress, by your involvement--

MS. CAPPS. Good.

MR. SAPER. --by your advocacy through that legislation. And that allows those of us in the field treating people like Captain Pruden the influence with insurers and other parts of the community when we have to fight back. We don't have much to fight back with right now.

MS. CAPPS. Well, we need to continue to help you more in this area, and I hope that we will. This will be the beginning of more work that we can do. We have had some legislation that I was dismayed that we responded to in terms of end of life pain treatment as well, but I want to, because this is like almost two full hearings in one Charity, I am so taken by the newness with which your situation has even been as treatable and isolated and diagnosed. All three of you were excellent in opening my eyes to something I didn't know as much about, even though I am a nurse, but in a different era. This was one of those unexplained kind of things that we just saw the side effects.

Two things I need. One of the things, just generally, we don't deal enough with so-called orphan situations, and NIH, you are our only hope. Until you walk through the door as an advocate or a patient, or you are a doctor trying to get a trial or some research approved, you realize that the popular diseases or entities, and they are important, too, but we are not on an even playing field in this country, in terms of the needs that we have. And that is what I feel like we need to be educated about. And

that is why I am so thankful that we have some built-in advocates here in Congress to remind us.

Charity, this is my question to you. You were a teenager when you were diagnosed or when you began to have symptoms, but you don't want to have to carry this huge burden of trying to demonstrate to society that there is something that needs to be treated.

MS. TILLEMANN-DICK. But Congresswoman Capps, you bring up an interesting issue, which is diagnosis. Pulmonary hypertension is invisible. You can't see it. It takes very invasive treatments to find it. I think that we will find, as we study more, as we put more money into research for pulmonary hypertension, that it may very well be an epidemic. I had a dear friend who died at 19 years old from heart failure who was perfectly healthy, by all accounts. There was no indication that she was going to die. She very well could have had pulmonary hypertension. It is very difficult to find unless you look for it after someone dies, you know, in an autopsy. I have been suffering from symptoms since I was a very little girl. When I was talking about playing soccer, I was 6 years old, so that was a long time ago. I remember going on hikes with my grandmother when I was 13. And she would be like, "Charity, really, you have to exercise more." And it wasn't that I didn't exercise, because I did. I would exercise for a half an hour every day when I was young, and then I would go out and we would play. With 11 kids in the family, you can't really avoid that. But I think that identification is one of the biggest battles that we have to face with pulmonary hypertension, and I think that as we invest more in research that we are going to find that there are many more people who suffer from secondary pulmonary hypertension and idiopathic pulmonary hypertension than we ever imagined.

MS. CAPPS. Well, thank you. You have been very eloquent today.

MS. TILLEMANN-DICK. Thank you.

MS. CAPPS. Thank you.

MR. DEAL. Thank you.

Dr. Burgess.

MR. BURGESS. Thank you, Mr. Chairman.

And again, I want to thank the panel, each of you, for being here today. Charity, I apologize. I had to leave the room while you were giving your testimony. I did read your written testimony. And as I was reading that, in another life, I was a physician, and I couldn't help but think, gosh, how lucky you were to get to a doctor who was actually able to make the diagnosis. Colonel Hicks, I don't know what your experience was with your daughter, but I can just imagine. Well, Dr. Gladwin, perhaps you could tell us, is that unusual for someone to see the physician and be diagnosed at that visit that they possibly have

primary pulmonary hypertension? Or is it usual, is that your history, that someone sees various physicians for various ailments and then ultimately comes to the diagnosis?

MR. GLADWIN. Yes, absolutely. As Charity said, there is no visible evidence. We really only have three major tools to diagnose it, one, a relatively new one, a blood test. A brain natriuretic peptide can be elevated in the blood of patients that have pulmonary hypertension, but that is also elevated in patients with kidney failure and heart failure, which are much more common. An echocardiogram can have the ability to tell us non-invasively. That is shown on the poster over there that the pressures are elevated in the heart. And there are big advances. The technology of echocardiography is really improving and the fidelity of these measurements is improving. But even so, I would say, if you would just ask for an echo to be performed on your patient, you have probably had this experience, I would say less than 10 percent, even in academic medical centers, will actually measure the pulmonary pressure. They focus on the left ventricle, and they tell you that left ventricular function. They ignore the pulmonary pressures. That is changing. For example, at the NIH, every echo requires a 20-minute assessment of the pulmonary pressure. We have recommended that in patients with sickle cell, and I think there is growing awareness. More and more echoes now report the estimate of pulmonary pressure, and then the final test that Charity eluded to is a right heart catheterization where you actually put a catheter in the jugular vein and pass a very large thin catheter, a 70-centimeter catheter, through the heart chambers into the pulmonary artery to directly measure the pressure. So what she had was a physician who did the physical exam, you know, took the time to do a good physical exam, took an excellent history, and as you know, the history and physical exam are invaluable, and was smart and attentive. Oftentimes, even as a pulmonologist seeing patients, you know, I have this asthma clinic I do every other week just as a volunteer in the district, and I get patients with pulmonary diseases. And typically, we rule out lung disease with CAT scans. We rule out left ventricular disease with echoes. We almost rule everything out, and then when everything is normal, we go, "Ah, maybe it is the pulmonary vasculature."

So I do think that this is a vital element in future research and this is where the field of proteomics can really help us; the ability to identify small molecules and mediators in blood so that we could have blood tests to predict whether people have pulmonary hypertension, essentially like the PSA. And there are some tasks, but we are not there yet, and that is somewhere I think where we are going, too.

MR. BURGESS. Very good. What sort of educational activities is the NIH undertaking to make clinicians and first-line physicians and nurse practitioners more aware of pulmonary hypertension?

