



FOCUS ON RARE DISEASES



THE OFFICE OF RARE DISEASES NEWSLETTER
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HIGHLIGHTS OF THE OFFICE OF RARE DISEASES RESEARCH ACTIVITIES

NIH Undiagnosed Diseases Program

The National Institutes of Health (NIH) has launched a program to evaluate patients with disorders that have evaded a diagnosis. Often such patients seek help from multiple physicians and other health care providers over many years. The Genetic and Rare Diseases Information Service, sponsored by the Office of Rare Diseases (ORD) and the National Human Genome Research Institute (NHGRI), has frequently received requests for help from such patients, who assume that their condition is rare because no one knows what is wrong with them. Over the course of three years, approximately 600 of the 10,000 requests received were for undiagnosed conditions.

Using a unique combination of NIH scientific and medical expertise and resources, the Undiagnosed Diseases Program pursues two goals:

- To provide answers to patients with mysterious conditions that have long eluded a diagnosis
- To advance medical knowledge about rare and common diseases

The program is trans-NIH in scope. It is organized by NHGRI, ORD and the NIH Clinical Center. Senior attending physicians with many different medical specialties from NIH research centers and institutes contribute the expertise needed to achieve the goals of this clinical research program.

Any longstanding medical condition that eludes diagnosis by a referring physician can be considered undiagnosed and may be of clinical interest. However, of the total number of cases that may be referred, only a limited number of cases will be taken into the program at the discretion of the program's

medical team. There is no cost to the participants and travel is provided.

Patients must be referred by a physician nurse practitioner, or physician assistant. The referral should include a summary letter describing the condition, when it was first noted and the current health status, a list of treatments and medications that have already been tried and their effects, and copies of reports and results of pertinent diagnostic tests, along with X-rays, MRI results, and other imaging records/studies. Copies of the actual imaging studies are preferred.

Generally, referred individuals must be at least six months old, with a disease or condition that remains undiagnosed despite ongoing care and follow up by a physician or other health-care provider, and must be able to travel.

The program's medical team will review the information submitted for each case. Cases meeting the criteria will be presented to the Undiagnosed Diseases Program's board of specialists for further consideration. Plans call for inviting up to 100 patient participants to the NIH annually (about two per week) for a thorough evaluation and consultation.

Patients in the program will be evaluated by many NIH senior attending physicians who

will consult on the cases using the resources of the NIH Clinical Center in Bethesda, Maryland. Their specialties include rheumatology, immunology, oncology, psychiatry, nephrology, hematology, ophthalmology, neurology, laboratory medicine, pain and palliative care, bone disorders, endocrinology, dermatology, dentistry, genetics, pathology, pulmonology, cardiology, internal medicine, pediatrics radiology and hepatology.

As a part of the program, the referring provider and the patient will receive the information resulting from the NIH evaluation. Long-term care will not be provided by the NIH, but selected patients may be eligible for an ongoing research study.

Although it is not anticipated that all admissions will result in a diagnosis, the evaluations should yield valuable information that medical researchers will be able to use to help identify previously unrecognized rare diseases, suggest new ways to treat and prevent common illnesses, and determine promising options for continued medical research.

For more information please call (866) 444-8806

Rare Diseases Clinical Research Network (RDCRN) Update

- **Request for Applications (RFAs) for the RDCRN**

In February 2008, in collaboration with ten NIH institutes, the following Requests for Application (RFA) to continue the RDCRN Program were published:

- 1) Rare Diseases Clinical Research Consortia (RDCRC) for the Rare Diseases Clinical Research Network (U54)
<http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-08-001.html> (RFA-OD-08-001)

This is an open competition. Both new and existing groups can apply for U54 cooperative agreement awards.

- 2) Data Management and Coordinating Center (DMCC) for the Rare Diseases Clinical Research Network (U54)
<http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-08-002.html> (RFA-OD-08-002).

The University of South Florida in Tampa successfully competed for the DMCC. The Principal Investigator is Dr. Jeff Krischer.

