

MUSCULAR DYSTROPHY

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TUESDAY, FEBRUARY 27, 2001

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN
SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9:30 a.m., in room SH-216, Hart Senate Office Building, Hon. Arlen Specter (chairman) presiding.

Present: Senators Specter and Craig.

Also present: Senator Wellstone.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. We have delayed slightly by just a few minutes the opening of this hearing so that I could go into the anteroom and brief the witnesses who are going to testify here today. This is a hearing of the Appropriations Subcommittee for Labor, Health, Human Services, and Education, and this is a hearing in a long line of hearings where we focus on particularly distressing ailments.

Today, as you know, it is muscular dystrophy. At other times we have special hearings on amyotrophic lateral sclerosis, on Alzheimer's, on cancer, on Parkinson's, and we do this at the request of the various groups. Today, the hearing has been scheduled at the specific request of the Parent Project Muscular Dystrophy as part of their first annual legislative conference. Approximately 110 Parent Project Muscular Dystrophy parents are going to participate in the conference, and there are 20 young entertainers participating in the Kids for Kids Project to focus on this particularly disabling childhood ailment.

Muscular dystrophy refers to a group of genetic diseases characterized by progressive muscle weakness and control of movement, frequent falls, problems walking, eyelid-drooping, skeletal and muscle deformities. The research efforts on muscular dystrophy have been very, very extensive.

On a bipartisan basis, together with Senator Tom Harkin, Democrat of Iowa, this subcommittee has taken the lead to vastly increase the funding for the National Institutes of Health. Four years ago, the funding level was about \$12 billion. Now it is in excess of \$20 billion, and we are moving on what is a glide path to try to double NIH funding over a 5-year period, and we have set a very ambitious mark this year to try to add \$3.6 billion which is our hope, perhaps more specifically our expectation, and it has been a real battle, because the funding for the National Institutes of

Health comes from Health and Human Services generally, where there are so many other vital programs, and it is also lumped together with the Department of Education, and there is no priority in America higher than education, and also with Labor, with workers' safety, so we have our work cut out for us.

I frequently say that the National Institutes of Health are the crown jewel of the Federal Government, and then I quickly add, perhaps the only jewel of the Federal Government. That is with the exception, of course, of those assembled here in this hearing room today.

One item that I want to comment about is our continuing effort to promote research on stem cells. Stem cells burst on the national scene in November of 1998, and this subcommittee then moved very quickly into a series of hearings. We had some seven hearings with a view to eliminate the prohibition against using Federal funds to extract stem cells from embryos.

Embryos are created, as you may know, for in vitro fertilization, and they are to be discarded. They are not going to be used. I would never advocate taking an embryo that could produce a live person for research, but when they are going to be discarded, it's a question of either having them used for nothing, or having them used to save lives. They are a veritable fountain of youth. These stem cells can be substituted for cells in the body. They are especially helpful on Parkinson's already, with the projection of a cure within 5 years, and on spinal cord problems, and they may be useful on muscular dystrophy as well. The sky really is the limit.

At the moment there are grants pending in the Department of Health and Human Services, where it is now lawful, according to an opinion by the General Counsel, to use Federal funds on stem cell research after they have been extracted from the embryos, and that is something which I personally feel very strongly about ought to be maintained, and we really ought to eliminate the limitations. This is a matter for the scientists, not a matter for the Congress, in my opinion.

STATEMENT OF AUDREY S. PENN, M.D., ACTING DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Senator SPECTER. We will now move to our first witness. Dr. Audrey S. Penn, Acting Director, National Institute of Neurological Disorders and Stroke. Dr. Penn comes to this position having served as Deputy Director of the Institute. She is a member of the American Academy of Neurology and the American Association for the Advancement of Sciences, past president of the American Neurological Association. She received her M.D. from Columbia and her B.A. from Swarthmore, parenthetically a suburb of Philadelphia.

Welcome, Dr. Penn. We look forward to your testimony.

Dr. PENN. Thank you, Mr. Chairman. I am here to discuss the muscular dystrophies with you. As an academic neurologist and investigator working on neuromuscular diseases, and now—

Senator SPECTER. I am told we have some 20 people outside who cannot gain entry. They are welcome to come in, and they can be Senators for a day. For a higher rank they can be staffers for a

day, sitting behind the Senators' seats, but if the guards would let all the people in, we have plenty of room here.

Dr. Penn, please proceed.

Dr. PENN. Yes, sir.

I have been well aware of the muscular dystrophies and the problems they present. As you stated, they are inherited, degenerative diseases of skeletal muscle which result in progressive muscle weakness. The muscles involved vary. The FSH dystrophy, facioscapulohumeral involves face, shoulders, and upper arms, limb girdle, shoulders and hips, oculopharyngeal, eyes and swallowing. They also vary in age of onset, rate of progression, degree of ultimate disability, pattern of inheritance, and the specific genes which are missing or defective.

Now, the diagnostic tests used are the same: clinical examination, electrophysiological testing, and measurement of muscle-derived enzyme in serum. This morning, I will focus on Duchenne muscular dystrophy.

Duchenne strikes males, starting in infancy, when it may be clinically suspected either by an extremely high serum enzyme, or subtle weakness as children start to walk. There is rapid progression. On average a wheelchair is needed at about age 12. Early in the process, there are obvious signs of regeneration of muscle, but degeneration progressively outpaces regeneration.

After years of work, much of which was funded also by MDA, the gene was identified, then its protein product, named dystrophin. Now, dystrophin is a giant protein which provides structural support to a critical complex of muscle membrane proteins, and links the internal muscle cell structure to the membrane surface. The Becker dystrophy, a milder form of Duchenne, reflects a defective rather than a missing dystrophin gene. It is less destructive, and slower to progress.

The relatively numerous and heterogeneous limb girdle dystrophies reflect the loss of other proteins at that same dystrophin complex, suggesting that the loss of stability of this set of proteins is critical to many of the dystrophies.

Now, there is still no cure for any of the muscular dystrophies. Physical therapy, tendon-lengthening to prolong walking and measures to preserve lung and heart function may all improve the quality of life. Corticosteroid usage at certain stages may help, but the side effects are especially troublesome in growing children.

There have also been continuous efforts to replace that gene since it was first identified in 1987, and scientists today are concentrating on new strategies. Studies of a mouse model indicate that the use of viruses as vectors to carry genes into muscle cells is possible. However, the dystrophin gene is so big, it does not fit inside usable viral vectors, and vectors may also trigger an immune response.

Other innovative approaches currently being investigated in the mouse include direct administration of DNA, the use of trimmed-down minigenes, strategies which can alter how the gene makes the protein, and replacement of dystrophin with a similar but smaller protein found in a very specialized region of the muscle membrane. Utrophin can fit inside usable viral vectors, and can restore strength in mice. In mice which carry a dystrophin mutation

that causes an erroneous genetic signal to stop making protein, a specific type of antibiotic can override the signal. A similar mutation is found in about 15 percent of children with Duchenne, and we are currently testing gentamycin in clinical trials.

All of this contrasts with the autosomal dominant FSH dystrophy, in which both men and women are affected. It may be hard to discern weakness by inspection or exam in some, while others are in wheelchairs. Even after the revolution on molecular genetics and over 12 years of work, we have still identified only the chromosomal region which is deleted in FSH. The specific gene has not been identified. The deletion probably acts indirectly on neighboring genes.

NIH Institutes, with the Parent Project for Muscular Dystrophy, organized a workshop last spring to address possible therapeutic approaches for Duchenne, and a second workshop on FSH organized by NIH with the FSH Society focused on that disease.

To follow up on these workshops, we have set aside funds, and we have called for new applications. We value our relationships with all of the voluntary organizations who work so hard to move ahead and cure these diseases, and we want to recognize their contributions: the MDA, which for years under the tireless efforts of Jerry Lewis has fostered research on muscular dystrophy, the Parent Project, which has brought a renewed sense of urgency to the field, and the equally dedicated FSH Society.

We believe we achieve results faster when we partner with these organizations. We dedicate ourselves to ensuring that the best science and scientists tackle these disorders, and put research funds to the best possible use to begin effective therapies.

PREPARED STATEMENT

Mr. Chairman, I appreciate the opportunity to discuss these disorders, which have long been a concern of mine, and I am pleased to respond to any questions you may have.

[The statement follows:]

PREPARED STATEMENT OF AUDREY S. PENN

Mr. Chairman, Ranking Member Senator Harkin, and Members of the Subcommittee, I am Dr. Audrey Penn, Acting Director of the National Institute of Neurological Disorders and Stroke. I am here to discuss with you the muscular dystrophies. I have been actively involved with this group of diseases throughout my career as a physician and scientist, working in academia, with voluntary organizations, and at the National Institutes of Health.

WHAT ARE MUSCULAR DYSTROPHIES?

The muscular dystrophies are a group of diseases which weaken the skeletal muscles that we use to move voluntarily. These disorders vary in their age of onset, in severity and in the pattern of which muscles are affected. All forms of muscular dystrophy, however, grow worse as muscles progressively degenerate. In some types of muscular dystrophy, the heart, the gastrointestinal system, endocrine glands, the skin, the eyes and other organs may be affected. All of the muscular dystrophies are genetic disorders, although the types of inheritance vary, and Duchenne muscular dystrophy, the most common and best known of the childhood muscular dystrophies, often arises from new mutations.

CAN WE TREAT MUSCULAR DYSTROPHIES?

Research has revealed most—but not yet all—of the gene defects that cause the different forms of muscular dystrophy. Unfortunately, the life expectancy and quality of life for people with muscular dystrophy have not improved substantially since

those discoveries. There is still no specific treatment that can stop or reverse the progression of any form of muscular dystrophy. For Duchenne muscular dystrophy, corticosteroids may help, but have side effects that can be especially troubling with children. Symptomatic treatment, though not able to stop the disease process, may improve the quality of life for some people with muscular dystrophies, through physical therapy, wheelchairs and braces used for support, corrective orthopedic surgery, and drugs.

The failure so far to produce a definitive therapy for any form of muscular dystrophy reflects the difficulty of the problems that we must confront to cure these diseases. Some of these problems are unique to a particular type of muscular dystrophy, some common to all muscular dystrophies, and others are shared by many genetic disorders. The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) lead efforts of several components of NIH against these diseases. The shared responsibility recognizes the value that various medical specialties and disciplines bring to research and treatment. The muscular dystrophies affect many aspects of physiology, benefit from a wide range of fundamental biological research, and require exploration of diverse diverse strategies for treatment. What is most encouraging is the range of scientific approaches that research is bringing to bear on these diseases. Molecular biology has given us a foothold to understand what goes wrong. To examine the list of therapies being explored for the muscular dystrophies is tantamount to taking a tour through the most active frontiers of modern medicine, including gene therapy, cell replacement, and innovative approaches to drug development.

Time will not allow me to describe all forms of muscular dystrophy. I will discuss three common types—myotonic muscular dystrophy, facioscapulohumeral (FSH) muscular dystrophy and Duchenne/Becker muscular dystrophy—and try to make some general points along the way.

MYOTONIC MUSCULAR DYSTROPHY

Myotonic muscular dystrophy (MMD) is probably the most common adult form of muscular dystrophy, partly because people with this disorder can live a long life, with variable but slowly progressive disability. Myotonia refers to impaired muscle relaxation which is associated with MMD along with muscle wasting and weakness. This form of muscular dystrophy affects many body systems in addition to skeletal muscles. These include the heart, endocrine organs, eyes, and gastrointestinal tract.

Myotonic muscular dystrophy follows an autosomal dominant pattern of inheritance. This means that the disorder can occur in either sex when a person inherits a single defective gene from either parent. The gene defect that causes MMD is a triplet repeat expansion in the untranslated region of a gene that encodes a protein kinase (DM-PK). To attempt to translate this into English: the inherited gene defect arises from a long repetition of a three-letter “word” in the part of the genetic code that carries the instructions for making a protein. The protein is one of a class called “kinases” that help regulate the function of other proteins. In this case the “word” is not in the part of the gene that specifies the makeup of the protein itself, but in a region that may help control when the gene is turned on and off. We don’t yet understand how this genetic defect leads to muscle degeneration, but the “triplet repeat” mechanism has now been found in at least 15 other disorders. Scientists have found some clues, both for myotonic dystrophy and triplet repeat disorders in general, and research is continuing. The fact that the repetition in the genetic code tends to get longer with each generation explains the phenomenon of “anticipation” in which the disease shows itself earlier and more severely in each generation.

FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

Facioscapulohumeral muscular dystrophy (FSHD) initially affects muscles of the face (facio), shoulders (scapulo), and upper arms (humeral) with progressive weakness. Symptoms usually develop in the teenage years. Life expectancy is normal, but some affected individuals become severely disabled. The pattern of inheritance is, like myotonic muscular dystrophy, autosomal dominant, but the underlying genetic defect is poorly understood. Most cases are associated with a deletion—that is, a missing piece of chromosome—near the end of chromosome #4. These deletions don’t appear to disrupt a particular gene, but may affect the activity of nearby genes. This complicates the search for the relevant gene and suggests a novel mechanism may be involved.