MR. GLADWIN. Well, I guess this is all very new, these five drugs, another five coming. They are hitting at a breakneck pace. So physicians typically, once they have tools, as you know, once you have the tool, you really start trying to learn how to develop those tools. But now that there are two pills, this lowers the bar for the ability to treat now. And while experts don't recommend this, the practicing doctors are starting to treat patients. And with the ability to treat, you lose what follows that, and doctors start saying, "I really need to know about this. Those five drugs, I have got to learn." So I think there is a great focus on that. In fact, I was at the ACCP meeting a few months ago, and the pulmonary hypertension sessions, you couldn't get in the rooms. They were bursting with so many people wanting to get in there and learn about these new drugs that were available. But the ACCP has put out an expert consensus statement on the guidelines and treatment of pulmonary hypertension. There has been a new classification scheme to try to educate people on the classification of pulmonary hypertension in collaboration with the PH Association. I think that is a very important collaboration. NHLBI and the PH Association are funding young, career-development awards. Betsy Nable, again, is a very dynamic leader. She is speaking at the American Society of Hematology meeting this Sunday. And following her, an investigator from our group is going to be giving a preliminary presentation on the use of biomarkers to predict pulmonary hypertension. And I am giving an educational session talk at the ASH meeting on pulmonary hypertension and sickle cell disease.

So I think that the process of science, in terms of education, the development of practice guidelines, the important advocacy. I received an e-mail from you guys about this meeting. So I mean, they have networked with the community, which is fantastic. So those things are working, but clearly, more can be done.

MR. BURGESS. And Dr. Gladwin, let me just ask you. You talked about, of course, primary and secondary pulmonary hypertension. You also talked about the two pathways by which it develops: one being dysregulation and the other being proliferative. Does primary or secondary pulmonary hypertension, does one have the propensity to be dysregulation and the other proliferative, or is it equally dispersed?

MR. GLADWIN. It really is equally dispersed. One of the remarkable things, to me, I think, is that regardless of the cause, you see the final similar end stage effect. So in patients with sickle cell disease where we think hemolysis, the breaking up of red cells, the releasing of

hemoglobin out of a red cell into plasma, releasing red cells enzymes into plasma, all of those things poison the endothelial cells. And those things block nitric oxide. They block Prostacyclin, and they result in this proliferation. That ends up causing this proliferative filling of blood vessels and this vasoconstriction. Patients with idiopathic pulmonary hypertension, which could be caused by this mutation, could be caused by an unknown virus. They end up with the same abnormality, and the drugs cross talk. So we are seeing tremendous efficacy of Viagra, which has been shown in a very large article just published in the New England Journal of Medicine that works in patients like Charity with primary pulmonary hypertension. So these drugs work in primary pulmonary hypertension, scleredema pulmonary hypertension, and the HIV-associated pulmonary hypertension, and we are seeing effects in patients with sickle cell. So the great news is that it appears to be working across types of disease. There is one big exception, and that is one of the most common cause of pulmonary hypertension in the world is heart failure, left heart failure, with a backup of pressure that leads to secondary pulmonary hypertension. Some of the drugs are dangerous for patients that have left heart failure. Some of the drugs, like Viagra, may be effective in those patients. So not every one of them is the same, but the vast majorities do behave similarly.

MR. BURGESS. Now you mentioned that there are five drugs that are FDA approved. Has there been any difficulty with the regulatory burdens that the FDA imposes for people who are critically ill and might benefit from fast tracking of the new medication?

MR. GLADWIN. I will only talk from my own experience, but I would say no, that this is exciting. In a lot of areas, pulmonary hypertension is a very exciting and informative area, because I also have one friend in the sickle cell field, and I study what is happening in pulmonary hypertension as an example of what you can do with an orphan disease. With the combination of advocacy, industry involvement, and state-of-the-art basic science, they came together, as I said, in this perfect storm. And the FDA, I think, is another example where this regulatory agency has really come through in a great way with pulmonary hypertension, and I have a personal experience, because I served as a scientific advisor. I am on the steering committee for a clinical trial of Bosentan in sickle cell disease. I received special approval from Betsy Nable to allow me to testify as a scientist, not as a representative of the company. I don't receive any funding from them, but that was a unique industry and NIH collaboration. I was there to be able to testify to the FDA about sickle cell disease, but they asked for fast track, and they were immediately given that. You will see in the pulmonary hypertension field that almost always fast track status is given by the FDA. They have accepted as a

gold standard the 6-minute walk test, which is how far you can walk in 6 minutes, because that is what matters for patients and their symptoms. “Can I walk up the stairs? Can I vacuum the floor?” The FDA has accepted that surrogate, and they accept a single, pivotal, phase three study. So the bar for approval for this disease is low, but of course safety is ensured. So I think this is an example for orphan diseases of how these collaborations and how the FDA’s involvement from the beginning, from what I have seen, has really led to rapid approval of drugs.

MR. BURGESS. Thank you very much, Mr. Chairman. I thank you for your indulgence of the time.

MR. DEAL. Thank you.

Mr. Shimkus.

MR. SHIMKUS. Thank you, Mr. Chairman. This has been a wonderful hearing. I think we have learned a lot.

For Captain Pruden and for our stenographer here, I will just give you a “hooah”, and that is h-o-o-a-h. I appreciate your service.

In your testimony, which you stated and that I also read, I think we shouldn’t leave this hearing without making sure we close a loop. And as has been addressed by a couple of members, you raise a concern about these young soldiers who aren’t addressing their pain issues or the Walter Reeds, the Bethesdas, and the doctors that are not trying to close that loop. You know, a lot of us have gone through healthcare issues. I had open-heart surgery. I didn’t want to take my pain medication, and then when my body started flipping out because I had this pain that was all over, you know, it is not like I was just having pain here, but it was an all-over pain, that your body just starts doing stuff that it is trying to mitigate it. So it is in everybody’s best interest that people address the pain issues and probably for a quicker recovery, which was in my case, also. What do we need to do? And I mean, you are still on the payroll. How do we get you engaged? I mean, do we need a victim? Chairman Bilirakis, you know, has been really involved, many times, in veterans healthcare issues. And what my issue is, I want to make sure we close the loop that we have an advocacy or an intermediary or somehow that we make sure that these soldiers are being addressed and marines and all of these folks that are injured so that they know that they can go, that someone is talking to them, and someone who doesn’t need to use his rank or his knowledge that will address this. And that is one of the main reasons, you know, that I wanted to make sure I had a chance to ask this question.

