



4600 Devitt Drive
Cincinnati, Ohio 45246
+1 513 874 3020 phone
+ 513 874 2520 fax
+1 800 818 RETT (7388) toll free
www.rett syndrome.org

Testimony before the House Labor, Health and Human Services and Education
Subcommittee of Appropriations

By
Ms. Gail Smith
Parent
Kristi, MD

And

Dr. Antony R. Horton
Chief Scientific Officer
International Rett Syndrome Foundation (IRSF)

On behalf of
the International Rett Syndrome Foundation (IRSF)

May 12th, 2010

Testimony of Mrs. Gail Smith
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Mr. Chairman, Congressman Hoyer, and members of the Committee, thank you for the opportunity to testify before you today.

My name is Gail Smith and I reside in Maryland. My husband and I dreamed of raising a normal healthy family. It seems like yesterday when our first child, Kristi, was born. She was a perfect baby. When I first held her in my arms, I counted all her fingers and toes. Everything was seemingly okay. She babbled and cooed her way through the first year, a bouncy, happy baby. She played pat-a-cake and waved bye-bye, and began to feed herself and walk.

Suddenly after one year old, Kristi became aloof and began to lose skills rapidly. At 2 1/2 she literally overnight lost her ability to walk independently. The doctors were puzzled. We were terrified. For my husband, a pediatrician, it was especially frustrating. We pursued countless doctors and many, many medical tests, but still no answers.

By five years of age, everyone who had said nothing much was wrong, couldn't believe anything had ever been right. Her mind was trapped within a body that would not allow her to communicate or physically respond. We mourned the death of our normal child, and began to grapple with our changing life. We experienced fear, anger and a deep sense of sadness. I used to lie in bed trembling and praying that I could just learn to cope with the unknown. Despite the challenges, love brought me through.

I had access to medical libraries, so I searched fervently in journals and papers for any remote likeness to the symptoms that Kristi exhibited. Then one day a friend, Kathy Hunter, who had a daughter in some ways similar to mine, shared with me a paper on Rett syndrome. That was the first article on the condition ever published in English. I knew I had found Kristi's diagnosis. At 13 years of age, Kristi was one of the first girls in the United States officially diagnosed with Rett syndrome at Johns Hopkins by Dr. Andreas Rett himself.

Rett syndrome is a neurologic disorder that occurs almost exclusively in girls, who develop normally until between 6-18 months, when the child begins a regression that severely challenges her mentally and physically. At that time there was no known cause, treatment or cure.

Kristi spoke volumes with her eyes and spread love with her sweet smile. I knew she could understand certain things, recognize people and sense feelings. She cried when babies cried and flirted when she really liked someone. She and I became symbiotic, joined at the hip. The last word she could speak was "mama", usually when she was in distress. I became sensitive to her every need, but I couldn't help her frustration or take her plight from her. She endured many operations for scoliosis, tendon releases and the placement of a feeding tube. As her lungs deteriorated she was hospitalized many times

for aspiration pneumonia. I have never experienced anything so painful as watching Kristi suffer.

In 2006 Kristi slipped away from us to join the angels of heaven. She was 34 years old. Despite the struggles, we have been so blessed to have her in our lives. She has taught me more about life and relationships than any teacher I have ever had. I cry everyday since she's been gone, however, I am somewhat comforted knowing that she is smiling down on us knowing there is finally hope for others who have Rett syndrome.

It is my everlasting love for Kristi, and the hope that Rett syndrome can be reversed for those who have the disease, and the families caring for them, that brings me here today. Research is the only way to help us find a cure for the many thousands of girls who are today suffering as Kristi did for 34 years. Through research, we have now found the cause of Rett syndrome. Through research we now know it can be reversed. Researchers tell us we are at the point of testing treatments to reverse the symptoms of this disease. With your support, we can take the next steps on the path and begin testing the therapies that will help these girls live better lives. With your support, we could reverse this disease once and for all.

I loved Kristi so very much and it would mean so much to see funding appropriated to help avenge the devastating impact of this horrible disease. Please help us!

Thank you for your time and consideration. I especially want to thank Congressman Hoyer. Our families met at church, and he and Kristi shared a long and special relationship. He has worked tirelessly on behalf of Rett syndrome and rare diseases. God bless you.