In recent months, NIAMS has led NIH in a number of important steps to stimulate and support further work on this poorly understood form of muscular dystrophy. These include:

Research conference.—In May 8–9 of 2000, the NIAMS, together with the NINDS, the NIH Office of Rare Diseases, the FSH Society, Inc., and the Muscular Dystrophy Association of America, co-sponsored a scientific conference on the cause and treatment of FSHD. Researchers from the United States, Canada, Europe, South America, and Asia met on the NIH campus in Bethesda, Maryland, to share their latest findings and identify exciting directions for future studies of this disease. The recommendations that emerged from the conference fall into several categories, including: efforts to enhance our understanding of the molecular processes and tissue changes associated with FSHD; ways to explore possible therapies to treat the disorder; and strategies to promote the establishment of population-based studies of the disease, as well as needed research resources. NIH is using these recommendations as a guide in developing new program initiatives related to FSHD and other muscular dystrophies. A summary of the Workshop is available on the NIAMS web at: <http://www.nih.gov/niams/reports/fshdsummary.htm>.

Research registry.—In September of 2000, the NIAMS and the NINDS funded a research registry for FSHD and myotonic dystrophy. The long-term goal of the registry is to facilitate research in FSHD and myotonic dystrophy by serving as a liaison between families affected by these diseases who are eager to participate in specific research projects, and investigators interested in studying these disorders. The registry, based at the University of Rochester, will recruit and classify patients, and store medical and family history data for individuals with clinically diagnosed FSHD and myotonic dystrophy. Scientists will be provided with statistical analyses of the registry data, as well as access to registry members who have agreed to assist with particular research studies. The national registry will serve as a resource for scientists seeking a cure for these diseases, in addition to enhancing research to understand what changes occur in muscular dystrophy.

Research solicitations.—In November of 2000, the NIAMS and the NINDS jointly issued a request for applications for exploratory research on FSHD. This announcement is designed to encourage research proposals using creative, novel, potentially high risk/high payoff approaches that could produce innovative advances in this field. Successful projects may include feasibility studies, clinical protocol planning, and efforts to incorporate new disciplines and technologies into the study of FSHD. In developing this solicitation, the NIH built on the insights we gained from the scientific conference cited above. Based on that conference, we have focused this new request for research proposals on issues related to improving our understanding of the origins of this disease and how to characterize its molecular basis. Among other areas, such projects could include studies looking at changes in muscle as FSHD develops; exploring the role of inflammation in this disease; and creating new models of FSHD that could facilitate the eventual development of effective therapies.

In January of 2001, NIAMS and NINDS partnered again to issue a program announcement with funds set aside to support research on understanding and developing therapies for the muscular dystrophies, including FSHD. This solicitation is described in the following discussion of Duchenne muscular dystrophy discussion.

DUCHENNE AND BECKER MUSCULAR DYSTROPHY

Duchenne muscular dystrophy (DMD) is the most common childhood form of muscular dystrophy, affecting approximately 1 in 3,000 male births. About one third of cases reflect new mutations and the rest are familial. Because inheritance is X-linked recessive, DMD affects primarily boys, though girls and women who carry one defective gene may show some mild symptoms.

DMD is a particularly devastating and lethal form of muscular dystrophy. When the body's attempts to regenerate muscle cannot keep up with the destructive process, muscle wasting and progressive weakness result. DMD usually becomes evident when children begin to walk. Boys typically require a wheelchair by age 10 to 12, and usually die in late teens or early 20's. Becker muscular dystrophy (BMD) is a less severe but closely related disease. DMD results from an absence of the protein dystrophin, and BMD reflects a partly functional version of the same protein.

Research conference.—To explore what NIH can do to develop effective therapies for DMD and BMD, the NINDS, the NIAMS, and the NIH Office of Rare Diseases (ORD), working together with the Parent Project for Muscular Dystrophy held a "Workshop on Therapeutic Approaches for Duchenne Muscular Dystrophy" on May 15 and 16, 2000, on the NIH campus in Bethesda, Maryland. An international group of experts participated in this meeting along with representatives from United States and European muscular dystrophy associations and NIH staff. On May 17, following the Workshop, the scientific organizers, topic leaders, and NIH program directors met to summarize the discussion and formulate future research priorities.

A summary of the workshop is posted on the NINDS websites at: http://www.ninds.nih.gov/news_and_events/dmdmtngsummary.htm.

Understanding the disease.—More than 15 years ago, researchers supported by the NIH and the Muscular Dystrophy Association identified the gene for dystrophin that, when defective, causes DMD and BMD. The identification of the dystrophin gene stimulated research that provided new insights and directions for research on the biology of muscle and the mechanisms of disease, as evident in thousands of high quality scientific publications and several promising leads for developing new therapies.

One challenge the dystrophin gene presents is its enormous size. The gene is the largest gene yet identified in humans. Most vectors (usually modified viruses) available for gene replacement cannot incorporate a gene of this magnitude. The size probably also contributes to the high rate of new mutations in the gene and to the large number of different mutations that can occur within the gene. Definitive therapy may require precise knowledge of the particular gene defect in each patient.

The dystrophin protein was unknown before the discovery of its link to DMD. Subsequent studies have revealed that dystrophin is part of a complex structure involving several other protein components. The “dystrophin-glycoprotein complex” helps anchor the contents of muscle cells through the cells’ outer enclosing membrane to the material in which muscle cells are embedded. Defects in this assembly lead to structural problems that can disrupt the integrity of the outer membrane of muscle cells, resulting eventually in degeneration. One of the most remarkable spin-offs from the elucidation of the complex has been clarification of the interrelationships among DMD and other forms of muscular dystrophy. Several other forms of muscular dystrophy, whose relationships to DMD were obscure, result from mutations in other protein components of the same dystrophin-glycoprotein complex. These include several forms of limb girdle muscular dystrophy, named for the characteristic pattern of muscle weakness. Research to more fully understand the normal and abnormal functions of the dystrophin complex, and of other proteins closely related to dystrophin, is ongoing, and evidence is accumulating that these proteins play important roles in the brain as well as in muscles.

Therapeutic approaches.—Several new approaches have emerged for developing therapies to stop or reverse muscle degeneration in Duchenne muscular dystrophy. All of these strategies rely upon increased understanding of the underlying biology of the disease. However, one point made at the May workshop is the extent to which novel therapeutic strategies for DMD arise from research that is not focused on muscular dystrophy, muscle biology, or even therapeutics in general.

Logically, the simplest approach to treating DMD might seem to be to supply a good copy of the defective gene. An important advantage in studying DMD is the availability of the *mdx mouse* which is a useful model of the human disease. Results in mice with the same gene defect as DMD show that modified virus “vectors,” such as the adeno-associated virus, can carry the therapeutic genes into muscle cells and partially reverse the disease. Recent experiments have also shown that a genetically engineered “mini-dystrophin,” while much smaller than the natural form, seems able to carry out its essential functions. However, considerable advances are needed to make gene replacement workable for children with MD. The technology of gene replacement is just beginning to yield clinical success in some of the simplest diseases to treat. Treating DMD presents special problems not only because of the large size of the gene, but also due to the need to deliver the gene reliably and safely to muscle cells throughout the body. Improving the delivery of genes to muscle, optimizing the control elements that regulate the activity of therapeutic genes, and minimizing immunological and other potential safety problems are on-going areas of research. The first preliminary gene replacement trials for any form of muscular dystrophy have been designed by MDA for a form of limb girdle muscular dystrophy caused by a defect in a component of the dystrophin-glycoprotein complex.

Several other approaches to counteracting the gene defect, besides gene transfer by viral vectors, also show promise for DMD. The use of “naked DNA” is one approach under investigation for several diseases that may be applicable to DMD. Another approach uses chimeroplasts. These specifically designed synthetic molecules are hybrids of DNA and RNA that can guide the muscle cells’ own repair machinery to correct some types of defect in the dystrophin gene. “Antisense” nucleotides are another type of synthetic molecule that has therapeutic potential. These molecules, which are designed to bind specifically to certain parts of genetic material, alter how the cells’ internal machinery reads a gene to make protein, thus compensating for certain types of defects in dystrophin. Another strategy uses aminoglycoside antibiotics. Some children with DMD (perhaps 15 percent) carry a mutation in the dystrophin gene that creates an erroneous DNA code signal to stop making the protein. Dr. Sweeney, who will also testify today, did experiments in mice with the

same types of errors in dystrophin and found that antibiotics can cause the protein synthesizing machinery to ignore stop signals and allow muscle cells to make enough dystrophin. Gentamicin, an antibiotic of this type, is now being tested in clinical trials for DMD in children.

Finally, drug therapy for DMD has also been a focus of research efforts. One approach has used high-throughput screening (HTS) to try to find drugs that increase the muscle production of another protein, *utrophin*, that can help compensate for the loss of dystrophin. High throughput screening employs robotics and miniaturized assays (tests) to screen thousands of chemical compounds quickly to find leads for further drug development. Other pharmacological research areas of continued interest for DMD relate to the use of corticosteroids in the disease and to strategies informed by increased understanding of immunology and its relation to DMD.

Solicitations.—As noted above, in January 2001, NINDS and NIAMS issued a PA-S (program announcement with set-aside) entitled “Therapeutic and pathogenic approaches for the muscular dystrophies” to encourage research in areas highlighted as priorities at the DMD and FSHD workshops and in areas important for other forms of muscular dystrophy. The PA-S, unlike a regular PA, sets aside funds (\$5 million) for the purpose of this research. Unlike an RFA (request for applications), this mechanism does not restrict researchers to a single deadline for proposals. Unsuccessful applicants are encouraged to reapply after improving their proposals based on the suggestions of scientists on peer review panels.

Several other actions of NINDS, NIAMS and other components of NIH address priorities for muscular dystrophy research that also have implications for other disorders. These include extensive efforts, through workshops, solicitations, and other actions, to promote new technological approaches, such as gene replacement, and to encourage exploratory grants from researchers not currently working in the field. Planned workshops will also focus on issues such as review of steroids for treatment of DMD and clinical trial design for testing of these drugs and issues in screening of newborns for eventual identification of DMD when a treatment is available. NINDS has also placed an increased emphasis on expediting clinical trials for neurological disorders. In addition to grant mechanisms for pilot trials and planning of large trials, the Institute is enhancing its ability to work with researchers to design and conduct clinical trials. NIAMS is also supporting planning grants for clinical trials, including one on myotonic dystrophy.

In recent years, NIAMS and NINDS have also worked together to strengthen NIH Intramural research in muscle biology and disease. The Institutes have recruited outstanding scientists to lead research programs in this area. One consequence, for example, is that the resources of the NIH Intramural program have been used to expedite clinical trials of gentamicin therapy of DMD and to discuss the implications of findings so far with this strategy.

CONCLUDING REMARKS

The muscular dystrophies impose enormous burdens on people with these disorders and on their families. We at NIH recognize the need to target increased efforts against the muscular dystrophies. We are doing so through the workshops, then following up with targeted solicitations for applications, including set-aside funds designed to recruit new investigators to the field, and through other efforts in both extramural and intramural programs that I have cited above. The promising opportunities for developing therapies build upon what we have learned about these disorders, and we must continue to learn more even as we move toward testing the best candidate therapies. It is also worth noting that the therapeutic strategies we are now investigating arose from research not targeted to these diseases, so we must maintain a broad front of progress in neuroscience, muscle disorders, and biology generally.

Finally, we at the NIH want to recognize the contributions of the foundations represented here today—the Muscular Dystrophy Association, which for years with the tireless efforts of Jerry Lewis has fostered research in muscular dystrophy and other neuromuscular diseases, and the Parent Project, which has brought a renewed sense of urgency to the field. The NINDS stands ready and able to work in partnership with these organizations and others in the United States and abroad to take the lead in a new strategy that will build on all we have learned in the past 15 years and bring effective treatment for muscular dystrophy patients. We appreciate your efforts in increasing funding for NIH overall and the NINDS in particular, and we dedicate ourselves to the task of putting this money to the best possible use in helping patients with these diseases.

Mr. Chairman, I appreciate the opportunity to discuss these disorders, which have long been a major concern of mine, and I am pleased to respond to any questions you may have.

Senator SPECTER. Thank you, Dr. Penn. Will the folks who just came in on the center aisle, you are welcome to come up front and to sit on the chairs for the staffers, or to sit in the Senators' chairs, so why don't you walk forward, because you are obstructing the views of some.

Dr. Penn, could you give us an idea as to what the increases have been on the National Institute for Neurological Disorders, say, in the last 4 years?

Dr. PENN. Yes, sir. We have received increases in fiscal year 2001 of 14.2 percent over fiscal year 2000; in fiscal year 2000, 14 percent over fiscal year 1999; in fiscal year 1999, 15.6 percent over fiscal year 1998; and in fiscal year 1998, 7.4 percent over fiscal year 1997.

Senator SPECTER. And what is the total funding which is now available for the national institute?

Dr. PENN. In fiscal year 2001 our appropriation is \$1.176 billion.

Senator SPECTER. And in absolute dollars, what was the increase last year, up to that figure?

Dr. PENN. Our increase from fiscal year 1999 to fiscal year 2000 was \$126 million.

Senator SPECTER. Well, that is a very substantial increase.

Dr. PENN. Yes, sir.

Senator SPECTER. Let me ask you a highly dangerous question. Are you adequately funded?

Dr. PENN. There are always things that this institute could do with more funding. We are delighted at what we have been getting, and I do not think we could say anything else.

Senator SPECTER. Well, what would you like to do if you had more funds?

Dr. PENN. If we had more funding, we could stretch it further. We have a tremendous base of people that we are funding now, so we have committed to those folks, and when you subtract that even from the increases, you are somewhat surprised that it is not perhaps stretching quite as far as we want. We have major, major disorders, as you know, that we have to cover.

Senator SPECTER. What prospects are there, if any, for curing muscular dystrophy?