CAPTAIN PRUDEN. Sure. You know, I think that the Army and the VA, from what I have seen thus far, have actually done a good job in the recent years, especially since the war began, of focusing on pain

management and helping to provide, you know, pain clinics, and I think that that should be extended. I think where a disconnect oftentimes occurs, is between the physician and the anesthesiologist or whoever is running the pain clinic. I think physicians need more training in proper pain management so that they know what is available. And then also when they don't know and the patient is complaining of pain, they have the wherewithal and the understanding that they should when they don't know how to treat it and the patients are complaining of pain, send them to a pain care specialist and get them through there and make sure that someone follows the person through. Too often, you know, I think with the specialty clinics you have orthopedics and, you know, gastroenterology and different things, and they don't talk to the pain management people. They are not following them, and then the pain management gets the soldier or the individual, it gives them a treatment course, but they are not cross talking with the people who are dealing with the underlying cause of the pain. I think that is important.

MR. SAPER. Mr. Shimkus, that is a very important question you are asking. And I think, honestly, that if Congress were to pass H.R. 1020, which would give credibility and support to those of us in the pain care community, you know, many of us differ on how we should approach this or that, but the entire pain care community, patients, different disciplines, device makers, drug makers, the entire pain care community is behind H.R. 1020. That is a powerful initiative, and that will give us the influence and the authority to work within our own systems to bring about better pain care in America.

MR. SHIMKUS. Well, I can definitely see how you all here at the table as someone's healthcare is being addressed and that people need to know these options and the patient needs to be aware on all of those issues. And I would ask Chairman Deal and the Navy, because of Mike's persistence in this arena, that we may share that to the Veteran's Affairs Committee on this health issue, especially for our folks that we have closure or at least the availability of this testimony here that we submit over to them so that. I am just concerned. You know, the main reason I am here because I saw firsthand soldiers who slipped into the void. I don't want them to slip through the void. So I want to just close the loop on this as much as possible.

MR. BILIRAKIS. Thank you so much for bringing that up. And I have already told Gene that if I had gone out of time, I wanted to go into basically exactly this sort of thing with the Captain. And I will tell you that one of the chief causes of the Veterans' Committee right now is transition. And that is critical. And we make sure that this is a part of what we are looking at that.

I wanted to ask you, though, sir. What could have been done to have saved your decision or kept your decision from amputating, what is it, your right leg? Obviously the pain is what brought it on. What wasn't done that could have been done that existed from something like Medtronic is saying? What should have Congress done that would have kept that decision from being made by you?

CAPTAIN PRUDEN. You know, the decision that I made wasn't solely based on pain. That was a primary concern. Part of it was functionality. I mean, part of the reason that it didn't function well was because of the pain. My leg was short and deformed, and I was unable to bear weight on it without a great deal of pain. I don't know that I have a good answer as far as, you know, what would be appropriate to fix this problem.

MR. BILIRAKIS. Was Medtronic available to you in all of your counseling? Well, I guess that is really what Mr. Shimkus counts for that.

CAPTAIN PRUDEN. About pain care options?

MR. BILIRAKIS. Yeah, the options that were there that--

CAPTAIN PRUDEN. Well, I think what could be done is facilitate, again, research and education so that there is more awareness of things like this for patients like myself and for the physicians overseeing our care and the research to develop new techniques.

MR. BILIRAKIS. But Medtronic was available? Jerry Lewis, the entertainer, has been using it for quite some time, and that sort of thing. I don't know whether that would have been the answer to the question or not, but was anything made available to you? Did you know anything at all about it?

CAPTAIN PRUDEN. I didn't know anything about that specific device. I am not aware of that.

MR. VANDER ZANDEN. If I could just comment. I mean, that is one of the things that we are really working so hard to do, and that is why H.R. 1020 is so important. I mean, if you look at just our programs, we have got 350 million media impressions with Jerry Lewis. We have gotten 2 million hits to our website. We have 65,000 active members of Tame the Pain. The work that we have done partnering with the American Pain Foundation, especially, who is represented here today, the American Academy of Family Physicians. The biggest issue right now is having people really understand what this is. And I just feel the need to clarify for everyone--

MR. BILIRAKIS. Mr. Shimkus' time is long gone. I don't know. It is up to you, Mr. Chairman.

MR. VANDER ZANDEN. If I could just summarize one point. I mean, the patients we are talking about are patients who are not dealing with a backache. We are not talking about people who have an injury. We are

talking about people who have their hand on the iron or on the stove and have no ability to remove it. That is the kind of pain we are talking about. We are talking about people who have changed the function of their lives. They can no longer work. They have lost marriages. They have been drug addicted. They are so far beyond hope, by the time they even see a pain management professional. If they do, after, as we said earlier, 13 visits sometimes, by the time they enter that pain management practice, it may be 4 years before they actually get one of our therapies. Just improving the access, improving the awareness through H.R. 1020 will be tremendous.

MR. BILIRAKIS. I thank the Chairman for giving me the time.

MR. SHIMKUS. Mr. Chairman, if I can just have 30 seconds. I won't ask any more questions. I just want to make brief comments. One is, Dr. Gladwin, you make us proud. I mean, I don't understand one-fourth of what you said, but the fact that you are on our side working and with your knowledge, I thank you for that. And Mr. Hicks, we feel your pain. I just want to let you know that we do, also, with all of these other diseases, we have constituents. I have one who recently died from Lou Gehrig's disease, so we also have those meetings where we have people lobbying in support of these diseases who don't show up anymore, especially as Members of Congress. So we are with you, and we understand from whence you come.

