

THE CMTA REPORT

Providing information on Charcot-Marie-Tooth disease (a.k.a. Peroneal Muscular Atrophy or Hereditary Motor Sensory Neuropathy), the most common inherited neuropathy. Contents © 1995, CMTA. All rights reserved.

First Research Grants Awarded



Erasmio Perera and Lisa Baumbach

IN THIS ISSUE:

| | |
|--------------------------------------|-------|
| Items of Interest | p. 2 |
| Member Profile | p. 3 |
| MAB Meeting | p. 3 |
| Neurotrophic Drugs | p. 4 |
| Volunteer of the Year | p. 4 |
| CMTA President Retires | p. 5 |
| Post-Doctoral Grant | p. 5 |
| Physician's Handbook Published | p. 5 |
| Medical Advisory Board | p. 6 |
| Research Update | p. 7 |
| CMTX Test | p. 7 |
| Ask the Doctor | p. 8 |
| Letters | p. 9 |
| Honoraria & Memorials | p. 10 |
| Neuromuscular Diseases | p. 11 |
| CMT Contacts | p. 13 |
| Blood Test | p. 15 |
| Membership/Order Form | p. 15 |

The Board of Directors of the Charcot-Marie-Tooth Association announces the awarding of the Karol Hitt Student Fellowship to three CMT researchers and their students. These fellowships represent the first grants awarded from the CMTA Research Fund by the Association.

The first grant was given to Lisa Baumbach, PhD, of the University of Miami Medical School, and her student Erasmio Perera. Dr. Baumbach and Mr. Perera will be conducting research this summer on genetic anticipation. The title of their project is, "Genetic Anticipation in Charcot-Marie-Tooth Disease: Molecular Investigations of the CMT1A Locus". The premise of this research focuses on the hypothesis that an increasing severity of disease presentation within families is associated with DNA rearrangements which disrupt a number of normal genes in the CMT1A duplication region on

Winning Logo for CMTA Announced



The CMTA has a new, official logo. The contest to find a new logo, announced in the Fall issue of *The CMTA Report*, resulted in many entries and many excellent designs. The winning entry was created by Tiffany Weston, a graphic artist who is connected to the organization through her friendship with a CMT family. Tiffany's design was chosen by a committee of the Board of Directors of the CMTA, chaired by Rex Morgan. The winning design resulted in a \$50.00 award for Tiffany. The winning logo will be used in the newsletter and on the stationery of the CMTA.

We would like to thank all of the many members who took the time to design a logo and send it to us. The designs were very creative and demonstrated the artistic talents of our members. §

chromosome 17, thus giving rise to different disease manifestations. Mr. Perera is a graduate student at the University of Miami leading to an advanced degree in molecular biology.

The second grant was awarded to Carol A. Oatis, PT, PhD, and her student Steve Sepal. Steve, a graduate student in Physical Therapy at Beaver College, Glenside, PA, and Dr. Oatis will study, "Moderate Resistance Exercise: Its Effect on Patients with Charcot-Marie-

(cont'd on p. 2)

Items of Interest

Research Awards - cont'd from p. 1

Item 1: A book called, Taking Charge: Teenagers Talk about Life and Physical Disabilities, offers strategies for handling the tough issues- from siblings to sexuality, from over-protective parents to staring strangers based on the thoughts of 15 young people with disabilities. One section explores issues of self identity, the second looks at relating to other people, and the third addresses issues of how other people relate to youth with disabilities. For more information, write or call: Woodbine House, 5615 Fishers Lane, Rockville, MD 20852, 1(800) 843-7323.

Item 2: Four exercise videos are offered by One Step Ahead, Armchair Fitness Videos, 1050 Connecticut Ave. N.W., Suite 1250, Washington, DC 20036. The videos have been recommended by the President's Committee on Employment of the Handicapped, the American Geriatric Society, Physical Therapy, Diabetes Forecast, Modern Health Care, and MS News. Armchair Fitness is the exercise video for anyone who's unable or unwilling to take part in strenuous activities. There are four videos, including Aerobics, Gentle Exercise, Strength Improvement, and Yoga Health. The videos range in price from \$29.95 to \$39.95. For an order form, call 1-800-453-6280.