- **Clinical Protocols**

Currently there are more than 35 clinical protocols which have been approved by the Protocol Review Committees (PRC), Data

Safety Monitoring Board (DSMB), and the NIH. At this time 37 studies are included in ClinicalTrials.gov (<http://www.clinicaltrials.gov>) and 31 are actively recruiting patients.

The RDCRN consists of 10 consortia. Each consortium focuses on a group of between three to eight rare diseases, totaling approximately 50 rare diseases for the network. In addition, the network includes a data and technology coordinating center (DTCC) that serves the RDCRN. The collaborating patient advocacy groups, through a coordinating coalition, participate as members of the network's steering committee. The network consists of more than 70 sites and includes more than 30 patient advocacy groups. The distribution of research locations across the United States makes investigational studies and treatments more accessible to patients with rare diseases. The network through the DTCC collects clinical information to develop biomarkers and new approaches to diagnosis, treatment, and prevention of rare diseases; provides training of new clinical research investigators; and supports demonstration projects.

Collaboration, Education, and Test Translation Program for Rare Genetic Diseases (CETT)

People affected by rare inherited diseases need the reliable information that comes through quality genetic testing. The CETT Program goal is to help facilitate the translation of new tests for rare genetic diseases. The program's objectives are to

translate as many appropriate tests as possible, ensure that the best possible test in light of today's knowledge is offered, and ensure that the test meets the needs of the community. All tests are important whether

the specific condition affects 5 people or 50,000.

The CETT Program encourages clinical laboratory and research collaborations, and supports the electronic collection of genetic and clinical data in public databases to leverage the information into new research and new treatment possibilities.

The CETT Program's objectives require a strong collaboration between researchers, clinicians, patient advocates and clinical

laboratories. The CETT Program has several new enhancements to facilitate the development of collaborations, researcher consultation, and educational materials. Please review the NIH notice and share with your research community:

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-084.html>. To learn more about the CETT Program, visit the web site at: <http://www.cettprogram.org/>

For more information, see the CETT Program web site at www.CETTProgram.org or by email at info@CETTProgram.org

Scientific Conferences

The request for nominations for ORD scientific conference co-support was sent to the institute and center (IC) directors in early August 2008. The ORD reviewed the requests for support and made its decisions in October. Memoranda of intent were sent to IC Directors and other staff on October 20. A list of the FY 2009 scientific conferences has been posted on the ORD web site. A second request for scientific conference

nominations for FY 2009 will be sent to the IC Directors in early February. Fifty-three conferences were selected to receive support from ORD.

The Office of Rare Diseases is pleased to announce that from the time this program began in FY 1995 until the present ORD has co-supported more than 850 scientific conferences.

Educational Project with Office of Science Education

ORD worked with the NIH Office of Science Education (OSE) to publish a Request for Proposal (RFP) for the development of an innovative curriculum supplement targeting grades 5-7. (The solicitation also included a second request, in collaboration between OSE and 10 NIH institutes and centers, for an evolution supplement for high school biology classes.) The Rare Disease supplement will raise awareness of rare diseases and allow students to develop skills and knowledge relevant to their daily lives as well as their future academic and career pursuits. Both

supplements will be part of the ongoing NIH Curriculum Supplement series.

The Rare Disease supplement will introduce students in grades 5-7 to basic science concepts and students will employ the process of scientific inquiry to develop an understanding of the nature and methods of science and biomedical practices as they relate to rare diseases. Studying rare anomalies in living organisms, including humans, provides a window into normal biological functions. The lessons will highlight the role of science and medicine in

society and the relationship between basic science and personal and public health.

The Rare Disease supplement will help students gain an understanding of the nature and impact of rare diseases and how scientific discovery benefits from studying these diseases. It will allow students to practice critical, creative and ethical thinking skills, deepen their understanding of the impact of medical research and the study of rare diseases, and stimulate their interest in health topics and careers. It will provide teachers with accessible and rigorous lessons on rare diseases and will be sensitive to the needs of teachers with diverse student populations in classrooms across the nation, as well as be consistent with the goals of the National Science Education Standards and the Science Framework for the 2009 National Assessment of Educational Progress (NAEP) exam.