And just a final note on Medtronic. I know that we were handed these. There were, I guess, some successful technologies you brought up that failed or didn't pass the screening. And it is just a comment to be made about our continued beating up of corporate America, because they do great work. They try to perform need. They need a return on their technology and their investment, and so I am glad you are on the team to try to address these things, and all corporate entities are not bad and evil.

Thank you.

And I yield back, Mr. Chairman.

MR. DEAL. Thank you.

Ms. Myrick.

MS. MYRICK. Well, thank you, Mr. Chairman.

And I would like to identify with your remarks earlier.

And Mr. Shimkus, thank you for bringing that up with the Captain.

Captain, thanks for still serving your country. We can't express our gratitude enough to you for what you have been through and what you are doing.

And Dr. Gladwin, again, you have given us hope. And as John said, we don't understand all of it, but we can understand enough to know that this is good and you are making progress.

And for Mr. Hicks and Charity, thank you for having the courage to come today and share with us. We do appreciate it.

Dr. Saper, I would like to ask you a question. I am concerned about an area that we haven't really talked a lot about when you talk about chronic pain, and that is the mental health side. I have a husband who has suffered with chronic pain for almost 20 years, and I know how it can drag you down. When doctors treat people for chronic pain, do they do anything to deal with, I guess what you would call, the depressive side that comes through that, too? Is that a normal course of treatment in the chronic pain field? Is this something that should be looked at more in what we are talking about with all of this cross-pollination at NIH that we are going to be doing?

MR. SAPER. Yes, that is a very important area. You know, there are different approaches to pain. There are very narrow approaches, such as injections or pills, and then there are the comprehensive centers. I direct a comprehensive center in Ann Arbor. And the boundary between mental pain and physical pain is an uncertain boundary. All pain, mental and physical and mood, is biochemical, and they influence each other. And appropriate care for chronic pain should include dealing with the emotional side of the pain problem, so we have centers. We have doctors who give pills and then centers who put in stimulators and we have doctors that give injections and some do surgery. And then we have comprehensive centers that try to put it all together for the more difficult cases, and every level of that pain care hierarchy is necessary to address this problem. Our field is in the young years. It is a young field. We are just beginning to credentialize doctors and train them. And the pillars of H.R. 1020 provide us those tools: education and research and access. And the mental side of pain care is very important, and I agree with you.

MS. MYRICK. Well, it just concerns that we are sitting here listening to all of you talk about the chronic pain side and then that this is an issue that we have not, as a group, paid a lot of attention to. And a lot of people do grin and bear it. I mean, you know, you can have a minor chronic pain that you put up with. And I think, as John said with not taking pain medication when he had his heart problem, people don't realize how that really affects their overall body. And so you know, what we can do to help in those areas, I hope that you all will stay in communication with us, because I think it is very important that we make people realize that this is something, that it is not bad to take pain medication. They are not bad to get help, Captain, as you are trying to tell your guys when they really need it. It is not something that you are, you know, a weakling if you do.

But I thank all of you for being here today. It has been extremely informative.

And I yield back.

MR. DEAL. I thank the gentlelady.

Once again, you all have been an incredible panel. You have done something that very few panels in hearings do: you have not only put the personal face on the issues; you provided the clinical expertise, you provided the mechanical radius of trying to deal with this. Mr. Vander Zanden, I apologize that you were sort of left out of the discussion. That was certainly not deliberate, because, as Mr. Shimkus says, we recognize the importance of what companies like yours are doing, because you are truly the link sometimes between the doctor who knows what needs to be done, the patient who is feeling the pain, and you provide a mechanism of delivering that relief, and we appreciate what your company and others are doing in this field.

For those of you who are the victims of these diseases or these problems and the advocates on the behalf of them, I couldn't think that anybody could have selected better representatives than the ones that have appeared before this committee today.

Thank you all so very much. This is truly a memorable event. Now the responsibility is ours to try to take the education and the information that you have provided to us and try to, as Mr. Shimkus says, close the loop of making something positive and meaningful happen as a result of your testimony today.

Thank you all so very much.

The hearing is adjourned.

[Whereupon, at 12:20 p.m., the subcommittee was adjourned.]

[Additional material submitted for the record follows.]

Question from the Honorable Ed Towns

**Dr. Mark Gladwin, Chief, Vascular Medicine Branch
National Heart, Lung, and Blood Institute
National Institutes of Health
December 8, 2005**

**Subcommittee on Health Hearing entitled: "Improving America's Health:
Examining Federal Research Efforts for Pulmonary Hypertension and Chronic
Pain"**

While many Americans are suffering from pulmonary hypertension and chronic pain, communities of color are being devastated.

1. What specific measures are being taking to address the higher prevalence of chronic pain and pulmonary hypertension among communities of color?

ANSWER:

[NOTE: While the response in relation to pulmonary hypertension was prepared by Dr. Gladwin, who testified before the Subcommittee on the issue of NIH pulmonary hypertension research, the response in relation to chronic pain research was prepared by Mitchell B. Max, M.D., Clinical Pain Research Section, National Institute of Dental and Craniofacial Research, NIH.]

Dr. Max: Recognizing that pain is experienced differently across various racial and ethnic groups, the NIH is soliciting grant applications to determine which behavioral treatments are most effective for specific subgroups of patients according to factors such as age, gender, race, and ethnicity. Research applications are also being invited to develop and test biobehavioral pain interventions for persons of various ethnic minority groups, either as a unique study or comparing interventions and outcomes across populations. NIH also is actively looking to fund studies to investigate the prevalence and effectiveness of the use of complementary and alternative therapies for pain treatment in diverse populations such as ethnic minority groups, the elderly, the terminally ill, patients with HIV-AIDS, and patients with other acute and chronic illnesses that are associated with pain.¹

Several NIH Institutes and Centers are addressing pain prevalence, pain treatment and management, and responses to analgesic drug outcomes as part of their Health Disparities Strategic Plans. A range of pain conditions are being addressed that include among others: evaluating chest pain and cardiovascular disease, osteoporosis, osteoarthritis, surgical pain, cancer pain, and end-of-life and palliative care.