Item 3: In the CMTA Report, Fall, 1994 issue, there was an item about Lubidet, a personal care product. One of our readers, John Meeker, wrote to tell us that he is an authorized Lubidet dealer and is offering the item at a substantial discount. For more information about the product, call John at (602) 868-5654.

Item 4: The Social Security Administration has a number of publications of both general and particular interest to those with disabilities. These include:

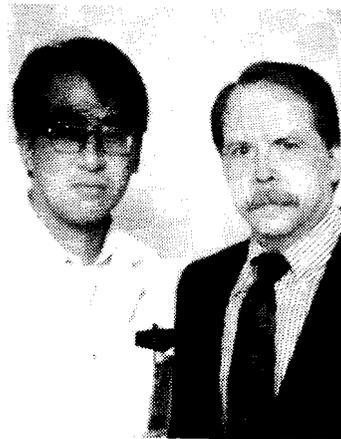
* SSA Publication No. 05-10069, "How Work Affects Your Social Security Benefits."

* Form SSA-7004-SM-OP2 is a "Request for Earnings and Benefit Estimate Statement." All wage earners should periodically submit this statement to be assured that all Social Security deductions have been properly credited to them. The form takes only a few minutes to complete.

* SSA Publication No. 05-11000, "Supplemental Security Income," explains what SSI is, who can get it, and how to apply.



Carol Oatis & Steve Sepel



Harohito Sago and Roger Lebo

* SSA Publication No. 05-10029, "Disability," explains Social Security disability benefits.

* SSA Publication No. 05-10153 is "When You Get Social Security Disability Benefits...What You Need to Know."

* SSA Publication No. 05-11002, "A Desktop Guide to Social Security and SSI Work Incentives," compares the applicable work incentives that apply under each program.

These publications may be requested from:

Department of Health and Human Services
Social Security Administration
Baltimore, MD 21235

Item 5: There is an excellent guide for people with disabilities who are seeking new or changed employment called Job Strategies for People with Disabilities. It

deals with many of the basic issues relevant to anyone who is job-searching, as well as those areas of specific interest and importance for people with disabilities. A few chapter titles are: **A Whole New Ballgame**. Now You Can; **ADA at Work for You**: With an Assist from the Rehabilitation Act of 1973. **Career Decision Making**. The Real World of Work; **Self-Assessment**: Able to Do the Job; **Making the Job Fit You**; **Job Clans**: Understanding Them Can Help You Make a Great Alternative Career Choice;

deals with many of the basic issues relevant to anyone who is job-searching, as well as those areas of specific interest and importance for people with disabilities. A few chapter titles are: **A Whole New Ballgame**. Now You Can; **ADA at Work for You**: With an Assist from the Rehabilitation Act of 1973. **Career Decision Making**. The Real World of Work; **Self-Assessment**: Able to Do the Job; **Making the Job Fit You**; **Job Clans**: Understanding Them Can Help You Make a Great Alternative Career Choice;

In the Fall issue of the CMTA REPORT the results of these studies will be reported. Congratulations are extended to these three members of the Medical Advisory Board and their colleagues. §

deals with many of the basic issues relevant to anyone who is job-searching, as well as those areas of specific interest and importance for people with disabilities. A few chapter titles are: **A Whole New Ballgame**. Now You Can; **ADA at Work for You**: With an Assist from the Rehabilitation Act of 1973. **Career Decision Making**. The Real World of Work; **Self-Assessment**: Able to Do the Job; **Making the Job Fit You**; **Job Clans**: Understanding Them Can Help You Make a Great Alternative Career Choice;