Testimony of Dr. Antony R. Horton
Before the House Labor, Health and Human Services
Subcommittee of Appropriations
March 29, 2006

Mr. Chairman, Mr. Hoyer and members of the Committee, thank you for allowing me to be here today and to follow Mrs. Smith's moving testimony. My name is Dr. Antony Horton; I am the Chief Scientific Officer of the International Rett Syndrome Foundation. I am here to testify about exciting new research into the causes of Rett syndrome and to tell you that hope lies just around the corner in the form of new therapies to treat symptoms and potentially reverse this disease.

Since the discovery of the gene *MECP2* 10 years ago and because of the generous support of this subcommittee over the last several years, we have gained an enormous amount of knowledge on this unusual disorder called Rett syndrome. We now understand much more about its clinical features. We now understand much more about the fundamental details underlying this disease, and through our increasing knowledge, we have already improved the lives of individuals and families affected by this disease. For brevity's sake, you will find more of the specifics regarding the status of our research efforts in my written testimony.

Once thought to be incurable, critical research funded by our foundation, has now established the proof-of-principle that Rett syndrome is a potentially reversible disease. In concert with this discovery, over the past five years, NIH funding has allowed clinical research teams to chart the progress of this disease over time through a consortium collecting natural history data on the progression of Rett syndrome. This work is paving the way towards a targeted approach to clinical trials, by providing researchers with the resources they need to conduct more informed studies, thereby allowing them to match the right patients to the right treatments.

I am here today to ask that you continue to support this incredible progress we're making towards treatments and a cure, by funding Mr. Hoyer's request of \$500,000 for Rett syndrome which IRSF will match. These funds will be used to perform critical data collection and educational activities and directed towards crucial resources needed to investigate new medicines that have great potential to improve lives of the many people living with Rett syndrome.

Thank you all for your time.

Rett Syndrome: A Potentially Reversible Neurologic Disorder

Rett syndrome is a serious childhood neurological disorder characterized by distinctive hand movements, slowed brain and head growth, seizures, mental retardation, inability to walk correctly, breathing difficulties and a cluster of other symptoms caused by the abnormal development of the nervous system. Rett syndrome strikes randomly, it affects females almost exclusively. The course of Rett syndrome, including the age of onset and the severity of symptoms, varies from child to child. In the United States there are 4,000 diagnosed cases, however, researchers have estimated the total number of women living with Rett syndrome could be much larger with as many as 15,000 affected individuals living with the disease in the U.S. alone.

Ten years ago, with private and Federal support, researchers located the *MECP2 gene*; it was identified as the gene responsible for causing more than 90% of Rett syndrome cases. In 2007, with additional private and Federal support, researchers using an animal model of Rett syndrome successfully reversed the disease in mice, indicating potential to reverse it in humans. Genetic similarities have recently been identified between Rett syndrome and other neurological disorders such as Fragile X, autism and schizophrenia, suggesting the work accomplished so far as a private/public partnership can be applied to these different disorders.

Rett syndrome is classified as a rare or "orphan" disease, meaning that the population of patients affected by this disorder are often underserved by the pharmaceutical industry, whose financial motives direct the course of decision making in favor of targeting diseases that affect large numbers of people. To redress this balance, the United States Government has wisely opted to draft legislation that seeks to promote the development of therapies targeting underserved populations through the Orphan Drug Act.

To this end, previous funding provided by the United States Congress has been directed towards meeting the unmet needs of people living with Rett syndrome through the support of clinical trial networks and studies seeking to document the progression of the disease over time. More recently this has fostered the connection of pooled knowledge through the assembly of blue-ribbon panels of experts which included thought leaders from academia, the pharmaceutical industry, members of the National Institutes of Health and the U.S. Food and Drug Administration. The consequence of bringing together the wealth of this nation's intellectual capital has been the identification of new and existing therapies which qualify for an Orphan Drug designation. The impact of an Orphan Drug designation cannot be understated; this will bring rapid and tangible benefits to patients in tandem with academic researchers and the pharmaceutical and biotechnology industries who employ thousands of dedicated professionals that daily pursue the dream of finding cures for the diseases which in one way or another, affect us all.

With leadership from Congressman Hoyer, the support of Congress and the Centers for Disease Control, Federal funds will be used to continue the trend and build upon the success of recent discoveries. The funds we seek will augment matching funds

provided by IRSF to meet several critical needs for people living with Rett syndrome, their caregivers and professionals seeking to develop treatments and an eventual cure.