NIH is also addressing the issue of opioid treatment. Opioids are the most powerful treatments available for most forms of pain, but they can have negative health consequences and may result in abuse and addiction. In a recently released Request for

¹ PA-03-12 Biobehavioral Pain Research. Release Date: July 11, 2003, Expiration Date: July 30, 2006 unless reissued. Includes NINR, NIA, NIAMS, NCI, NICHD, NIDCR, NIDA, NIMH, NINDS, NCCAM

Applications (RFA), NIH is soliciting new research to examine risk and protective factors related to opioid abuse and addiction in the context of pain, develop pain treatment protocols that are tailored to reduce the probability of these negative health consequences, and develop ways to ameliorate these problems when they occur. As part of this RFA, NIH is encouraging research on the prevalence of physical dependence, abuse, and addiction to opioids in pain patients in relation to age, gender, and ethnicity as well as studies on how pain perception and willingness to report pain might vary by age, gender, and ethnicity.²

NIH is also addressing persistent pain that is associated with disorders of tissues of the head and face such as migraine disorder, trigeminal neuralgia, temporomandibular joint and muscle disorders, and dry eye syndrome. As part of this research initiative, NIH is looking to determine factors that underlie gender, age, and ethnic variations in pain experience in order to provide more appropriate and individualized pain management.³

As you are probably aware, NIH policy requires that women and members of minority groups and their subpopulations must be included in all NIH-funded clinical research as well as Phase III clinical trials, unless a clear and compelling rationale and justification that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. This policy applies to research subjects of all ages in all NIH-supported clinical research studies.

Dr. Gladwin: Although primary pulmonary hypertension (which arises without any clear-cut underlying illness to precipitate it) affects people of all racial and ethnic backgrounds, secondary pulmonary hypertension (which is the result of an underlying illness) is a serious complication facing African Americans who have sickle cell disease. As mentioned in my testimony, studies conducted by the NHLBI Division of Intramural Research have shown that almost one-third of patients who have sickle cell disease develop pulmonary hypertension by age 18 and that patients who have both pulmonary hypertension and sickle cell disease have a 10-fold greater risk of death compared with sickle cell disease patients who do not have pulmonary hypertension. The findings prompted NHLBI to announce plans to award contracts for a multi-center, placebo-controlled clinical trial of sildenafil therapy in this patient population to assess the drug's safety and determine whether it improves patients' exercise capacity, pulmonary pressures, and symptoms. If the research demonstrates that sildenafil benefits patients who have pulmonary hypertension as a consequence of sickle cell disease, sildenafil

² RFA DA-06-005 Prescription Opioid Use and Abuse in the Treatment of Pain Release Date: November 18, 2005. NIDA, NIDCR.

³ PAS-03-173 NEUROBIOLOGY OF PERSISTENT PAIN MEDIATED BY THE TRIGEMINAL NERVE RELEASE DATE: September 16, 2003 PA NUMBER: PAS-03-173 EXPIRATION DATE: July 01, 2006, unless reissued. NINDS, NIDCR

therapy is expected to greatly reduce the burden that pulmonary hypertension places on the African American community.

Now that we know that sickle cell patients have a dramatically increased risk of developing pulmonary hypertension, physicians who care for adult sickle cell disease patients are being encouraged to screen for pulmonary hypertension so that the patients can begin life-saving treatments. When the findings of the NHLBI intramural study mentioned above were published in the *New England Journal of Medicine*, the NIH press release emphasized that screening represents an opportunity to address a major cause of disability and death in the adult sickle cell disease population. Our results were featured in popular press articles such as the one from the health section of the *Washington Post* (March 2, 2004) that was displayed on a poster during my testimony. Programs at NHLBI Comprehensive Sickle Cell Centers and elsewhere, including the Sickle Cell Adult Provider Network managed by the University of Colorado Health Sciences Center and the Sickle Cell Information Center at Emory University School of Medicine, also are promoting the benefits of screening through newsletters and electronic mailing lists. Furthermore, my fellow researchers and I are continuing to educate physicians by emphasizing the findings at scientific conferences and through publications in peer-reviewed journals.

PAIN CARE COALITION

A National Coalition for Responsible Pain Care

American Academy of Pain Medicine • American Headache Society • American Pain Society •
American Society of Anesthesiologists

VIA HAND DELIVERY

January 20, 2006

The Honorable Edolphus Towns
Subcommittee on Health
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

Re: December 8, 2005 Hearing on Chronic Pain

Dear Representative Towns:

I was privileged to testify before the Subcommittee on Health on December 8th on subjects related to chronic pain, and I appreciate your question concerning one very important aspect of that hearing, which was the critical need for pain research. You have asked "What advancements in treatment will be gained from ongoing federal research about chronic pain management?" and I am pleased to offer these additional views for the hearing record.

As I pointed out in my testimony, pain is woefully under-funded at the National Institutes of Health relative to the burden pain imposes on the general population. Furthermore, unlike its approach to other diseases such as cancer, diabetes, arthritis or HIV-AIDS, and despite Congress having declared the decade ending in 2010 as the "Decade of Pain Control and Research," NIH lacks a comprehensive research agenda for pain. Because pain cuts across virtually all categories of disease and injury, this lack of a co-ordinated and comprehensive approach to pain research severely limits the potential for discoveries in one area to lead to rapid clinical enhancements in others.

As you are aware, pain is a gigantic and compelling public health problem in this country. Millions of individuals of all ages and from all walks of life suffer from chronic, disabling pain. At best, it is a continuing annoyance that restricts daily activities and detracts from quality of life. For far too many, it is a serious disease, injury or condition that leads to disability, often accompanied by depression, and virtually destroys quality of life for the sufferers and often their families. Twenty percent of surveyed Michigan chronic pain sufferers had considered suicide as an option.