(continued on p. 4)

Member Profile... A Mother Recognizes Her Son's "Special"ness

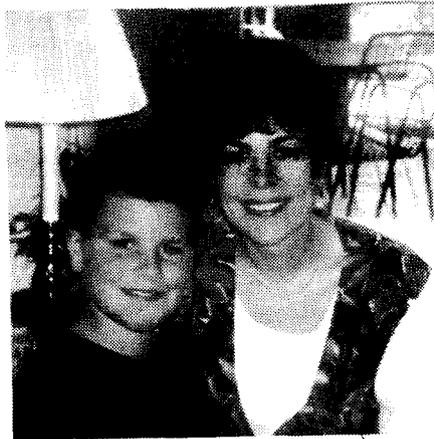
Janice Clay is a wife and mother of three. Her son Danny loves to play baseball and it was there, on the baseball field, that Janice first noticed how "different" Danny's abilities were in running. As she described her concern, she said, "Playing baseball made me aware of what was going on. He tried to run, but he didn't get anywhere. When I watched him, I knew something was wrong."

Danny was diagnosed last year with CMT and at the same time his father, Allan, was also diagnosed, but with a less severe case of the disorder. Danny is the youngest member of the Clay family, having two older sisters, Lisa, 14 and Amy, 13.

Janice works thirty hours a week in a dentist's office, but she was inspired to do something to help Danny adjust to his diagnosis of CMT in her free time. What she discovered was that it was quite difficult to explain CMT to grandparents and teachers, no matter how interested they were. In response to the need for CMT children to be able to share their experiences in dealing with the disorder with their friends and families, Janice hit on the concept of writing personalized books centering on experiences common to all children but made unique by a disabled child's special means of adaptation. Her first book was called The Most Valuable Player which was specialized to include Danny's name, his coach's name, and some of his friends. The book explains how everyone worked together so that Danny could play his favorite sport, baseball.

From this first book on Danny and his experiences with CMT, came the idea to create books called, "Somebody Special Books." Janice will offer personalized books for all children facing special challenges and will donate a portion of the proceeds from the sale of each book to the organization which supports patients and families with that disorder. Currently, Janice will offer books on cerebral palsy, diabetes, Down syndrome, paralysis and, of course, CMT. Currently, the only books available are about asthma and CMT. The last page of each book discusses the disorder and offers the name of the support organization for it.

In addition to the baseball theme, Janice has written a book about a girl with CMT who discovers horseback riding as a way



Janice & Danny

to experience the thrill of running without her feet ever touching the ground.

If you are interested in ordering a personalized book for your child, you can contact Janice Clay at "Somebody Special Books", 1315 Hillcrest Road, West Chester, PA, 19380. The books are \$ 8.95 each with \$ 1.25 postage and handling, plus state tax, if applicable. Each book can be personalized with your child's name, the names of his/her friends, school, and family, as well as his/her teacher's name and any specific details about your child's handicap you care to include. When ordering, include how CMT affects your child's daily living and what special exercises or devices your child uses. For specific questions about the books, call Janice at (610)696-2809.

Exactly how "special" Danny is can be illustrated by an update on his baseball experiences. This spring baseball began with Danny behind the plate as the catcher. A foul ball broke Danny's nose and threatened to end baseball for the season. After surgery to correct his nose and the sinus problems the break caused, Danny is back behind the plate and played in the opening game of the season, April 22, 1995. §

Medical Advisory Board Meeting

The CMTA medical advisory board (MAB) met in May at the general meetings of the American Academy of Neurology in Seattle, WA. The program chairman for the meeting was Dr. Thomas Bird of Seattle. Dr. Jeffrey Vance of Duke University gave an update of current genetic research. There are now nine known CMT gene sites, but there has been nothing new reported since the last MAB meeting. Dr. Vance reported that their findings indicate that CMT 1A accounts for 90% of type 1 CMT. Of those patients 80% have the duplication on chromosome 17 with the other 10% showing point mutations. Concerning type 2 CMT, Dr. Vance's work indicates that CMT 2A comprises 40% of the patients. The remaining 60% of type 2 CMT is caused by as yet unidentified genes. Dr. Vance believes that type 2 is more common than previously thought.