Dr. PENN. I personally think that there are excellent prospects, because the energy is so high and the possibilities are so great, and I tried to outline them, and I think you will hear more from Dr. Sweeney.

However, it was never easy. If it had been easy, it would have been done a lot sooner than this, and I think a lot has happened. A lot has happened in terms of the viruses, both a lot of good as well as some bad. We have a major hurdle which involves immune responses both to any vectors used and to the protein. If you have never had this protein from the beginning because your gene is missing, then an immune response will occur, so that has turned out to be a deleterious effect, even in the mouse.

Senator SPECTER. What assistance would you think possible in the long run, by the use of stem cell research?

Dr. PENN. We think that stem cell research, and in particular a muscle cell, something called the myoblast, which is always in muscle, including in adult life, could be extraordinary, because a great deal of work and a great deal of funding has gone into taking a cell which is further along in the differentiation path but can make muscle.

Myoblasts do not last very long when they are put in there, and they do not really disperse through the muscle, so the big problem is, how are you going to take myoblasts, which you can isolate and put them in a large muscle like the muscles of your thigh, and get them all through the thigh.

Senator SPECTER. But you think stem cells do have potential—

Dr. PENN. They may be able to do this.

Senator SPECTER [continuing]. For possibly finding a cure for muscular dystrophy?

Dr. PENN. And even more, a cell in muscle now, which can be isolated and actually cause to differentiate further, something called the satellite cell. That cell is a certain form of stem cell. What is so interesting is that it is similar in ways to cells in the blood, and, as we know, the bone marrow has stem cells. That kind of stem cell is already there.

Senator SPECTER. The lights have not been working, but I think my 5 minutes has expired, so I will turn to Senator Wellstone.

STATEMENT OF SENATOR PAUL WELLSTONE

Senator WELLSTONE. First of all, Dr. Penn and all that are here, I thank Senator Specter for his graciousness. I am actually not a member of this Appropriations Committee, but I am very, very committed to everybody that is here and to the work that you do, Dr. Penn.

I will just follow up very quickly on two questions that the chairman asked you, one on the overall question of budget and what would you do in the best of all worlds. Sometimes I see you when we are talking about Parkinson's and other neurological diseases. Today it is muscular dystrophy, and I have been working with the people in Minnesota on Duchenne's disease, and it seems to me that the one thing I think all of us hope and pray for, more than anything else, is that we have the kind of budget where we do not have one group of people who are struggling with an illness played off against another group of people. I mean, that is not what this is about.

So I think it is very, very important, and I appreciate your work, Mr. Chairman, in really bumping up the appropriations. Sometimes when we talk about some diseases, there may not be that large a number of citizens affected. Take Duchenne's disease. Children are affected, and whatever the numbers, for the families this disease is the most important thing of all. Today we are focusing on muscular dystrophy including Duchenne's, and I want to tell everybody here, that you are the most powerful citizen lobby imagined. I mean, if you are not here, and you are not speaking for yourselves with loved ones, it just will not happen, and I thank you.

So I think we really ought to work on the budget, and then on stem cell research. I know this is a very controversial question, but

boy, I just have to say, Mr. Chairman, I was listening to a report on National Public Radio this morning about the debate, and I think that done the right way, with all the safeguards that there is no question that stem cell research must be allowed to continue. It would be so tragic if we cannot go forward with this research, which has such promise in terms of finding cures for terrible diseases and helping so many people and so many families.

So we are really at a very, very critical point when it comes to the research and what we need to do as a Nation. I consider this to be an historic hearing, so I thank you, and I look forward to listening and when I do leave it is not for lack of interest, it is because I have another commitment, but I wanted to be here and I thank you for allowing me to be here.

Senator SPECTER. Thank you very much, Senator Wellstone.

Thank you very much, Dr. Penn.

Dr. PENN. Thank you, sir.

STATEMENT OF LEE SWEENEY, Ph.D., SCIENTIFIC DIRECTOR, PARENT PROJECT MUSCULAR DYSTROPHY

Senator SPECTER. I would like to turn now to the second panel, Dr. Lee Sweeney and Dr. Leon Charash.

Dr. Sweeney is chairman of the physiology department of the University of Pennsylvania School of Medicine, and serves as a professor of medicine and surgery. He is the scientific director for the Parent Project Muscular Dystrophy, and directs the neuromuscular disease program at the Institute for Human Gene Therapy. He has a bachelor's in biochemistry from MIT, and Ph.D. in physiology and biophysics from Harvard University. Thank you for joining us, Dr. Sweeney, and we look forward to your testimony.

Dr. SWEENEY. Thank you, Senator, and I greatly appreciate your invitation to testify today, and especially to be allowed to represent the muscular dystrophy community.

Dr. Penn made a number of points that I wanted to make, and they are reiterated in my written testimony so I will not go through them again, but I would say that her point about there being multiple forms of muscular dystrophies that have different ages of onset and different severities of the diseases is a point worth remembering, and the fact that we have very little insight into some of these diseases, such as FSH and other diseases. We know a lot about what causes them, but the commonality there is we can do very little to treat any of these diseases.

When most people think of muscular dystrophy they think of Duchenne muscular dystrophy. It is hard not to remember the images of the young boys afflicted with this disease. It afflicts one out of every 3,500 newborn boys throughout the world, and it arises spontaneously in about a third of the cases, that is, no family history of the disease prior to the newborn child.

As I said, and as Dr. Penn said, work that was sponsored by the NIH and by the Muscular Dystrophy Association led to the discovery of the dystrophin gene in 1987, and yet since then there has been really very little done to change the way we treat these boys, and very little Federal research has actually gone into developing new treatment options.

An increased commitment is needed on the part of NIH to focus on basic muscle biology research, muscular dystrophy research, and DMD in particular, in order to drive new initiatives and drive new discovery. Admittedly, Congress has been very generous to NIH. However, research on the muscular dystrophies has not proportionally benefited from your attempts to double the NIH budget.

I think in large part it is because muscle biology and muscle diseases research was historically an underfunded field. The entities primarily responsible for funding them were not funding to the highest levels within NIH. This has been compounded, certainly in recent years, by in my opinion what is an inadequate review process for muscle disease grants in place, for muscular dystrophy grants in particular, and so even though more money is available, it is not really benefiting these diseases to the extent that it should be.

It is not due to a lack of opportunity in basic and disease treatment research—I gave several examples, parenthetically all from your home State—but these include viral gene therapy, drug-based therapies, even stem cell therapies, so there are a lot of opportunities there, and we are getting to the point where you can probably cure a mouse, but we are a long way from actually treating a boy or an adult with any of these muscular dystrophies.

Now, last year, Congress passed the Children's Health Act of 2000, which included language that increased the coordination among the appropriate Institutes at NIH to maximize resources in efforts specific to muscular dystrophy research. This has had a major effect, and the NIH, in particular the NINDS and NIAMS, have made significant progress in working with the research community, exploring new ways to encourage researchers to focus on these diseases. You heard about the workshops that Dr. Penn spoke of. H.R. 717 is another attempt, directed in this case at DMD in particular, to move forward.

So again, I commend Chairman Specter and the committee for their support of NIH, their commitment to double its budget, and I believe it will have a great impact on the muscular dystrophy community. We are on the verge of making meaningful progress in the treatment of these diseases for the first time in history, but we cannot do it without the Federal Government continuing to express its interest and really pressing NIH to focus on these diseases.

PREPARED STATEMENT

So as you begin your appropriations process, I encourage you to consider the lives of the people afflicted with these diseases, and the lives of their families. Especially consider that these are equal opportunity diseases. They cross all racial, ethnic, and socioeconomic barriers. They can arise in any family, even your own.

Thanks for your compassion, and I would be happy to answer any questions.

[The statement follows:]

PREPARED STATEMENT OF LEE SWEENEY

My name is Dr. Lee Sweeney, and I am the William Maul Measey Professor and Chairman of the Physiology Department at the University of Pennsylvania School of Medicine. Today, I am testifying at the request of the Parent Project MD, as an expert in muscle biology, regarding muscular dystrophy in general, but with a focus

on Duchenne muscular dystrophy, and its weaker form, Becker muscular dystrophy. I appreciate the invitation to testify today and I want to especially thank Senator Specter and Senator Harkin for allowing me the opportunity to speak on behalf of the muscular dystrophy community.

There are five key points that I would like to make in my testimony today:

(1) There are many forms of muscular dystrophy, many of which are poorly understood, and for most of which we have made no progress in treatment of the disease;

(2) Duchenne Muscular Dystrophy (DMD) is the most common lethal childhood genetic disorder, affecting one in every 3,500 newborn boys worldwide;

(3) Although the dystrophin gene that is defective in DMD was successfully identified by medical researchers in 1987, federal research devoted to potential treatment options has been minimal;

(4) Increased federal commitment to medical research for basic muscle biology, muscular dystrophy in general, and DMD in particular, is critical for supporting promising new research initiatives and to drive new discovery;

(5) While Congress has been generous to NIH, research on muscular dystrophies needs special attention to attract new investigators into a historically under-funded area.

Muscular dystrophy is a broad term that refers to a number of primary diseases of muscle. These include dystrophinopathies (Duchenne and Becker), myotonic dystrophy, distal myopathies, Emery-Dreifuss, facioscapulohumeral, oculopharyngeal, and the limb girdle muscular dystrophies. Many aspects of these diseases are not understood, and treatments are either unavailable or minimally effective. The age of onset and severity of these diseases is highly variable.

Mention muscular dystrophy and Duchenne muscular dystrophy (DMD) is the one that most people think of, whether or not they know its name. Images of its victims, the young boys, don't easily leave your mind. DMD is the most severe of all of the muscular dystrophies. It is the world's most common and catastrophic form of genetic childhood disease. DMD represents 90 percent of all childhood onset muscular dystrophy cases, and is characterized by rapidly progressive muscle weakness that results in death, generally by 20 years of age. One in 3,500 male children will be born with the disease, about a third of them into families with no previous history of the disease. These boys will lose the ability to walk by age 10, and will gradually lose their ability to breathe, until they die in their late teens or early twenties.

Although we have known the gene (dystrophin) that is affected in DMD and Becker muscular dystrophy since 1987, no significant treatment that extends the lifespan of DMD children has been developed. The only drugs that are known to provide any benefit are steroids, which have serious side effects in the children. Less than 1/1000 of the NIH budget is focused on research linked to muscular dystrophy. Of the \$17.8 billion budget for NIH in fiscal year 2000, only \$9.2 million was invested in medical research specific to DMD. Because of the limited federal support for medical research specific to various forms of muscular dystrophy, current treatment options are minimal in efficacy, and are aimed at simply managing the symptoms in an effort to optimize quality of life, without impacting lifespan.

This is not due to a lack of opportunities in basic and disease-treatment research. There are significant advances being made that could someday be translated into treatments that would drastically change the progression of the disease. For example, researchers at the University of Pittsburgh have recently engineered a possible gene therapy for DMD. They were able to fit the critical elements of the dystrophin gene into what currently appears to be the safest and most promising viral vector for the treatment of muscle disease. Their work demonstrated that a small piece of dystrophin could be delivered to muscle when placed into adeno-associated virus (AAV). The virus causes the muscle to begin making the piece of dystrophin, which may be sufficient to stop the progression of the disease. In mice, the dystrophin expression has continued for more than one year, and likely will go on much longer.

My own lab at the University of Pennsylvania has used AAV to produce a growth factor in muscle (IGF-I) that we think can be used to treat many forms of muscular dystrophy, as well as stop the loss of muscle in all of us as we get old. Our tests in old and dystrophic mice have been dramatic, in that muscle function has been preserved throughout life by the over-expression of this growth factor in muscle. My lab also recently demonstrated that a common antibiotic might be used to treat a small percentage of DMD patients, again based on successful studies in mice.

These are but a few examples (all from Senator Specter's home state) of many that I could provide. Yet there should be many more and there should be more rapid progress in bringing these treatments from mouse to man. Although Congress has been extremely generous with NIH, proportionately little of the increase has benefited the muscular dystrophies. This is in part because of the reticence of new and established investigators to enter a historically under-funded area; namely, muscle

biology and muscular dystrophy. Until the last few years (and only then likely due to Congressional interest) NIH has put little emphasis on the muscular dystrophies. Scientists will not enter a research area unless they perceive that funding is available for research. Furthermore, in my opinion there have been significant problems in the manner in which grants that deal with muscle disease have been reviewed, resulting in too few being funded. Attention is now being given to this problem, again because Congress has expressed its concern. Last year the Congress passed the Children's Health Act of 2000, which included a title that increased coordination among the appropriate Institutes at the NIH in order to maximize resources and efforts specific to muscular dystrophy research. The NIH, and in particular the National Institute for Neurological Disorders and Stroke and the National Institute for Arthritis and Musculo-Skeletal Disease, have made significant progress in working with the scientific research community on exploring new ways to encourage researchers to focus on all aspects of the muscular dystrophies. The support of these Institutes has been invaluable, and our hope is that they will continue to support the muscle research community in its endeavor. We also hope that the Center for Scientific Review within NIH will become more responsive to the inadequacies in the review of muscle research.

A recent Congressional initiative that could further benefit DMD research is the recent introduction of H.R. 717, the DMD Childhood Assistance, Research and Education Act (also referred to as the DMD CARE Act). Due to the advocacy efforts of the Parent Project MD and the leadership of Representatives Roger Wicker and Collin Peterson who co-introduced the bill, H.R. 717 now has over 100 co-sponsors. This important legislation would establish an MD interagency committee within the NIH in order to expand opportunities for collaboration. Additionally, the bill calls for the creation of three Centers of Excellence through NIH and CDC so that leading research institutions will have an opportunity to compete for federal support towards both epidemiological and clinical research.