Pain takes many forms: migraine, low back pain, head, neck or jaw pain, chest pain, neuropathic pain from nerve injury and disease, arthritic pain in the joints, and on and on. In some cases pain accompanies other diseases like cancer, diabetes and arthritis for which the federal government has ongoing disease-specific research agendas. In other examples, like migraine, low back pain, or jaw pain, pain itself is the disease, and these areas get less focused attention in the current NIH structure and funding priorities.

The most comprehensive study of the ongoing federal research effort to date, based on 2003 data, was recently published in *The Journal of Pain* Vol. 6, No. 5, May 2005, and I am submitting a copy of that report and accompanying editorial commentary for the hearing record. Principle findings of that review included the following.

First, only 1% of NIH research dollars are currently committed to research grants with a primary focus on pain. When grants with a secondary focus on pain are included, the figure approaches 2.5%. (See Abstract.)

Second, slightly more than half of the pain-related grants are for basic science research, and slightly less than half for clinical research. (See Table 4.) Third, the current effort is widely dispersed between and among different Institutes and Centers at NIH, with the top five institutes accounting for only one half of the grants, with the other half spread across 23 different organizational units. (See Tables 5 and 7.)

Fourth, some diseases and organ systems currently receive much more attention than others, seemingly irrespective of the connection between those diseases or systems and the incidence of chronic pain suffering. For example, despite the prevalence of chest and other pain among those suffering from heart disease, there is virtually no funding for cardiac pain. And while severe headache affects millions, often daily (4% of general population), it receives scant attention at NIH. (See Tables 13 and 14.)

As with other aspects of scientific research, predicting which basic science projects will lead to promising areas of clinical research, and which clinical research efforts will lead to improved or even "breakthrough" treatments for pain sufferers is quite difficult. In the case of pain, this difficulty is enhanced by the limited funding currently available and the lack of a more systemic and co-ordinated approach. Notwithstanding these limitations, there are areas of ongoing research which suggest possible treatment applications in the reasonably near term.

* Researchers in one area of NIH-funded activity are beginning to understand that many common painful conditions are accompanied, in some individuals, by a greatly increased sensitivity to pain elsewhere in the body. This amplification of pain may help explain conditions like fibromyalgia, Gulf War-related chronic pain, idiopathic low back pain, and temporomandibular joint disorder ("TMJ"). Research elsewhere suggests that genetic variabilities contribute to this pain amplification. Further research is underway to extend this genetic inquiry. If certain genes are confirmed to be linked to pain amplification, it may be possible to predict who is likely to develop particular pain

syndromes. Similarly, certain genes appear linked to drug susceptibility, and genetic research may provide clues to developing new drugs to treat chronic pain conditions.

Another area of promising but early research relates to visceral pain. It appears that internal organs signal pain by somewhat different chemistry than do skin, bone, and joints. Animal studies have identified a pain receptor that may signal angina when a piece of heart muscle is deprived of oxygen. This particular receptor can be blocked by a commercially available and very low cost diuretic. These discoveries in animals could have implications for treatment of angina, esophageal and stomach pain, kidney stones, or childbirth pain in humans. But there is currently little NIH-funded research on cardiac pain or other pain related to the internal organs. With most clinical pain research now in just a few medical specialties (neurology, anesthesiology, and dentistry), NIH desperately needs a comprehensive approach to moving pain out of limited "silos" and across researchers and clinicians in different specialties if rapid advancements in treatment are to result.

Cardiac pain is among the best examples of the mismatch between research priorities and patient needs. Current surgical and other interventional approaches are major "drivers" of health care costs. For some patients, these expensive procedures reduce chest pain without prolonging life. For others, they are not appropriate or particularly effective in reducing pain. If alternative approaches to treating the pain could be developed, the savings potential could be enormous. Yet, as noted above, there is virtually no NIH pain research on heart disease, and few cardiologists conducting clinical research in pain.

A third area of promising research illustrates both the potential for cross-institute discoveries and the limitations of current approaches. Chronic neuropathic pain is generally associated with damage to nervous system tissues. That damage can come from traumatic injury like that experienced by returning Iraq War Veterans, many of whom will face persistent pain, or from invasive diseases that damage tissue, like cancer, arthritis, and diabetes. Researchers are working on diabetic neuropathy and progress is being made. Others have had success in animal studies with application to cancer and arthritis. But moving these discoveries into applications for neuropathic pain generally is limited by the current disease-oriented focus at NIH. Until NIH looks at pain as a disease in itself, getting research out of current "silos" will be difficult.

Moving basic and animal research results from one area into widespread clinical trials in multiple areas is also impeded by the simple dearth of clinical researchers that focus on pain. That shortage is a result of years of under-funding at NIH, and it will take years to correct.

The above examples of ongoing research are merely illustrative and hardly exhaustive. They only hint at the potential to alleviate human suffering were NIH to focus more clearly on pain as a public health priority, maintain and increase funding for clinical research in particular, and better coordinate both basic and clinical research efforts across existing Institutes and Centers.

I hope this additional information is responsive to your question, and would be pleased to explore these issues further with you and your staff at any time. If there is any particular research area on which you would like more in-depth information, I would be pleased to identify researchers with whom you and your staff could consult directly.

Respectfully submitted,



Joel R. Saper, M.D.