The following programs and projects will meet these needs:

Rett syndrome Natural History Study Traveling Clinics: Clinical trials are conducted to allow safety and efficacy data to be collected for the registration of therapeutic interventions (e.g., drugs, devices, therapy protocols). In order to be prepared for the implementation of clinical trials in Rett syndrome, it is important to develop accurate information on the natural history pattern of progression among individuals with Rett syndrome. The study's purpose is to gather detailed historical and physical information on a large group of females with Rett syndrome.

Enrollment was initiated in March, 2006. Because of Federal support, hundreds more have been enrolled in the study. At present, there are well over 800 participants. Without this support the study would not have achieved the current enrollment success. Ongoing support for the Traveling Clinics fulfills a dual role by facilitating the rapid recruitment and ongoing retention of patients enrolled in the Natural History study and offers specialized medical advice for families and caregivers. This is only achieved by bringing this leading team of clinical experts to meet patients they would otherwise never see.

Rett syndrome Patient Registry & Informational Databases: Federal support of a Patient Registry helps avoid delay in bringing treatments to those afflicted with this disease. Because patients self-identify it improves the ability of researchers to recruit sufficient numbers of candidates that meet the entrance criteria of a clinical trial. Many rare disease organizations are designing patient registries and clinical systems to identify patients for clinical trials and to provide research data for investigators. Gathering data from patients, clinicians and other databases is an essential step in building clinical trials. The informational databases currently supported by IRSF will be combined under the aegis of a unified Patient Registry. Since, small populations of individuals are affected by rare diseases; this requires the collection of patient information on a global scale. Federal support of these databases permits the identification of subsets of Rett syndrome patients enabling clinical investigators to target drug therapies to the patients' individual genotypes. This tailor-made approach to treatment both maximizes efficacy while minimizing the adverse effects of a drug by matching the right patient to the right treatment.

RettSearch Clinical Research Consortium: Federal support has allowed for vast improvements in the collection of scientific information on clinical aspects of the disease. The RettSearch International Clinical Research Consortium is coordinated through a central hub based at the Kennedy Krieger Institute, at Johns Hopkins University in Baltimore, Maryland. This is the coordinating center for all Rett syndrome clinical research conducted across the globe. This clearing house of information has led to reduced duplication and increased effectiveness of research efforts. Its mission is to promote the development of new approaches for the treatment of Rett syndrome,

develop guidelines for medical practitioners, collect and disseminate information in areas of relevance to clinical research and to coordinate clinical trials with newly emerging therapies for Rett syndrome.

Meeting on Therapeutics for Rett syndrome and Related Autism Spectrum Disorders: Federal support for meetings such as this enables IRSF to gather scientists and clinicians with varying areas of expertise to stimulate and exchange new ideas, combine skills, disciplines and resources. This has already resulted in a vast network of individuals working in tandem to strategize facilitating the discovery, development and testing of new treatments and advancing them to patients with Rett syndrome and other related neurodevelopmental disorders, thereby accelerating the drug discovery process. Meetings such as this greatly foster cross-disciplinary collaborations and inform researchers where treatments that are in development for one disorder could be applied to aid patients suffering with a similar condition.

The proposed workshop will convene a group of leading scientific researchers working on Rett syndrome and other autism spectrum disorders (ASDs) which together, are known to affect 1:110 individuals. The meeting will seek to involve other patient advocacy groups within the Autism Spectrum who are seeking treatments for related diseases such as Fragile-X syndrome, Tuberous Sclerosis, Angelman syndrome and Prader-Willi syndrome as well as classic autistic disorder. Presently, there are few opportunities for specialists to focus on translating research discoveries from various disorders with the specific goal of informing others of new therapies to treat these diseases.

Medical Education & Family Support: Through education and support American families touched by Rett syndrome can take advantage of the most recent information and developments in the field and serve as advocates for their children and their treatment with the medical community. Rett syndrome is a rare, complex neurologic disorder affecting 1:10,000-15,000 females; most physicians and specialists will never encounter an individual with Rett syndrome in their practice. Since the majority of Rett syndrome patients are severely handicapped and nonverbal, they cannot independently communicate the status of their health, pain or illness. IRSF is a trusted source of vetted, expert medical advice via electronic and print media for families, caregivers, and health providers seeking assistance during a health or medical crisis. This helps to remove barriers to good health for the affected individuals and the families, caregivers, health providers and general public who support and live with those diagnosed with Rett syndrome.

We seek your support to continue our vital work.