Again, I commend Chairman Specter and the Committee for their support of NIH and their commitment to doubling the NIH budget. I believe that this will have a great impact on the muscular dystrophy community. A mere increase of \$20 million a year directed at muscular dystrophy research could transform our treatment and understanding of these diseases. We are on the verge of making meaningful progress in the treatment of DMD for the first time in history, but we cannot do it without support from the federal government.

While all of the muscular dystrophies have significant impact on the quality of life of the affected individual, the childhood muscular dystrophies, and DMD in particular, have tremendous repercussions for the family members and caregivers. Currently there exists only a small quantity of public information about DMD and other childhood muscular dystrophies, and what little information does exist remains inadequately disseminated and insufficient in addressing the needs of specific populations and other under-served groups. Many family physicians and health care professionals lack the knowledge and resources to detect and properly diagnose the disease at an early state, thus exacerbating the progressiveness of the symptoms that go undetected or misdiagnosed. Educating the public and the health care community throughout the country is of paramount importance, and is in the public interest and will benefit all communities.

Today's hearing is a major step towards creating a greater public awareness of muscle disease, and I'd like to personally thank the Members of the Committee and their staff for showing their interest in the DMD and other muscular dystrophy communities. As you begin this year's appropriations process, I encourage you to consider the lives of those affected by these diseases. Especially consider the lives of your own sons and grandsons when thinking about DMD, as it is a disease that knows no boundaries.

Thank you for your time and compassion. I would be happy to answer any questions.

Senator SPECTER. Dr. Sweeney, the subcommittee and the full Congress is very concerned about the lives of the people who are affected here, and you have accurately characterized it as generous by any standards, but you are really making a fairly severe indictment, as I listen to you, that NIH is not doing the job. Do I hear you wrongly?

Dr. SWEENEY. I would not say not doing the job. I think the problem is—

Senator SPECTER. Well, they are not pursuing avenues to get the maximum use for the money to solve the problem.

Dr. SWEENEY. Well, I think the problem is that when an area lies fallow for too long and scientists do not go into it, then just making money available across the board does not do anything.

Senator SPECTER. Well, has it lain fallow? There have been very substantial appropriations for the Institutes, always, and you heard the particularization of the increases of about 16 percent, and \$1.4 billion. That is a very substantial sum of money.

Dr. SWEENEY. Yes, the overall budget is certainly very generous, and it is just, I think in this case something needs to be done, as the Institutes have started doing in the last year, to encourage investigators to move into this area, to highlight that there are research opportunities.

Senator SPECTER. Well, have they encouraged investigators to move into this area only in the last year? If so, that is a strong indictment, Dr. Sweeney.

Dr. SWEENEY. Well, I would say that the only significant efforts have really been within the last year or so, although I cannot characterize going back much more than 10 years, because then you go back beyond my career.

Senator SPECTER. Well, that leaves 9 years for analysis.

Dr. SWEENEY. Yes.

Senator SPECTER. I would like to ask staff to meet with you, Dr. Sweeney, and get the particulars, because if you are right, some changes need to be made.

Please note that I said, if he is right.

Dr. Penn, why don't you come forward and make a response here. What do you think? Is Dr. Sweeney even partly right?

Dr. PENN. I think, Senator, that more people, more really good investigators, as I sort of indicated, could definitely be working in this problem, and I think some things have now come forth where we need those people. We need people that know about these viruses. We need—

Senator SPECTER. Well, don't you have good investigators working on it now?

Dr. PENN. We do now, but remember, the revolution in molecular genetics is really not that old either, so—

Senator SPECTER. You are talking about identifying the gene in 1987.

Dr. PENN. Yes, but identifying the gene, as I said, produced information which nobody was ready to really take care of, because it is so big. I mean, we did not know exactly—we still do not know precisely what that protein does.

I will not say that more could not have been done in this disorder by NIH over time to take advantage of all the new information coming out, and making sure that all that new information was applied to the dystrophies. I think that the workshop helped. We certainly knew who was out there working.

We always say that we need more good scientists in all of our particular disorders, and I do not want to say that any of the institutes at NIH that are working on this disorder have not contributed to what has happened. I understand the issues about review. We will have a big meeting in the middle of March, which I am

sure Dr. Sweeney will attend, to talk more with our Center for Scientific Review about how to review these applications. If people do not get funded, they get discouraged.

Senator SPECTER. Well, Dr. Penn, your comments are just too high a level of generalization.

Dr. PENN. Yes, sir.

Senator SPECTER. More could be done, and you would not say that some progress has not been made. You have been very handsomely funded.

Dr. PENN. Yes, sir.

Senator SPECTER. And for that money the Congress expects results, and I would like you to sit down with Dr. Sweeney and staffers and get down to brass tacks as to what his complaints are and what your responses are.

Dr. PENN. I would be pleased to do that, sir, and I think we know a lot about what Dr. Sweeney has in mind.

STATEMENT OF LEON CHARASH, M.D., CHAIRMAN, MEDICAL ADVISORY COMMITTEE, MUSCULAR DYSTROPHY ASSOCIATION

Senator SPECTER. Dr. Charash, thank you for joining us, chairman of the Medical Advisory Committee and spokesman for the Muscular Dystrophy Association. Since the 1980's, Dr. Charash has provided a guiding hand on research programs, continues his private practice, is associate clinical professor of pediatrics at Cornell, M.D. from Cornell, specializing in pediatric neurology.

Thank you for joining us, Dr. Charash, and the floor is yours.

Dr. CHARASH. Mr. Chairman, Senator Craig, and Senator Wellstone, I have some exceptions to some of the things that have been stated here.

There was a question made about whether we have been sub-optimal in treating patients. The Muscular Dystrophy Association, founded in 1950, has expended over \$1 billion to treat patients. We have a clinic in every major medical school in the United States, one in Children's Hospital here in Washington, where free care is given to anyone who needs diagnostic and therapeutic services.

The Muscular Dystrophy Association, incidentally, was founded by a group of parents in 1950, and with Jerry Lewis' leadership has expanded to the point where it has a worldwide program sponsoring research around the world.

The critical question you asked, Senator, was, is there anything we would like to do? There is something we must do, because we have been successful. In these 50 years of research since MDA was founded, all the knowledge of muscle disease would fit into three paragraphs in Cecil's Textbook of Medicine. Now there are volumes on it. We have learned everything we wanted to know about muscle biology, histology, physiology, chemistry, and we have also now found the gene for every single disorder, essentially, that produces muscular dystrophy.

And by the way, we did find the gene, Senator, in 1957, and 2 years later we convened the first world conference of what is called myoblast therapy, and a year after that we treated the first human being with myoblasts, which are stem cells, and we expanded that to other clinics, and then we have used viral vectors. What we have gotten out of, though, is not something we should do, it is some-

thing we must do, because we built up a platform of information. All of this knowledge, in 50 years, has swelled the platform to where we can now shoot a rocket up. We have never been able to translate all of this knowledge into effective treatments.

We have strategies, and Dr. Penn very eloquently described antibiotics, stem cells derived from muscle or bone marrow, viral vectors to do this. MDA started it, initiated the first and only human trial to give a gene to muscular dystrophy patients, a virus, to a gentleman seated over here. Where is he? Over there. I was present in Columbus, Ohio, when he got his first injection. It is the only trial ever done.

We have to plan. We have to be proactive. We got all the information. We have not done anything about it, but we have not had that very long. We just got it now. The iron is hot. We have to strike. To do that, we have to have a focused program to translate all that we know into treating muscle diseases, and I might suggest this. If we can treat muscle disease, we can treat all genetic disease, and muscle is the best tissue to use.

Diabetes is a disease of the pancreas with islet cells. Muscle is the biggest tissue in the body. Muscle is accessible. We can see it. We can see if it has atrophied. We can see what its tone is like. We can biopsy it. We can do electrical studies on it.

If we can find a way to crack open genetic treatment of muscular dystrophy with stem cells, or with viral vectors, or whatever else, the door will be open. If you are watching the progress of treating diabetes, to take a needle biopsy of the pancreas is invasive and dangerous. We can take needle biopsies of muscles as often as we want, safely.

PREPARED STATEMENT

So I think the Muscular Dystrophy Association, which has devoted itself to all the dystrophies for 50 years, is passionately interested in seeing the NIH not only increase its funding, but set up a protocol where there can be a research body, and set up institutions, satellite institutions and help break down all genetic diseases.

Thanks.

[The statement follows:]

PREPARED STATEMENT OF LEON CHARASH

Thank you Mr. Chairman, Senator Harkin and members of the Subcommittee for this opportunity to address you. I'm here today to call your attention to a matter of life and death for tens of thousands of children and adults affected by muscular dystrophy. Muscular dystrophy is the name given to a group of disorders caused by genetic defects and characterized by weakening and eventual wasting of voluntary muscles. The muscular dystrophies can weaken the muscles of the heart and those required for breathing. By profession, I'm a pediatric neurologist and I've treated many children with muscular dystrophy.

In 1950, a group of parents and other relatives of muscular dystrophy patients, concerned that virtually nothing was being done to combat these diseases, organized to form what is now the Muscular Dystrophy Association. For over 50 years, the Association has provided help through medical services and hope through research for youngsters and adults with any of the nine forms of muscular dystrophy. And it's thanks to hundreds of millions of dollars in research funded by MDA that tremendous developments in understanding the causes of these disorders have occurred. Today, virtually all of the genetic defects that cause the muscular dystrophies are known.

The obvious next step is the development of effective therapies. A number of strategies are being pursued to correct the gene defects in the muscular dystrophies. Some are in the early stage of development and have shown encouraging results. Others are in the clinical trial phase. One approach now in clinical trials involves the use of antibiotics. MDA-funded studies of how cells make proteins led to the discovery that some antibiotics can override a "stop" message in genes that make the critical muscle protein dystrophin. Also, therapies using resident stem cells have shown encouraging results in early studies and, based on those results, will eventually be applied in clinical trials. Another strategy is gene therapy designed to replace missing or defective muscle proteins.

Scientists are optimistic about the therapeutic potential of these new techniques. However, the price tag is high. MDA funded and initiated the first gene therapy clinical trial in a muscle disease in September 1999. The project was a phase-one trial in which only six individuals were slated to receive gene therapy. The budget for this initial trial alone was nearly \$5 million. It's clear that continuation and expansion of these studies depends upon an increased financial commitment. For the first time in the history of these terrible diseases, we are not limited by science.

While MDA will not only continue to press ahead but will increase its efforts in search of treatments and cures, we believe strongly that a major investment through the National Institutes of Health will be essential to advance to the next level in muscular dystrophy research. To this end, we propose that the projected \$19.9 million NIH annual commitment for muscular dystrophy research be increased by \$100 million. We also propose that an NIH study group be established for neuromuscular disease research.

An analysis of NIH expenditures on diseases that affect a number of people similar to that affected by muscular dystrophy shows a great disparity in spending. In fact, spending on some of these disorders, and even on some that affect far fewer people, is many times the amount allocated for muscular dystrophy research. We seek this Subcommittee's support in our effort to meet the challenge of taking muscular dystrophy research to the next level—the development of effective treatments for 250,000 American children and adults.

Thank you.

Senator SPECTER. Thanks very much, Dr. Charash.
Senator Craig.

STATEMENT OF SENATOR LARRY CRAIG

Senator CRAIG. Mr. Chairman, on this issue my learning curve is about like this, and I am pleased that you are holding this hearing, because it is tremendously important that we cause our institutions to focus.

This Congress has been committed now for several years to advancing increasingly large sums of money to go directly at and to pay for the quality of research and bring folks online who are dedicated to these areas, and these kinds of hearings, as I think Senator Wellstone said, help us focus, and they help the institutions of our Government that are dedicated to these kinds of efforts focus along with us.

I will continue, as certainly this committee has, to support increased funding. We now are fortunate enough to have the resources to attack in ways that we have not in the past, and we also have the knowledge and the technologies to do so, so thank you all for being here this morning to help us.

Senator SPECTER. Senator Wellstone.

Senator WELLSTONE. Maybe I will try to build on, Mr. Chairman, a question or really a comment on your part to Dr. Sweeney.

Dr. Sweeney, you had talked about DMD, and until I met Cheri Gunvalson from Minnesota who is here today, I just really had so little knowledge of this terrible disease. Part of the problem it seems to me has been the invisibility of muscular dystrophy, at least as it affects children, especially with Duchennes, and that

there has been such a small number of families that have been affected in the whole country that there just has not been the presence and the clout, or the focus to get the research that is needed, or is it something else going on here?

Dr. SWEENEY. I think it is a number of factors, and I think there is good visibility. I mean, the MDA has for a number of years raised the visibility of the muscular dystrophies in this country. I really think that the problem I perceive, and I guess we can debate whether there is a problem, within NIH is really not a lack of interest on the part of the institutes, but it is more—

Senator WELLSTONE. No, I do not think there is a lack of interest.

Dr. SWEENEY. It is more of a problem, as I said, in sort of the way these grants get reviewed. I mean, the vagaries of the review process at NIH in large part dictate what sort of work gets funded. Study sections get set up that focus on a certain area. There is not a good home to review grants that deal with the muscular dystrophies, and because of this I think they are chronically underfunded, and because of that, new investigators are discouraged from going in to the area.