Attachments

CC: The Honorable Nathan Deal
The Honorable Mike Rogers
The Honorable Sherrod Brown



Oncology Nursing Society

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December 8, 2005

The Honorable Nathan Deal
Chairman
Subcommittee on Health
House Energy and Commerce Committee
US House of Representatives
Washington, DC 20515

Dear Chairman Deal:

On behalf of the Oncology Nursing Society (ONS) – the largest professional oncology group in the United States composed of more than 33,000 nurses and other health professionals which maintains a long-standing commitment to promoting excellence in oncology nursing, teaching, research, administration, education in the field of oncology, and the provision of quality care to individuals affected by cancer – we respectfully submit these written comments to your subcommittee to be part of the official record for the December 8th hearing, *“Improving America's Health: Examining Federal Research Efforts for Pulmonary Hypertension and Chronic Pain.”*

As part of its mission, the Society stands ready to work with policymakers at the local, state, and federal levels to advance policies and programs that will reduce and prevent suffering from cancer, including initiatives that improve pain and symptom management and enhance quality-of-life. To that end, ONS commends you and your subcommittee colleagues for recognizing the importance of examining federal research efforts related to chronic pain. We thank you for the opportunity to submit these comments.

Under-treated Pain – A Major Public Health Problem

Pain is a major health problem in the United States, especially the kind of pain that is often experienced by individuals with cancer. The treatment and management of pain and accompanying symptoms such as fear, anxiety, depression, weakness, nausea, and vomiting need to be improved significantly. When pain is severe, it interferes with activities and quality-of-life; diminishing physical, psychological, and interpersonal well-being. It is perhaps one of the more tragic realities in health care today that, despite the existence of many drugs and techniques for treating pain, countless individuals continue to suffer needlessly from unrelieved pain.

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Greater emphasis on quality-of-life for individuals at end-of-life and the growth of hospice care in this country have done much to validate the role of opiates in treating pain and suffering. Although considerable progress has been made to improve the adequate treatment of pain through efforts at educating health care professionals and the public, still less than half of patients with cancer get adequate relief of their pain and approximately one in four patients with cancer die with unrelieved pain. Much of the failure to relieve cancer-pain stems from patient, provider, and family misconceptions and fears. Moreover, recent controversies and negative media attention regarding the use of opiates have begun to erode much of the progress that has been achieved in this arena. It is, indeed, an unfortunate reality that the class of drugs that has the potential to alleviate pain and suffering also has the potential to be abused. Adequate pain control further is complicated by regulatory agencies that scrutinize professional licensure and restrictively regulate controlled substances – practices that are well-intended but unintentionally can obstruct legitimate use rather than stem diversion. However, while it is essential to strike a delicate balance between legitimate access and efforts to prevent diversion and abuse, it is critical to note that there is abundant evidence that the vast majority individuals – including people with cancer – who use these drugs for their legitimate and intended purposes, do not go on to abuse them.

Under-managed pain often results in emotional and economic consequences both of which have long term costs to affected individuals and their families. Therefore, it is essential that improved quality-of-life through expert pain control be available to all who experience pain, not just a select class of patients with specific diagnosis. More must be done to ensure that appropriate pain management is the standard of care for the young as well as the elderly, and for those with chronic illness or at end-of-life. ONS believes that the inadequate treatment of pain is a significant public health problem in the United States and requires the necessary public health response.

Cancer-related Pain

While we have made significant gains in cancer survival rates, unfortunately each year another 1.3 million Americans will receive a cancer diagnosis and more than 570,000 Americans will lose their battle with this terrible disease. For these individuals and their families, it is essential that we take all the steps necessary to ensure that throughout their treatment – and through survivorship or end-of-life, that their pain and other symptoms are managed appropriately. Moreover, as cancer risk increases with age, so do the risk and incidence of other chronic conditions. Therefore, many who develop cancer also suffer from other co-morbidities and underlying painful conditions associated with their other health problems such as arthritis, diabetes, or prior trauma.

Additionally, concurrent advances in the treatment of cancer have yielded a growing population of patients who are living longer with cancer as well as an increased number of people who are cured and transition to cancer "survivorship." Many of those patients who live long-term continue to experience pain that may be related to their treatment rather than the malignancy itself. These patients often suffer moderate to severe pain on a daily basis which

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compromises their ability to function in various life activities. Therefore, this cohort has more in common with the non-malignant pain patient than the patient who has pain associated with advancing disease. For example, pain may be due to nerve injury or scar tissue formation from cancer-related surgical intervention. As such, ONS advocates increasing access to – and ensuring the availability of – quality, comprehensive pain and symptom management, psychosocial support, follow-up, and end-of-life care for people with cancer.

Opioid Treatment Essential to Managing Cancer-related Pain

Cancer patients typically have two types of pain – continuous, persistent pain that is always present and intermittent or breakthrough pain that occurs with activity. While surgery, radiation, and chemotherapy may be used to control the pain by shrinking the cancerous tumor, drugs such as non-opioids, opioids, and adjuvant medications are the mainstay of pain treatment. For years, morphine has been the standard opioid of comparison to treat severe pain in cancer patients. However, as knowledge about pain physiology and pharmacology translates into better analgesics or new formulations of opioids with fewer side effects, morphine has not remained the drug of choice. Morphine has several active metabolites including morphine 6-glucuronide and morphine 3-glucuronide that may accumulate in patients with renal disease, renal dysfunction, or elderly persons because of decreased clearance and prolonged elimination half-life. When this occurs, patients taking morphine may become confused, disoriented, sedated, and may experience other side effects. Because of these problems related to morphine's active metabolites, the trend has been to use semisynthetic opioids such as oxycodone, fentanyl, and hydromorphone.

People with cancer usually need to be treated with continuous release opioids (usually dosed twice a day) for the persistent pain and short acting opioids (usually dosed every two to four hours) for the breakthrough pain. At present the only continuous release opioids that are available are morphine (MS Contin®, Oramorph®, Kadian®), oxycodone (OxyContin®), and fentanyl (Duragesic patch® typically dosed every 72 hours). Some cancer patients cannot tolerate morphine because of side effects of nausea and vomiting while others need to take high doses of continuous release oxycodone because they are not able to use the fentanyl patch as they would need multiple patches to equal the OxyContin® dose they are taking. With the availability of controlled release oxycodone, cancer patients are able to have access to another analgesic for relief of persistent pain. If access to opioids, such as OxyContin®, were to be restricted severely, such a limitation could pose a major problem – and threat to health and well-being – not only for people with cancer but a multitude of patients with chronic nonmalignant pain who are enjoying an improved quality-of-life because of OxyContin®.