Through these lessons, students will have had the opportunity to investigate the elements that constitute scientific evidence and how to use their knowledge to find appropriate resources for rare disease information. They will understand the fundamentals of inheritance and why some rare diseases are more prevalent in certain groups than others. They will understand that environmental and

inherited factors affect the function of an organism and may contribute to the occurrence of rare diseases, and that many people with rare diseases can lead meaningful lives and should not be stigmatized because they have inherited such disorders.

The core of the supplement will be a sequential set of lessons that easily fit into five, 45-minute class periods and are integrated into topics commonly studied in grades 5-7 science classes nationwide. The lessons may include laboratory and computer-based activities that enhance the students' learning experience. The supplements will enrich existing curricular materials, assist teachers in attaining their educational goals, and engage students in developing critical thinking, as well as enhancing skills in reading, mathematics, teamwork, and communication.

NIH intends to print the materials, make them freely available for educational use, and will allow free access to all online materials developed under this contract. The materials will not be used by any organization or business for sale or profit. The full text of the RFP solicitation can be found at FedBizOpps (www.fbo.gov) under solicitation # NIHOD2008072.

International Conference on Rare Diseases and Orphan Products (ICORD 2008)

ORD, the Food and Drug Administration (FDA) Office of Orphan Products Development, the Centers of Disease Control and Prevention (CDC), the Genetic Alliance, and NORD sponsored the 4th ICORD 2008 on May 20-22, 2008. Major Sessions focused on the following subjects:

- The Value and Need for International Research Collaboration with Rare and Neglected Diseases
- Strategies to Link Government and Academic Discoveries and Industry
- Linking Patients to Research Programs and Treatment Centers

- Research Methodology and Statistical Analyses for Trials of Rare Diseases and Orphan Products
- Rare Diseases Research Activities at the NIH
- WHO International Classification of Diseases with an Emphasis on Rare Diseases
- Global Policy Needs and Development of National Plans for Rare Diseases and Orphan Products
- Genetic Testing and Approaches to Screening
- Meeting Patient and Family Healthcare, Psychological and Social Support Needs Across the Lifespan
- Gaining Access to Appropriate Information

Four Working Groups were established with the appointment of chairs to address the numerous needs and opportunities identified in the individual sessions with an emphasis on continued activities during the year with reports on the status of activities expected to be presented at the 5th ICORD meeting in Rome, Italy in February 2009 and in Buenos Aires, Argentina in 2010. The website for ICORD is: <http://www.icord.se/>

The agenda and speakers' presentations can be found at the following website: http://www.icord.se/washington_2008.php?p=speaker_presentations , and http://www.icord.se/washington_2008.php

ORD Website

The Office of Rare Diseases website (<http://rarediseases.info.nih.gov>) has been completely redesigned and recently was launched as the new public site. In addition to a more user-friendly layout, the new site features a more robust search engine, allowing visitors to find all relevant information in a format that is very similar to commercial search engines. Visitors to the new site have the option of going directly to a subject page using the tabs at the top or using

the subject sections below to find out what links are being featured. Like the tabs at the top, the headings of the subject sections will take the visitor to the subject page where an expanded selection of links is available. We are continuing to make website improvements and will highlight some of these changes in future editions of the newsletter. The ORD welcomes feedback regarding our website, as we continually strive to make it as useful as possible.

NORD Invites You to Become a Rare Disease Day Partner



The National Organization for Rare Disorders (NORD) is coordinating the observance of Rare Disease Day in the United States on February 28, 2009. On that day—and in the weeks leading up to it—we will join with others around the world to conduct a variety of activities to raise awareness of rare diseases and the need for safe, effective treatments.

We invite all patient organizations, companies, medical societies, government agencies, and others with an interest in rare diseases and orphan products to join us in this global effort. You can do this by writing to rarediseaseday@rarediseases.org and signing up as a Rare Disease Day Partner. This will be the 2nd Annual Rare Disease Day. The special day was observed for the first time last year in Europe and was coordinated by NORD's partner organization, EURORDIS. It is the hope of NORD and EURORDIS that this will become an annual global event, taking place on the last day of February each year.