This was brought home—I went to a workshop that NIAMS held a few weeks ago, a very small one, where we were talking about better diagnostics that could be used in the skeletal muscular dystrophies, and all the technology that we were talking about had originally been developed in skeletal muscle now is being used in the heart. When the experts were asked, well, why isn't it being used in skeletal muscle, for those diseases, they said, well, there was no funding, and so we went to work on heart.

So I mean, it is a perception in the community, and you know, where there is a perception, it needs to be addressed.

Senator WELLSTONE. Let me ask you this, and Dr. Charash can also respond. Senator Specter said he would like to get a number of you all together to sit down and deal with concerns and answers, and I do not assume anything but good faith on the part of NIH, but what would you recommend for muscular dystrophy, and in particular for DMD? I guess my question is: What would you say specifically we need to do?

Dr. CHARASH. We have been working on Duchenne. It is a big gene. We cut it down to a smaller size, which works. We have taken the virus and stretched it as a vector. We have used it in animals. We cannot separate Duchenne research from all the other dystrophies, for this critical reason. We cannot treat a child without informed consent. We do not believe it is moral or ethical to have a—or even to ask a parent to sign—now, we—

Senator WELLSTONE. You do not have to separate out what would be the priorities for overall research? What would you change right now?

Dr. CHARASH. A task force funded by the NIH, translate all that we now know about—we have identified the genes. We know ways in which we can enter it into the body, and the stem cells that can be harvested from adults, and we need a task force—incidentally, I think Jerry Lewis is going to make a request to this committee for what he thinks should be done, and that is the view of MDA.

Senator WELLSTONE. Dr. Sweeney.

Dr. SWEENEY. I think a couple of things could be done. I think whenever you have got an area that needs a jump start, like this one now needs to reinvigorate it, I think some initial targeted funding for the area is justifiable, but I think moreover, the long-term solution comes in addressing the review process and to create a study section that can deliberate on disease, muscle disease-related grants and muscle biology in general. I mean, this is true for cardiac issues. It should be true for skeletal issues.

And then centers to bring about more rapid translation of research, such as has been suggested in the case of DMD and H.R. 717, that would set up translational centers that could take the basic biology and the preclinical data and begin to move it.

So I think, you know, in the long term it is not about giving more money to NIH. It is about directing some money in the short term and fixing the review process for the long term.

Senator SPECTER. Thank you, Senator Wellstone.

Dr. Charash, you commented about, I mean, now I have all the information, it is time for action plan, a task force. We did not just get all the information this morning. How long have we had it?

Dr. CHARASH. Well, you know, we have explored a number of—we started the first human trial, but for safety alone, and we chose adults, and if it works in adults—

Senator SPECTER. Dr. Charash, the point I am making is, why have we languished? How long have we had the information which would warrant an action plan, and have not done it?

Dr. CHARASH. Well, we have had it for 1½ years, and we have started on the first—it has cost us \$5 million just for the first trial on safety alone. If we're going to expand that to efficacy, it is going to be a fortune, and it overwhelms—

Senator SPECTER. Do you know how many \$5 million there are in \$1.4 billion?

We have another panel to hear from, but the subcommittee is going to pursue this to find out what the answer is, and we would appreciate, Dr. Charash, if you would join Dr. Sweeney and Dr. Penn in telling us what we need to do to get some concrete results.

It is a very difficult matter for Congress to instruct the scientists. Saying it is difficult is an understatement. It is an impossible matter for the Congress to instruct the scientists, but other scientists can instruct the scientists. Independent scientists can come in and take a look at it, and that is what we would appreciate it if you would do.

Okay. Thank you very much, Dr. Charash, Dr. Sweeney, Dr. Penn.

Dr. SWEENEY. Thank you, Senator.

Senator SPECTER. We now turn to panel three, Mr. Donavon Decker, Mr. Chris Rosa, Ms. Patricia Furlong, Mr. Benjamin Cumbo, and last but not least, Mr. Jerry Lewis.

We are going to have Mr. Lewis serve as clean-up hitter here, and we are going to start with Mr. Donavon Decker, an air traffic control specialist for the Federal Aviation Administration with the Huron automated light service station in Huron, South Dakota. He was diagnosed with limb girdle muscular dystrophy at the age of 15. He has four sisters and two nieces who have muscular dystrophy. In 1999, Mr. Decker was the first patient to undergo gene

therapy for muscular dystrophy. He has participated in the past seven muscular dystrophy telethons.

STATEMENT OF DONAVON DECKER, LIMB-GIRDLE MUSCULAR DYSTROPHY PATIENT, HURON, SOUTH DAKOTA

Senator SPECTER. Mr. Decker, we welcome you here, and look forward to your testimony, and when it is convenient for you we would like to know what the gene therapy was that you undertook.

Mr. DECKER. Thank you, Mr. Chairman. I will start off by reading my testimony and then follow up with any questions.

Thank you, Mr. Chairman and members of the subcommittee for permitting me to speak to you today. My name is Donavon Decker from Huron, South Dakota. I am employed at the Huron Automated Flight Service Station as an air traffic control specialist for the Federal Aviation Administration.

I am 38 years old, and have a form of muscular dystrophy that affects arms, shoulders, legs, and hips. It is called limb-girdle muscular dystrophy. Limb-girdle muscular dystrophy is a genetic disorder. My family is a classic example of how the disease can affect many members of the same family while skipping a generation. There are 8 children in the family, and I have 19 nephews and nieces. Four of my sisters and two of my nieces have limb-girdle muscular dystrophy. Neither my mother nor my father had any symptoms of the disorder.

In 1999, as you stated, I had the opportunity to become part of a milestone in research, the first-ever gene therapy clinical trial for muscular dystrophy. The Muscular Dystrophy Association funded the trial, which cost approximately \$5 million.

As part of the historic project, I was the first person in the trial to receive injection of billions of new genes. One foot muscle was injected with new genes and the other received a sham injection. This is a phase 1 safety clinical trial, and was a collaboration among researchers representing three universities, the Ohio State University, University of Pennsylvania, and the University of Iowa. The test results will be done in a month or so.

This research has the capacity to be used on all types of dystrophies, therefore helping individuals from young children to adults. I believe this trial would have not taken place if it were not for the Muscular Dystrophy Association. I would like to recognize the person who has served as the national chairman of the MDA for over 50 years, Mr. Jerry Lewis, and I am certain that you all know Jerry for his dedication each Labor Day you are aware of when he hosts his telethon for the association.

In the United States, some 250,000 people have one form of the nine muscular dystrophies, which affects all children as well as adults, regardless of race, creed, or color. Last year, the Federal Government budgeted \$19.9 million for muscular dystrophy research. I must say this is very disappointing to myself and my family. I am certain that many other families living with muscular dystrophy share my disappointment. But this can change. We can only win the battle much quicker with your help. The support of your subcommittee could make a positive difference in the lives of young people and adults with muscular dystrophy. It can make a difference in my life.

I urge this committee's consideration of support of a substantial increase for the allocation of funds for muscular dystrophy research. The Muscular Dystrophy Association is doing its job. I am now asking for additional support from NIH-funded researchers.

When I am at home, I do not use a wheelchair. However, when I travel I do, because it is easier on myself and the people that travel with me. I can no longer walk very far, and I cannot walk inclines without stairs or a wall to lean on. Three of my sisters use a wheelchair for daily activities.

PREPARED STATEMENT

I know that in a couple of years, if nothing is done I will be confined to a wheelchair for the rest of my life. The lives of others will be cut far too short if a cure is not found. Together, we can make this work so it will not happen. We need to do whatever it takes to keep this from happening. I and thousands of others affected by muscular dystrophy are counting on you.

I would answer any of your questions at this time.
[The statement follows:]

PREPARED STATEMENT OF DONAVON DECKER

Thank you Mr. Chairman, Senator Harkin, and members of the Subcommittee for permitting me to speak to you today. My name is Donavon Decker from Huron, South Dakota. I am employed at the Huron Automated Flight Service Station in Huron as an Air Traffic Control Specialist for the Federal Aviation Administration.

I am 38 years old and have a form of Muscular Dystrophy that affects the arms, shoulders, legs and hips. It is called Limb-Girdle Muscular Dystrophy. Limb-Girdle Muscular Dystrophy is a genetic disorder. My family is a classic example of how the disease can affect many members of the same family while skipping a generation. There are eight children in my family and 19 nephews and nieces. Four of my sisters and two of my nieces have limb-girdle muscular dystrophy. Neither my mother nor my father had any symptoms of the disorder. My mother is still living while my father was killed in a construction accident in 1987.

In 1999, I had the opportunity to be a part of a milestone in research the first ever gene therapy clinical trial for muscular dystrophy. The Muscular Dystrophy Association funded the trial, which cost approximately \$5 million. As part of the historic project, I was the first person in the trial to receive an injection of billions of new genes. One foot muscle was injected with new genes and the other received a sham injection. This phase I clinical trial was a collaboration among researchers representing three Universities: Ohio State University, University of Pennsylvania and the University of Iowa. For the researchers to properly monitor my progress, I had to have muscles taken from both feet six weeks after the injections. The test results will be done within a month or so.

This research has the capacity to be used on all types of dystrophy's, therefore helping individuals from young children to adults. I believe this trial would not have taken place if it weren't for the Muscular Dystrophy Association. I would like to recognize the person who has served as the National Chairman of the MDA for over 50 years, Mr. Jerry Lewis. I am certain that you all know Jerry for his dedicated efforts each Labor Day Weekend when he hosts his Telethon for the Association.

I want to thank Jerry for making it possible for me to participate in research that may lead to a treatment for limb-girdle muscular dystrophy. I want to say thanks to the millions of people who volunteer countless hours of their time to help MDA. I can't say enough about all the doctors and researchers funded by the MDA and the magnificent things they are doing to combat muscular dystrophy. But most of all, I want to say thank you to the generous public for their support in terms of dollars to help MDA. The Association has done a great job in putting those dollars to the best possible use. Again, Jerry, "Thank You".

In the United States some 250,000 people have one or another of the nine forms of muscular dystrophy, which affects children as well as adults regardless of race, creed or color. Last year, the Federal Government budgeted \$19.9 million for muscular dystrophy research. I must say this is very disappointing to myself and my family. I am certain that many other families living with muscular dystrophy share

my disappointment. But this can change. We can only win the battle much quicker with your help. The support of your subcommittee could make a positive difference in the lives of young people and adults with muscular dystrophy. It can make a difference in my life.

I urge this subcommittee's consideration of and support for an increase in the allocation of funds for muscular dystrophy research in the amount of \$100 million annually to be awarded to researchers by the National Institutes of Health. The Muscular Dystrophy Association is doing its job. Now I am asking for the additional support from NIH funded researchers.

When I am at home or work I do not use a wheelchair, however when I travel I do because it's easier on myself and the people that travel with me. I can no longer walk very far and I cannot walk up inclines or go up stairs without a wall to lean on. Three of my sisters use a wheelchair for daily activities. I know that in a couple years if nothing is done I will be confined to a wheelchair for the rest of my life. The lives of others will be cut too short if a cure isn't found. "TOGETHER WE CAN WORK SO THIS WILL NOT HAPPEN". We need to do whatever it takes to keep this from happening. I and thousands of others affected by muscular dystrophy are counting on you.

Senator SPECTER. Thank you very much, Mr. Decker.

STATEMENT OF PATRICIA FURLONG, PRESIDENT, PARENT PROJECT MUSCULAR DYSTROPHY

Senator SPECTER. We turn now to Ms. Patricia Furlong, president of the Parent Project Muscular Dystrophy, mother of four children. Two of her daughters are with her today. Regrettably, both of her sons died of muscular dystrophy. She is a nurse practitioner and a nurse educator. She served as Chair for Kids for Kids Project, and we welcome you here, Ms. Furlong, and look forward to your testimony.

Ms. FURLONG. Thank you, Senator Specter. It is an honor to be here today. Parent Project Muscular Dystrophy would like to thank you, Senator Specter, Senator Craig, and Senator Wellstone for being here, and Bettilou Taylor and members of this committee for this opportunity. We are indeed honored that voices are heard here in this city and in this place.

I represent the Parent Project Muscular Dystrophy. It is a non-profit voluntary health organization comprised of parents and grandparents whose children are diagnosed with Duchenne and Becker muscular dystrophy. Our goal was to add in the options to expedite therapies for Duchenne muscular dystrophy.

Mr. Chairman, today I ask the Members to focus on Duchenne muscular dystrophy. For years, we have been witness to the public information that we are almost there, we are around the corner, answers are on the horizon. Are they? Mr. Chairman, we are not there. Although there are emerging strategies leading to therapy and treatment in the future, the NIH investment has been minimal.

On a sunny day in June 1984, my sons were diagnosed with Duchenne muscular dystrophy. To this moment, I recall those words, Mrs. Furlong, your sons have Duchenne muscular dystrophy. There is no hope and no help. The prognosis is the same. It has been the same. They may not survive. The physician then asked me if I had any questions. I wondered why the sun was shining. I asked him that.

My personal story has to be more than this. It has to be a collective story about all boys diagnosed with Duchenne and Becker muscular dystrophy and, following their exposure to medical intervention, losing all independence. Mr. Chairman, there is nothing

that has changed in 100 years. Nothing will change without increased investment in Duchenne research.

One day, long ago, my son Patrick was trying to convince me of a crazy argument he had. He said to me, mom, pretend I am in a midlife crisis. In fact, he was. He was 8. Duchenne, the most common lethal genetic disorder of childhood has not had sufficient attention, and the ordinary person has no recognition of this disorder, and yet, due to the high spontaneous mutation rate, every person is at risk.