**Risk Management, Diversion Control, Abuse Prevention, and Legitimate Access:
 A Delicate But Necessary Policy Balance**

ONS maintains a long-standing commitment to ensuring that all people with cancer-related pain have access to the quality pain and symptom management care, services, and therapies they need and deserve. Specifically, our organization believes that all people with legitimate

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need must be assured access to the medication and therapies that they and their health care providers deem most appropriate. We recognize and appreciate that with the potential for abuse, our nation must develop and implement appropriate, yet reasonable practices and regulations to ensure that these drugs do not fall into the wrong hands and are not abused.

As you may know, ONS is one of 21 national organizations that lent its support in 2001 for the "Joint Consensus Statement" on "Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act" articulating the need for balance between the treatment of pain and enforcement against diversion and abuse of prescription medications. This important document reflects a consensus among myriad health care providers, patient advocates, and law enforcement agencies that the prevention of drug abuse is an important public health and societal goal that can – and should – be pursued without impeding appropriate patient care.

As the Joint Consensus Statement asserts, "Effective pain management is an integral and important aspect of quality medical care, and pain should be treated aggressively." Moreover, the Joint Consensus Statement also recognizes that, "Focusing only on the abuse potential of a drug, however, could erroneously lead to the conclusion that these medications should be avoided when medically indicated – generating a sense of fear rather than respect for their legitimate properties."

Clearly, there are classes of drugs that should be regulated in an appropriate fashion so as to prevent and reduce diversion and abuse. However, in these important efforts, we must not increase the burden to patients or the health care professionals who are administering their pain-related care. Regulations that limit reliance on professional clinical judgment and unduly restrict access encumber the provision and delivery of appropriate pain management for patients with legitimate needs.

The percentage of the population who take prescription drugs for non-medical purposes has remained stable for the last decade at 1-1.5 percent as has the percentage of the population with an illicit drug problem (6-7 percent). This suggests that while periodic hotspots develop around a particular drug in certain communities, overall our nation's policies are working to minimize drug abuse. To that end, a study of opioid use and abuse published in the Journal of the American Medical Association concluded that the increase in medical use of opioid analgesics does not contribute to the increase in abuse.¹ However, we unfortunately always have had to be aware that an individual's request for a certain drug could be based in real need/response but also could be based on its street value. Yet, as noted above, we continue to see significant numbers of people with cancer dying in pain. This indicates that while our policies work to stem the tide of abuse they may be standing in the way of providing legitimate and necessary quality care for those in need. ONS agrees that drug abuse is a serious problem and that its prevention is an important societal goal; yet, ONS maintains – as stated in the Joint Consensus

¹ Data from 1990-96, Joransen DE, Ryan KM, Gilson AM, Dahl JL. Trends in medical use and abuse of opioid analgesics. JAMA 2000; 283(13):1710-1714.

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Statement – that [efforts to prevent drug abuse] “should not hinder patients’ ability to receive the care they need and deserve.”

ONS Recommendations

Oncology nurses have been leaders in providing pain education and our organization provides education to our members through our journals, at conferences, and at special events. ONS maintains a long-standing commitment to ensuring that all people with legitimate pain have access to the relief they need and deserve. To that end, ONS recommends that the federal government:

1. Support additional basic, translational, clinical, and health services research into chronic pain management and addiction and treatment, including efforts to identify, capture, and disseminate more meaningful information about the use and potential abuse of prescription pain medications. To complement this, we urge additional research on the prevalence and root causes of prescription drug abuse and the exploration of the development of non-addictive pain therapies.
2. Establish and maintain an ongoing dialogue between the DEA, the FDA, and health care professionals to encourage cooperation and mutual understanding in an effort to ensure a balanced and rational approach to effective symptom management and minimization of illicit drug use.
3. Work with health care professionals to develop guidelines for practice that will assure access to opiates based on sound clinical judgment and patient need, while increasing early recognition of problem behaviors.
4. Develop educational materials for patients and family members that will reassure them of the legitimacy of opiates in treating pain while giving them guidelines for safe use and the prevention of diversion or abuse.
5. Allocate resources to educate health professionals about the appropriate use of opiates and associated pain management techniques, both pharmacological and non-pharmacological. Such educational efforts should address how to stop drug diversion, how to keep records, and how to document proper assessment and prescription distribution.
6. Support projects aimed at identifying and eliminating system-level obstacles that preclude effective pain management in acute pain, cancer pain, and chronic pain.
7. Assure that federal publications delineate clearly between substance abuse and legitimate pain management in acute pain, cancer pain, and chronic pain as the evidence that addiction is very rare in patients who have pain should be acknowledged more widely.

Summary

On behalf of ONS and our members who are involved in the provision of cancer-related pain and symptom management, we thank the Subcommittee for its consideration of our views on this important public health matter. ONS affirms its commitment to promoting the relief of cancer-related pain and suffering and urges the Subcommittee – as well as the FDA and the

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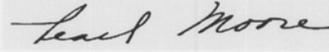
DEA – to consider first and foremost, the needs of those who suffer needlessly from unrelieved pain and to take steps to assure their continued access to the pain relief they need and deserve.

Please know that the Society stands ready to work with your subcommittee and other stakeholders to achieve ensure that patients with legitimate pain have access to quality, appropriate, and legitimate relief. If we can be of any assistance to you, or if you have any questions, please feel free to contact us or our Washington, DC Health Policy Associate, Ilisa Halpern (202/230-5145, ihalpern@gcd.com).

Sincerely,



Karen Stanley, RN, MSN, AOCN®, FAAN
President



Pearl Moore, RN, MN, FAAN
Chief Executive Officer