NORD will provide a press kit and other materials to all Rare Disease Day partners, along with a Rare Disease Day logo to display on their websites. The partners will

be encouraged to come up with their own creative initiatives within the spirit and stated goals of Rare Disease Day.

As a recipient of this email, you are being invited to:

- Become a Rare Disease Day Partner by writing to rarediseaseday@rarediseases.org
- Display the Rare Disease Day logo on your website
- Link to the global Rare Disease Day website (to be launched very soon)
- Ask the governor of your state to declare Feb. 28, 2009, Rare Disease Day in the state
- Personalize the Rare Disease Day press kit NORD will provide and share it with your media contacts
- Nominate researchers to the Rare Disease Hall of Fame to be posted on NORD's website
- Share information with NORD about your Rare Disease Day activities so that NORD can tell other Rare Disease Day Partners about what you are doing
- Share human interest stories for posting on the NORD website or in the press kit
- Create blogs for online communities and/or videos for YouTube to be posted during the week leading up to February 28, 2009

A Message from Dr. Zerhouni to Nonprofit Advocacy Organizations Announcing His Departure from NIH

Dear Friends and Colleagues:

Today, with mixed feelings, I wrote to inform NIH scientists, administrators, staff, contractors, and trainees that at the end of October, I will be leaving NIH to explore new opportunities and to devote my attention to several writing projects.

I wanted to also thank and recognize the commitment and tireless efforts of the non profit organizations like yours that help NIH accomplish the great work that it does. For over six years, I have enjoyed and benefitted from your thoughtfulness, dedication, and devotion to our shared mission: to make a difference in the nation's health through the discovery of new knowledge. Together, we have faced great challenges posed by the unique times in which we live and where there are profound changes and shifts in the scientific environment, Government, and the world.

Each one of you is among the most extraordinary, committed group of individuals with which I have ever interacted. Whenever NIH asks for your ideas, input, suggestions, and, participation, you answer the call, regardless of the nature and the complexity of the question, concern, or issue under discussion. You have every right to share credit for the agency's achievements as you form a unique and essential component of our success. It is also because of you that NIH is one of the true "wonders of the world" and takes such a prominent place in rankings of Federal agencies.

NIH is the "Nation's Medical Research Agency," and with your continued guidance, support, and volunteerism, the agency will remain on the leading edge of health, medical, and scientific advancement. Our continued success depends on nothing less. I want to sincerely thank you for your kind support during my tenure.

Please feel free to distribute this message to your officers, advisors, and members.

Elias A. Zerhouni, M.D.

Mary Demory Retires

After over forty-two years of Federal service, the last fourteen with the Office of Rare Diseases, Mary Demory has retired.

Mary has been with ORD since its inception in 1993 and she has played a vital role in the growth of ORD and the scientific conferences program. Her tireless work with the Genetic Alliance, NORD and other patient advocacy groups has improved collaboration efforts throughout the rare diseases community.

When Mary is not enjoying her grandchildren in Virginia and Tennessee, she will continue to contribute to the mission of ORD as a part-time consultant. Thank you, Mary, for your dedication to the needs of the rare diseases community.

About ORD

The Office of Rare Diseases (ORD) was established in 1993 within the Office of the Director of the NIH, the Nation's medical research agency. Public Law 107-280, the [Rare Diseases Act of 2002](#), established the office in statute. The goals of ORD are to stimulate and coordinate research on rare diseases and to respond to the needs of patients who have any one of the almost 7,000 rare diseases known today.

Definition of rare diseases: (Orphan Drug Act as amended in 1984 by P.L. 98-551 to add a numeric prevalence threshold to the definition of rare diseases.)

“...the term, rare disease or condition means any disease or condition which (a) affects less than 200,000 persons in the U. S. or (b) affects more than 200,000 persons in the U.S. but for which there is no reasonable expectation that the cost of developing and making available in the U. S. a drug for such disease or condition will be recovered from sales in the U. S. of such drug.”

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