The clinical explanation does not clearly reflect this disorder. By the age of 12, most boys have lost their ability to walk. The child needs help with ordinary things, turning in bed, lifting a fork, wrapping their arms around someone they love. By the age of 17, breathing is sometimes difficult. Often, invasive ventilation is necessary. During the late teens or early twenties, young men with DMD are unable to manage oral secretions, and often have to have stool removed because they are unable to do it themselves. Remember, muscle is not just for moving bones.

The diagnosis of Duchenne is accompanied by a lifetime of progressive loss of function, loss of independence, and dependence on family. It is an extraordinary physical, mental, psychological, spiritual, and financial burden to the family, for all of us as a society.

Finally, the loss of these boys. Their absence diminishes us and the greatness of this country.

Before his death, my son Christopher said to me, if you will not fight for me, who will? It is for this reason we started the Parent Project Muscular Dystrophy. Beginning in 1997, the Parent Project Muscular Dystrophy members successfully initiated a legislative agenda. We began with a grassroots fundraising campaign. We began meeting with Members of Congress, Members of the Senate. We began talking about Duchenne muscular dystrophy here on the Hill.

Last year, we, with your kindness, saw the first title in the Children's Health Act. This was the first time in history a Federal mandate for DMD was initiated. This year, on Valentine's Day, H.R. 717, the DMD Care Act, was introduced in the House by Representatives Wicker and Peterson, with an unprecedented 92 co-sponsors.

Parent Project Muscular Dystrophy has established extensive collaborations with the NIH and the Center for Disease Control, but without adequate funding of these efforts, they will fall by the wayside, and another generation of children will see no change in prognosis.

Mr. Chairman, Congress is very generous to NIH, but this disease, the No. 1 lethal genetic disease of childhood, gets only 1/1,000ths of the NIH budget. No wonder there is nothing available for these children.

Our children are not out of their warranty period before their bodies wear out. They will never receive adult status to advocate on their own behalf. This generation, this disease sends ripples of pain and dysfunction through every family. On behalf of the children with Duchenne and Becker muscular dystrophy and their families, and all of these people you see here with muscular dystrophies, we ask the Federal Government to commit \$100 million

over 5 years specifically for Duchenne research. This would change the face of this disease forever and jump start an important field of research.

PREPARED STATEMENT

Today, we are not seeking exceptional funding for our children. We seek equity. Respected Members of this Congress, our battle is against Duchenne and Becker muscular dystrophy. We seek equity, equity in research opportunities, equity in set-aside funding, equity in the review process, equity in worth, the worth of every child with Duchenne and Becker muscular dystrophy, the worth of every person with muscular dystrophy.

Mr. Chairman, it is too late for my own sons, but with your help, this disease will change. Thank you.

[The statement follows:]

PREPARED STATEMENT OF PATRICIA FURLONG

On behalf of the Parent Project for Muscular Dystrophy Research, Inc. (otherwise known as the Parent Project MD), I would like to express the organization's sincere appreciation to Senator Specter, Bettilou Taylor, and members of this Committee for the opportunity to testify at today's Congressional hearing.

I represent the Parent Project MD, a nonprofit voluntary health organization comprised of parents and grandparents whose children have been diagnosed with Duchenne muscular dystrophy or its milder form, Becker muscular dystrophy. The Parent Project MD's mission is quite simple and straightforward: To mobilize people in the USA and Worldwide in collaborative efforts, enabling people with Duchenne and Becker Muscular Dystrophy to survive, thrive and fully participate into adult age. We wish to expedite treatment and a cure for this heartbreaking muscle disorder by increasing support for research.

Mr. Chairman, today I ask the members to focus upon the most common, lethal genetic disorder of childhood—Duchenne MD. For years, we are witnesses to public information that we are “almost there” or “around the corner”. Answers are on the horizon—or are they? Mr. Chairman, we are not there. Although emerging strategies leading to treatment and therapy in the future are in the works, NIH investment in DMD is abysmal, the peer review process and structure is not conducive to muscle research—simply stated the mechanism to foster science and research in this is broken. We have to commit adequate resources and support before the prognosis of DMD will see significant change.

On a sunny June day in 1984, my sons were diagnosed with Duchenne muscular dystrophy. To this day, I recall the exact words: “Mrs. Furlong, your sons have Duchenne muscular dystrophy, you are therefore a carrier, one or both of your daughters will perhaps be carriers. Your marriage will fail and your daughters will suffer due to the amount of care you will necessarily provide for your boys. Do you have any questions?” I wondered why the sun was still shining.

THE JUXTAPOSITION OF DUCHENNE

It simply isn't fair to be bright, handsome, and full of potential. To be well adorned in a good family, having so much to give the world, to be so loved and then to die so young. Worse, is to both see and feel the life force deteriorate slowly, finally and completely—until there is nothing left. Mr. Chairman, we live in a proactive, positive world, though children with DMD are ultimately powerless. It just isn't fair and great injustices must be righted or we are no better than a “killing field” through our apathy.

The barriers to progress on this disease says little for us as a society and as a nation—that due to a lack of significant resources, clinical outcomes of this disorder are predictable and remain unchanged. Boys die before reaching 20, before reaching adulthood, before experiencing life. One day, long ago, my son Patrick was trying to convince me about one of his crazy ideas and I recall smiling at his comment “Mom, pretend I am having a midlife crisis.” Sadly, age 8 was midlife for Patrick—his argument was sound.

Duchenne, the most common lethal genetic disorder of childhood, has not had sufficient attention—and the ordinary person has no recognition or understanding of

this disorder; and yet, due to the high spontaneous mutation rate, every person is clearly at risk.

My personal story therefore, is a collective story about all the boys diagnosed with Duchenne, and following his exposure to myriads of medical intervention, losing all independence and finally his life. Mr. Chairman, in this, NOTHING has changed in the last 100 years, the story remains unchanged and will remain so without increased investment in DMD research. In this remarkable land of medical miracles, we should all hide our faces in shame on that one statistic; let alone the harsh reality of this progressive, heartbreaking degenerative process known as Duchenne.

Duchenne Muscular Dystrophy (DMD) is the most common lethal childhood genetic disorder in the world, affecting 1:2328 male newborns worldwide (1997 German study). The disease can be inherited through X-linked recessive transmission within families, or it may be caused by a spontaneous mutation in individuals. Children who are born with DMD follow a predictable clinical course. Young children often develop difficulty walking and begin falling due to muscle weakness, and by 8–10 years of age the muscle weakness has progressed to the point where most children are wheelchair-bound. By their late teens, most DMD children have succumbed to their disease, usually as victims of respiratory failure.

This rather clinical explanation does not clearly reflect the disorder. Children with DMD experience a lifetime of medical intervention. As toddlers, boys with DMD look quite normal. At diagnosis—informed physicians refer to baseline studies, night splints, AFO's and PT—an excessive barrage of medical lingo that will soon become a second language for the family. As a mechanism to prevent contractures of the Achilles tendon, hamstrings and ileotibial bands, gait changes, lordosis, walking on their toes and finally loss of ambulation, boys with DMD require aggressive physical therapy, ankle-foot orthosis (AFO's), and long leg braces. By the age of 12, most boys have lost their ability to walk and, for the rest of their life, will require an electric wheelchair. In an effort to prevent spinal curvature, respiratory compromise and bone loss—long leg braces are utilized in combination with several hours of upright posture in “standers”. Hand in hand with loss of function is loss of independence. The child will need help with ordinary things: associated issues related to schooling, toileting, lifting a fork, turning in bed. By the age of 15, the breathing apparatus of these children is severely compromised. When laying flat in bed, these children do not have sufficient respiratory effort to exhale, blow off CO₂; hence mechanical (noninvasive) is instituted. They sleep with a mask over the nose and mouth (BiPap ventilation), which provides forced air into the lungs and therefore enhances their ability to exhale. Finally, the young man with DMD will require invasive ventilation—tracheotomy and ventilators due to extraordinary weakness of the pulmonary apparatus. Often we forget that muscle encompasses much more than moving bones—the Heart is a muscle as is the Digestive tract, which is comprised of smooth muscle. No muscle escapes degeneration in Duchenne. Children with Duchenne have cardiomegaly (enlarged heart), decreased cardiac output and congestive heart failure in their late teens. During the late teens or early 20's, young men with DMD are unable to manage oral secretions, have difficulty with digestion and require manual removal of stool. The Diagnosis of DMD is accompanied by a lifetime of progressive loss of function, loss of independence, dependence on family/care-givers and extraordinary physical, mental, psychological, spiritual and financial burden for the family and for all of us, as a society. Finally, the loss of these boys—their absence—what we miss as parents, siblings, relatives, communities as a society is great. This greatest country on earth is diminished by our irreverence for the lives of these children.

PARENT PROJECT MD

Before his death, my son Christopher asked, “if you will not fight for me, than who will?”. I was devastated at this question, for one feels complete defeated when they cannot help protect their own child, instead having to simply watch the child suffer this long, agonizing death. Parents from around the United States, indeed the world, wanted to advocate for their child, for this disease. In 1994, a small group of parents founded Parent Project Muscular Dystrophy, a national nonprofit dedicated to expediting research and cure for DMD/BMD.

Mr. Chairman, the obvious question for the Committee is, “What can we do?” Parents sitting around a table in 1994 raised the following issues, which are still valid today:

- (1) How can we improve the quality of life for our children and extend their life span?
- (2) How can we initiate the development of standards of care to provide families, physicians and care-givers access to state of the art information and knowledge

about care options to extend function and improve the quality of life for DMD/BMD children?

- (3) How can we help provide for genotyping of all DMD/BMD Children?
- (4) How can specific mutations be identified and compared to clinical progression?
- (5) How can subsets of the population who have a less severe clinical progression be identified to understand the underlying mechanisms (compensatory) involved?
- (6) Can genotypes/phenotypes be determined based on the impact of specific regimens (steroids/nutrition/future)?
- (7) Can subsets of the Duchenne population be isolated as candidates for future clinical trial?
- (8) Can the incidence/prevalence be updated? The statistic used of 1:3500 has been thrown around for years. Is it accurate? In light of genetic counseling, are the numbers of spontaneous mutations increasing?
- (9) Is newborn screening an important goal? Would the children have better clinical outcomes if diagnosis could be known at an earlier age?
- (10) What is the role of steroids? Is there a window of opportunity to introduce steroids? After 17 years of trials—what are next steps to determine age of intervention/regimen—and is this outcome directly or indirectly related to specific mutations?
- (11) Can we develop strategies for identifying, supporting and disseminating promising research and its application?
- (12) What are the mechanisms required for translation of bench research to clinical trial—FDA, Biotech, who, how? And finally,
- (13) What is the Federal Investment in DMD research and advocate for equity for children with DMD/BMD?

In 1997, Parent Project MD members initiated a legislative agenda. Initially, we wrote letters to representatives—pleas on behalf of their sons. In 1999, the House Labor/HHS Appropriations Subcommittee heard our testimony. Last year, this Committee graciously included strong DMD report language in its conference report—and we thank the committee for this. We were further blessed to obtain a separate Title in the Children's Health Act of 2000—the first time in history there has been a federal mandate on DMD. This year, Valentine's Day, H.R. 717, the DMD Care Act, was introduced in the House by Representatives Roger Wicker and Collin Peterson with 90 original co-sponsors. Parent Project MD has established extensive collaborations with NIH and CDC, but without adequate funding these efforts will fall by the wayside and another generation of children will be lost to DMD.

Mr. Chairman, Congress has been very generous to NIH, and rightfully so. But this disease—the world's number ONE lethal, genetic disorder—gets less than 1/2000th of the resources of the NIH in research. It is no wonder there is nothing available for these children. Parent Project MD believes there are some structural issues that help account for this and we would be pleased to address them. Scientists uniformly do not believe that the peer review processes and structure of NIH encourage muscle research. We ask that you assist us in helping create the structural environment necessary at NIH to bring this disease to some semblance of parity to other disease groups of similar severity and prevalence.

Our children are not out of their warranty period before they wear out, our children will never have the adult status to advocate on their own behalf, our children's degeneration sends ripples of pain and dysfunction through generations of families.

On behalf of children with DMD/BMD and their families.—We ask the Committee to increase federal investment in DMD research and treatment. An overall increase of \$20 million per year over the course of 5 years specifically for DMD research would change the face of this disease forever.

Congress must do with muscle disease what it has done with many other diseases: It must allocate this small amount of the NIH budget specifically for research on DMD. This would jump-start an important research field that has been chronically short on research support, and would build the research infrastructure to an acceptable level.

TODAY, WE DO NOT SEEK EXCEPTIONAL EXPENDITURES FOR OUR CHILDREN: WE SEEK SOME EQUITY

Respected members of the 107th Congress, today, our battle is against Duchenne and Becker muscular dystrophy. We request EQUITY: Equity in research opportunities, equity in set-aside funding, equity in the review process and equity in worth, the worth of each child who has Duchenne or Becker muscular dystrophy. We ask that you listen now to the voices of these young men, as their voices will surely fade before they reach adulthood. We urge you to provide the first set-aside money for research that will investigate the territory of this devastating disease and the weap-

only needed to win this war. Without your help, our children will continue to have the same prognosis for another 100 years. Mr. Chairman and distinguished members of the Committee, we are honored to appear before you today, and grateful for this opportunity to testify.

Senator SPECTER. Thank you. Thank you very much, Mrs. Furlong, for that very moving testimony. We are heartsick to know of the death of two sons. It is a tragic loss. My wife and I have two sons. Fortunately for us they are healthy and still with us, but we have some understanding of your grief, and we admire the work you are doing to try to change things for other people's sons.

Senator WELLSTONE. Mr. Chairman, with your indulgence, may I take 1 minute to just make one quick comment? I wanted Ms. Furlong to know that really I first of all could not agree more with what the chairman said to you, and second to know that your work has really made a difference.

I had something to do with working on The Children's Health Care bill, and it was because of you all that we were able to get the language in that called for a coordinated approach on Duchenne disease, and I think the first appropriation was just \$5 million this January, but it was a start, but before your voices, and before the work that all of you have done, there had not been that kind of coordination and focus, and so I just want to make it crystal clear this is just the beginning of this journey, but the work that you and everyone else in this room has done has been terribly important, very, very important. Thank you for your very strong, passionate, wonderful voice.

Ms. FURLONG. Thank you, Senator Wellstone.

Senator SPECTER. Thank you, Senator Wellstone.

STATEMENT OF CHRIS ROSA, Ph.D., MEMBER, MUSCULAR DYSTROPHY ASSOCIATION BOARD OF DIRECTORS, MEMBER, PRESIDENT'S COMMITTEE ON EMPLOYMENT OF PEOPLE WITH DISABILITIES

Senator SPECTER. Our final witness on this panel is Dr. Chris Rosa, director of the office of special services for students with disabilities at Queens College, serves as Muscular Dystrophy Association board of director, steering committee of MDA national task force, earned his doctorate in sociology from Queens College. Mr. Rosa was diagnosed with Becker muscular dystrophy at the age of 9.

Thank you for joining us, Dr. Rosa, and we look forward to your testimony.

Dr. ROSA. Thank you very much, Mr. Chairman. It is really my honor to be here, along with you, Senator Craig and Senator Wellstone. Thank you for allowing me to come before you this morning to represent the more than 200,000 families, American families who are affected by muscular dystrophy.

I feel that I am uniquely qualified to comment upon the concerns of American families affected by the muscular dystrophies, because in 1976 the lives of members of my family were forever changed by my diagnosis of Becker's muscular dystrophy. When my condition was first diagnosed, very little was known about the muscular dystrophies. Doctors offered families little hope, and prepared them for lives of diminished opportunities, and the inevitable premature loss of loved ones.

However, over the past three decades, thanks to the work of the Muscular Dystrophy Association, the prospects for people with muscular dystrophy have improved dramatically. Through MDA's national network of clinics, people with MD are receiving the preventive health care and assistive technologies necessary for them to live more productive lives.

Indeed, thanks to MDA, I was able to graduate from college, to go on to graduate school, earn a doctorate in sociology, build a rewarding career, and dream of one day starting a family of my own. Moreover, through MDA's worldwide program of neuromuscular disease research, we have moved to the very threshold of treatments and cures.

While this progress is a source of tremendous hope for families affected by muscular dystrophy, it is also a source of great tragic irony. As those of us who have been empowered to pursue independence by research wait desperately for effective treatments and cures, the ravages of muscular dystrophy continue to exact tremendous human and social costs.

Muscular dystrophy will continue to weaken vibrant, productive people, ultimately rendering them unable to work and forcing them to be dependent upon disability benefits. It will continue to cut down talented, contributing members of our society in the prime of their lives, leaving gaping holes in the fabric of love and support that binds our families together.

PREPARED STATEMENT

Every day, without treatments for muscular dystrophy, costs us the very lives of dozens of bright and talented people. At this time, we therefore propose that you respond to the urgent need of thousands of American families by increasing NIH's projected \$19.9 million allocation annually for muscular dystrophy research by a significant amount.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF CHRISTOPHER ROSA

Mr. Chairman, Senator Harkin, and members of the Subcommittee, I feel that I am uniquely qualified to comment upon the concerns of American families affected by the muscular dystrophies because in 1976, the lives of members of my family were forever changed by my diagnosis of Becker MD. When my condition was diagnosed, very little was known about the muscular dystrophies. Doctors offered families little hope and prepared them for lives of diminished opportunities and the inevitable premature loss of loved ones.

However, over the past three decades, thanks to the work of the Muscular Dystrophy Association, the prospects for people with muscular dystrophy have improved dramatically. Through MDA's national network of clinics, people with MD are receiving the preventative health care and assistive technologies necessary for them to live more productive lives. Indeed, thanks to MDA, I was able to graduate from college, go on to graduate school, earn a doctorate in sociology, build a rewarding career, and dream of starting a family of my own. Moreover, through MDA's worldwide program of neuromuscular disease research, we have moved to the very threshold of treatments and cures.

While this progress is a source of tremendous hope for families affected by muscular dystrophy, it is also a source of great tragic irony. As those of us who have been empowered to pursue independence by research wait desperately for effective treatments and cures, the ravages of muscular dystrophy continue to exact tremendous human and social costs. Muscular dystrophy will continue to weaken vibrant, productive people, ultimately rendering them unable to work and forcing them to

be dependent upon disability benefits. It will continue to cut down talented, contributing members of our society in the prime of their lives, leaving gaping holes in the fabric of love and support that binds our families together. Every day without treatments for muscular dystrophy costs us the very lives of dozens of bright, talented people.

We therefore propose that you respond to the urgent need of thousands of American families by increasing NIH's projected \$19.9 million annual allocation for muscular dystrophy research by an additional \$100 million.

Thank you.

Senator SPECTER. Thank you very much, Dr. Rosa. We hear you, and we will take a close look at what NIH has been doing with muscular dystrophy to see, without unduly meddling with what the scientists are doing, if they might be of a mind to have some re-allocation.

Mr. Decker, I noted early on your comment about, or in your bio, you participated in gene therapy, first patient to undergo gene therapy. What was that like, and what were the results?

Mr. DECKER. Like I stated in my testimony, the results are not known yet. I did speak to Dr. Mandel last week because I thought it would be nice to have the test results for this hearing, but he advised me that in about a month or so the test results should be out.

As far as what it was like, it was a dream come true, because we went from 20 years ago, never knowing if there would be a cure, to where I am very optimistic on how things are going to go. Dr. Hansel Stedmans, who is in the audience today, was one of the researchers there, along with Dr. Jerry Mandel. You could not ask for any better doctors to be involved with. The Ohio State University was extremely—I cannot say enough about everybody there.

Being selected, because of the right genetic disorder was—it is very humbling. As far as which foot do I think the new gene was in, I do have my opinions, but the doctors tell me that the dosage was so low, set by the FDA, that they did not figure I could realize which foot it was in, but I do think I know which foot the new gene was in, and the muscle biopsies were taken 6 weeks after the injections, just like everything went, but I must stress the goal of the first phase is safety only.

They have done one patient other than myself. Neither one of us had ever had any soreness of the feet, and I have remained in contact with the other person, and they do feel that they know which foot the new gene was in, too.

Senator SPECTER. Thank you very much, Mr. Decker.

Senator CRAIG.

Senator CRAIG. Well, thank all of you for being here today and your testimony and your willingness to come forward and get involved. I think, Dr. Rosa, your statement about tragic ironies speaks well for all of you.

Ms. Furlong, H.R. 717, if it were to become law, would authorize three centers of excellence for DMD research at the NIH, and it authorizes three centers of excellence for DMD, data collection surveillance, epidemiology—would you give us a little of the background of your involvement of why the legislation was structured as it was, and do you believe it fills the needs that we currently understand, or you currently understand are there?

Ms. FURLONG. Yes, I would love to address those issues. The term, 1 in 3,500 male children worldwide, has been used for a very long time. The Parent Project Muscular Dystrophy Project has had questions about that.

If, for instance, two-thirds of that disorder is by familials, from families, and one-third is spontaneous mutation, one would assume that with genetic counseling, you could tip the scales so that the incidence would be less. It does not occur to us that the incidence is less, so one of the questions that we would like the Center for Disease Control to approach, or to ask, is, is the incidence of 1 in 3,500 accurate? Has it changed?

There has been a German study in 1997, and from the numbers of the German study, if you do the math, you could get the number 1 in 2,500, which certainly changes the incidence, and prevalence of the disorder, and certainly the need for research, so these are the questions, to start at the beginning and look at what incidence and prevalence, and finally—not finally, but in the process to look at the standards of care for these children, and make them consistent across the board.

When my sons were diagnosed, we visited five doctors in the course of the next 30 days. I must tell you that that is such a devastating blow that you are willing to try anything, go anywhere, and in those physicians we visited, and the same is true today, there was a wide degree of what might be appropriate in terms of these children, and perhaps it is related to the age of diagnosis, and, further, the mutation, the specific mutation of the child, so we need to know those things, what is the standard of care, will it vary for a child with a different mutation, and if there is a child or a young man with a different mutation that is doing very well, could we apply that compensatory mechanism, for instance, to the children who are not doing so well, to make them improve in their outcomes, so there are a certain number of questions that we think the bill addresses.

We also think that in your home State, Senator Specter, you have some very fine institutions, the University of Pennsylvania, University of Pittsburgh, with some very fine research. There are amazing scientists. The Muscular Dystrophy Association has developed a remarkable basis of information, and many of these people are collaborative, at the same institution.

Centers of Excellence create a critical mass. There is Washington, D.C., with Dr. Eric Hoffman, who is here. There are such critical masses that you could really isolate some sets of collaborators to do specific jobs to approach this systematically to improve the prognosis and life span of these young men, hence the bill.

Senator CRAIG. Thank you. Thank all of you very much.

Senator SPECTER. Thank you, Senator Craig. Thank you very much, Ms. Furlong, Dr. Rosa, Mr. Decker. We hear you, and we will try to help even more.

**STATEMENT OF JERRY LEWIS, INTERNATIONAL ENTERTAINER AND
NATIONAL CHAIRMAN, MUSCULAR DYSTROPHY ASSOCIATION
ACCOMPANIED BY BENJAMIN CUMBO, MUSCULAR DYSTROPHY ASSO-
CIATION'S NATIONAL GOODWILL AMBASSADOR**

Senator SPECTER. I would like now to call Mr. Jerry Lewis, at the center of the American stage for more than 50 years, a great humanitarian, striving to provide his kids with a better future. He has led the worldwide fight against neuromuscular disease as national chairman of the Muscular Dystrophy Association. He battles on behalf of more than 1 million Americans affected with these diseases.

Since 1966, his Labor Day Telethon has raised over \$1 billion for muscular dystrophy. His honors are legendary, and include being nominated for the Nobel Peace Prize, the only entertainer ever nominated for this honor, and received a Lifetime Achievement Award from the American Medical Association, the U.S. Defense Department's highest civilian award, the Medal for Distinguished Public Service, and accompanying Mr. Lewis is Mr. Benjamin Cumbo.

Mr. Lewis, Jerry Lewis, thank you for all you have done. Thank you for coming here today.

Mr. LEWIS. My pleasure. Thank you.

I have to tell you that I got in the elevator to come here, and this cute lady that works in the Senate was in the elevator when I got on and she said, you're Jerry Lewis. I said, no, I'm not. She said, yes, you are. I said, no, I'm not. She said, you are. I said, okay, I am. She said, no you're not.

I thank you, Senator Specter and Senator Craig, for this opportunity. I think that I have to mention the fact that most everything I have done in the 50 years working with MDA and working for my kids, I have never in 50 telethons ever read anything, other than possibly a scientific piece of data, but for the most part everything has come from my heart, and I think that is why the American people have been so responsive.

But because this is so vital today, I am going to do something I have never done before. In truth, it is the first time. I am going to read the text exactly as we put it together, because it is all too important, so if I am looking down a couple of times, I am not ignoring you, Senator. It is just that I am reading, which I learned to do many years ago.

I am grateful for this opportunity to speak on behalf of the quarter million Americans affected by muscular dystrophy. A quarter million. That is a big number. So you can put a face on this problem and understand in human terms why we are all here, I brought a short video for you to watch. Please, if you will.

Ben is now 13. He was MDA's National Goodwill Ambassador in 1996. He is what this is all about, and our presence here today.

For 50 years, I have been fighting an evil, insidious force that preys on people like my pal Ben. I vowed all those years ago that I would beat muscular dystrophy in my lifetime. I will be 75 in 3 weeks, and I am a tough bird, but don't you think that at this point I could use a little help?

Since 1950, the Muscular Dystrophy Association has been out there leading the charge against all nine forms of muscular dys-

trophy, not just Duchenne muscular dystrophy, about which you have heard a great deal today. Virtually every major discovery in these diseases was funded by MDA.

We have located the genetic defects for almost every form. We have tested countless drugs and compounds looking for the answers. We have developed techniques that are being used in the battles against scores of other diseases. We did not ask the Government for help, because we could do it alone. We did not need help.

My message to you today is this: Things change. Today, we need the help. MDA has laid all the groundwork. Now it is time to take what we have learned, this vast well of knowledge, and turn it into treatments and cures. We have worked so hard, received so much support from the American people it is incredible. It would be a tragedy and a sin for our march toward victory to be stalled now.

We are actually the victims of our own success. MDA has done such an outstanding job of providing vital services and directing revolutionary scientific research that everyone, including the Government, thinks we can do it all. Well, I am here to tell you we cannot, not any more. The clinical trials that we must conduct to test the things that we think could stop muscular dystrophy are expensive, unbelievably expensive. Without Government support, many trials will never happen, and those that do will take much longer.

This is unacceptable. I cannot tell a quarter million Americans that they are not a national priority. For years, Government research on muscular dystrophy was underfunded because everyone counted on MDA to carry the load. This has allowed a lot of money to go to research in other diseases.

You have heard testimony about how diseases affecting far fewer people get much greater funding through the National Institutes of Health. It is time for the quarter million Americans that I have the honor to represent to get their fair share. They waited long enough, and they deserve it. That is why I am asking for \$100 million annual increase in NIH funding for muscular dystrophy research.

Now, I know what you are thinking. This crazy comedian is asking for the world. No, I am not, not really. I am only asking for the weapon that we need to win the war against muscular dystrophy. I do not believe anyone would think a quarter million Americans represent acceptable casualties. I do not think the loss of even one is acceptable.

Other witnesses here today have given you all the facts and figures you need to justify another \$100 million for muscular dystrophy research. When it comes to those I fight for, I do not think in terms of facts or numbers. I think in terms of children, of mothers, fathers, or brothers and sisters. That is what this is all about, and has been for 50 hard years.

PREPARED STATEMENT

I carry in my heart the memory of every person with muscular dystrophy I have ever met. I hope you will carry the image of Ben, both the little boy and the young man, in your hearts when you consider this request. If you do that, I know you will do right by Benjamin and all the kids.

Thank you for your time.

[The statement follows:]

PREPARED STATEMENT OF JERRY LEWIS

Mr. Chairman, Senator Harkin and members of the subcommittee, I'm grateful for this opportunity to speak on behalf of the quarter million Americans affected by muscular dystrophy. A quarter million—that's a big number. So you can put a face on this problem and understand in human terms why we're all here, I've brought a short video for you to watch.

That cute little boy in the video is now the handsome young man sitting to my (right/left). Benjamin Cumbo, now 13, was MDA's National Goodwill Ambassador in 1996. He's what this is all about.

For 50 years, I've been fighting an evil, insidious force that preys on people like my buddy Benjamin. I vowed all those years ago that I'd beat muscular dystrophy in my lifetime. I'll be 75 next month. Now, I'm a tough old bird, but don't you think that at this point I could use a little help?

Since 1950, the Muscular Dystrophy Association has been out there leading the charge against all nine forms of muscular dystrophy, not just Duchenne muscular dystrophy about which you've heard a great deal today. Virtually every major discovery in these diseases was funded by MDA. We've located the genetic defects for almost every form, we've tested countless drugs and compounds looking for the answers, we've developed techniques that are being used in the battles against scores of other diseases. We didn't ask the government for help because we could do it alone. We didn't need help.

My message to you today is this: Things change. Today, we need the help. MDA has laid all the groundwork. Now it's time to take what we've learned—this vast well of knowledge—and turn it into treatments and cures. We've worked so hard, received so much support from the American people, it would be a tragedy, a sin, for our march toward victory to be stalled now.

We're actually the victims of our own success. MDA has done such an outstanding job of providing vital services and directing revolutionary scientific research that everyone, including the government, thinks we can do it all. Well, I'm here to tell you, we can't. Not anymore. The clinical trials that we must conduct to test the things that we think could stop muscular dystrophy are incredibly expensive. Without government support, many trials will never happen and those that do will take much longer. This is unacceptable. I can't tell a quarter million Americans that they aren't a national priority. For years, government research in muscular dystrophy has been underfunded because everyone counted on MDA to carry the load. This has allowed a lot of money to go for research in other diseases. You've heard testimony about how diseases affecting far fewer people get much greater funding through the National Institutes of Health. It's time for the quarter million Americans that I have the honor to represent to get their fair share. They've waited long enough and they deserve it. That's why I'm asking for a \$100 million annual increase in NIH funding for muscular dystrophy research.

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Other witnesses here today have given you all the facts and figures you need to justify another \$100 million for muscular dystrophy research. When it comes to "my kids," I don't think in terms of facts or numbers, I think in terms of children, of mothers, of fathers, of brothers, of sisters. That's what this is all about and has been for 50 years. I carry in my heart the memory of every person with muscular dystrophy I've ever met. I hope you'll carry the image of Benjamin, both the little boy and the young man, in your hearts when you consider this request. If you do that, I know you'll do right by Benjamin and all "my kids."

Thank you and God bless you all.

Senator SPECTER. Thank you very much for that very poignant and moving testimony, Mr. Lewis. We thank the Cumbos for being with us today, and for bringing Benjamin along.

Ben, you are not scheduled to have a speaking part, but let me ask you how you are.

Mr. CUMBO. I am doing all right. I am just a regular 13-year-old boy just trying to do everything I can, just trying to get a girlfriend, too.

Listening to hip-hop, and everything a regular teen boy will regularly do, but me, I just realize that I am extremely lucky, and God has blessed me because I mean, there are people that are a heck of a lot worse than I am, and I mean, don't just do this for me, though. I mean, there are other people in worse condition than I am, and if they can get funding, too, from NIH, this will be great right here, because if the Government can spend, like \$2 billion on one plane, and stuff like that, \$100 million will not hurt for 5 years.

Mr. LEWIS. Good boy, Ben.

Senator SPECTER. Ben, have you considered being a Senator?

Mr. CUMBO. I don't know. I just—I mean, with your help I hope I can pursue a career in the military as pilot, I guess, hopefully.

Senator SPECTER. Well, we may have to reserve one of those \$2 billion planes for you.

Ben, how are you feeling? Are you feeling okay?

Mr. CUMBO. Oh, yes, I am feeling very fine.

Senator SPECTER. Are you able to participate in sports?

Mr. CUMBO. Unfortunately, no. I mean, I used to, as you can see in the video that they just displayed earlier, but I mean, now I am getting a little weaker though, and I am not really able to do that, but one thing I can concentrate on is just being a good student and just trying to do the best thing I can with everything I can.

Senator SPECTER. But you are doing okay with the girls?

Mr. CUMBO. I don't know yet. I mean, I might have to wait, like, 3 more years. I don't know.

Senator SPECTER. Well, Ben, we thank you for coming here, and we thank your parents for making the video, because you bring to life the exact nature of the problem, and we hear you.

Jerry Lewis, we have watched you for years and years and years and years, and we have all seen your telethons, and we marvel at how you do them. How long do they last, more than 24 hours?

Mr. LEWIS. Well, including prep time they run about 38 hours.

Senator SPECTER. 38 hours?

Mr. LEWIS. Yep.

Senator SPECTER. Well, that is a phenomenal physical exercise.

Mr. LEWIS. There is no ham in my family. I got it all.

Senator SPECTER. We are going to take a look at the NIH budget on muscular dystrophy. The National Institute for Neurological Disorders gets slightly under \$1.2 billion, and muscular dystrophy is slightly under \$20 million, and there was an increase last year of almost \$147 million for the neurological institute. The NIH has been very, very expansively and expensively funded, and as you might suspect, the Congress does not make the allocations, but I think that NIH will hear what you said today. Dr. Penn will hear what you said today—she is nodding in the affirmative—and we have a couple of other experts. A little oversight by the scientists of the scientists is always a very healthy thing.

Mr. LEWIS. Senator Specter, may I make a point—

Senator SPECTER. Sure.

Mr. LEWIS [continuing]. About the fact that NIH had a budget of \$19.9 billion, came to that particular figure relative to muscular dystrophy research over a period of years, over the period of years of survey, examination, plotting, and planning, that figure came into play.

Since that time, we now are into genetic engineering. We are into DNA. We are into trials where we know the answer will come from. We are talking about \$5 million a trial. We will use 20 trials in the first year after you give us the \$100 million, and then we are going to have to look forward to the following year, when you do it again.

But we could ostensibly get the answer in the first series of trials, so what I am saying is, the Government of this country can put the cherry on the cake of the 50 years that I have put in. Please think about that cherry.

Senator SPECTER. Well, it is a very important matter. There is no doubt that you are representing, Ben is representing a lot of youngsters stricken with muscular dystrophy, and we do hear in this committee hearing room situations involving many, many tragedies, but none more important than muscular dystrophy.

Mr. LEWIS. And your two sons, Senator, that you alluded to earlier, are healthy, thank God, because of the work we do and have done in the 50 years. We have not the faintest idea how many innocent human beings have been saved by the work we have done, and that is a very, very strong comment, along with what we are talking about today.

Your sons are healthy, thank God, and what we do is to keep them from ever becoming my kids, so if the good Senate will look at this carefully—and I mean expeditiously, simply because we are dealing in life and death, and the answers, the sooner they come, we will get to the victory dinner quicker.

Senator SPECTER. Well, having identified the gene in 1987, I would like to have some answers as to what has been done in the intervening 14 years. That is a long time.

And we have to mount a very intensive campaign on stem cell research, which may hold the key—

Mr. LEWIS. Right.

Senator SPECTER [continuing]. For muscular dystrophy, as it appears to hold the key for many, many other ailments.

But this turn-out today has been a very impressive one. We thank all of you for coming. We feel the emotion and the electricity in the room, there is no doubt about it, and Senator Craig, you can have the last word.

Senator CRAIG. Well, thank you, Mr. Chairman. No, I am going to give Jerry Lewis the last word. He deserves it for the commitment and dedication you have had, but you know, Mr. Lewis, I think Benjamin upstaged you today—

Mr. LEWIS. Absolutely.

Senator CRAIG [continuing]. In a way that I know you will accept.

Mr. LEWIS. Yes, absolutely.

Senator CRAIG. The young man sitting beside me here from Lafayette, California, he tells me it is north of San Francisco. He just

slid me a note a few moments ago and said, you have got a very interesting and hard job.

His name is Scott, and Scott is right, we have a fascinating job, but it is a tough one. I am extremely pleased that Congress has committed itself to rapid increases in money that has gone to NIH in the area of health and medical research, and we will try to continue to do that. We are beginning to recognize the benefits, and humanity is beginning to feel them. We would like to see results.

Mr. LEWIS. You will all be blessed, Senator Craig.

Senator CRAIG. Well, what you have done and what all of these parents and this organizational work has done over the years—and you have said it well: It has set us up in a positive way. I will certainly work with Chairman Specter to see where we can get, both in money and in the structure necessary—the legal structure necessary to see if we cannot accomplish some of these things.

We as a country are blessed right now, in the sense that we have some resources. It is a matter of prioritizing. There are a lot of diseases out there, and all of them bring to us tough choices. Our resources are substantial, but they are limited. We will sort them out. Your presence here today, and the presence of all of you and these marvelous parents and young people send a very loud message. Thank you.

Senator SPECTER. Thank you, Senator Craig. Thank you, Ben, thank you, Jerry, and thank you all.

Mr. LEWIS. Thank you, Senator.

ADDITIONAL PREPARED STATEMENT

Senator SPECTER. The subcommittee has received the prepared statement of Jeff Baxter on behalf of the Parent Project MD. The statement will be placed in the record.

[The statement follows:]

PREPARED STATEMENT OF JEFF BAXTER

Mr. Chairman, I would like to begin by thanking the Committee for hosting today's hearing on this important children's health issue—and for inviting me to speak on behalf of the Parent Project MD, and more importantly for allowing me to speak for those who don't always have a voice in the political process—little boys with Duchenne Muscular Dystrophy.

Mr. Chairman, as a professional musician and guitar player, I have made a life's work of playing the guitar and making music. My profession requires me to use all my muscles on a daily basis—to play the guitar, to sing songs, to dance, to perform. I am ashamed to admit that I take my capabilities for completing these daily activities for granted. I can't imagine what it would be like to not be able to play, to sing, to dance, or to perform.

Unfortunately, children with Duchenne are so physically limited, that they will never have the opportunities I've had. We have distinguished medical professionals here today who can tell you all of the scientific and technical reasons why this is the case. But, I'm here to be the voice, the hands, and the legs for those boys who have no voice, no strength in their hands, no power in their legs. Children who have such difficulty raising their arms to feed themselves and lifting their legs to walk, that they can't even think about playing an instrument, dancing on stage, or performing for a crowd. Children who by the age of 14 need major surgery to stabilize their spine and a ventilator to breathe. Mr. Chairman, when these kids are at the age when they should be worrying about college, listening to the music, hanging out with their friends and enjoying and all the passions of youth—these boys are already gone.

Mr. Chairman, you may wonder why I'm here today? Well, I'm here for my friend's son Bill, an 11-year old with Duchenne, and all the boys suffering with this deadly disease. For now, Bill is doing as best as one can expect given his predicament.

ment—he can still walk, although even the smallest stair is a struggle. And he is the exception, because the majority of DMD cases are in a motorized wheel chair by the time they are Bill's age.

Bill is a bright little boy whose future is already mapped out in a defective gene—he won't play the guitar, he won't ever perform on stage, he will never be able to have children of his own . . . he and the other boys will never know their full potential because this disease is killing them.

Mr. Chairman, I'm here today to make a statement and plead a cause. Help Bill and the thousands of other children with Duchenne muscular dystrophy. Help these boys live. We have got to get serious about research, and it requires a commitment from the private sector, from people like myself, and from the federal government. I've helped the Parent Project Muscular Dystrophy raise some funds, but this is just a drop in the bucket for what is required for true progress. We need your help and the help of the NIH and CDC to get organized to fight this disease. Mr. Chairman, help me help the boys with Duchenne.

Let me end by reiterating how honored and grateful I am to be here today, and I applaud the Committee for holding this important hearing and giving me the opportunity to speak for the Duchenne boys.

CONCLUSION OF HEARING

Senator SPECTER. Thank you all very much for being here, that concludes our hearing.

[Whereupon, at 11:55 a.m., Tuesday, February 27, the hearing was concluded and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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