Barbara Lerner, a geneticist at Athena Diagnostics (formerly Genica), reported on the number of CMT diagnostic tests done since the test was first offered in July, 1993. One thousand eight tests were done in 1993 and 1,752 tests were done in 1994. So far in 1995, the average is 147 tests per month. Twenty percent of the tests were positive. Of all of the CMT tests ordered so far, 20 were positive for HNPP, and of the HNPP tests ordered, 3 were positive for CMT. (HNPP is the result of the deletion of the gene on chromosome 17 instead of the duplication of the gene.) The average age of the patient was 22 with the youngest being 4 and the oldest 88.

Dr. John Hsu, an orthopedist, strongly urges CMT patients to see an occupational therapist yearly for a comprehensive hand checkup. Dr. Hsu is just completing a twenty year study of surgical procedures on the CMT foot. These results will be published when available. §

Call for CMT-X Participants

If you are a CMT-X patient or a member of a CMT-X family, Dr. Michael Bennett, chairman of the Neuroscience Department at Albert Einstein College of Medicine, needs you! Dr. Bennett is conducting research on connexin 32, the malfunctioning chemical compound in CMT-X patients. If you have the diagnosis of CMT-X in your family, contact Dr. Bennett at the Dept. of Neuroscience, Albert Einstein College of Medicine, Bronx, NY, 10461 or call 718/430-2535. §

Volunteer of the Year



Dr. Gareth Parry

The CMTA is pleased to announce that Dr. Gareth J. Parry is the recipient of the Rebecca Sand Volunteer of the Year Award. This award is given annually to someone who either has made a significant contribution in the last year or to someone who has shown consistent commitment to the CMT patient/professional communities.

Three years ago Dr. Parry volunteered to be the editor of the proposed handbook, CHARCOT-MARIE-TOOTH DISORDERS: A Handbook for Primary Care Physicians. He assembled a group of outstanding scientists to write the book chapters, as well as writing a chapter himself. The task, now completed, was long and arduous, but is a significant contribution to the understanding and care of the CMT patient. We salute Dr. Parry and acknowledge his outstanding contribution to the CMT community. §

Items of Interest - cont'd from p. 3

Putting It All Together. Job Finding. To Disclose or Not to Disclose; Creating Standout Resumes and Cover Letters; Finding Job Leads; Researching Employers; Interviewing: A Chance to Show How Valuable You Are; Postscript: Positive Thoughts Pack Power. The book is available from Peterson's Guides, for \$ 14.95.

Item 6: A catalogue which provides books for children and those who care for them is available from Parenting Press, P.O. Box 75267, Seattle, WA, 98125. One book available through Parenting Press is entitled, Why Does That Man Have Such a Big Nose?, which is useful for children aged 3-8. Through text and

In the past three years, there have been several articles in the popular press about substances that promote nerve regrowth. The most recently investigated of these substances has the ability to preserve and restore two kinds of nerve cells, one in the brain and the other in the spinal cord. (The spinal cord cell is the one that activates muscle movements.) This specific substance is called glial cell-derived neurotrophic factor or GDNF. These substances in general are called neurotrophic growth factors.

GDNF was predicted to lead to treatments for Parkinson's disease and amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), and perhaps as a tonic for several other neurodegenerative diseases. Other scientists took a far more cautious viewpoint stating that there is no proof that these neurotrophic factors would lead to new treatments for neurodegenerative diseases. In the January 31, 1995, issue of The New York Times there was a review of neurotrophic drugs. One researcher's opinion as stated in the Times article reads, "I am a strong advocate of fundamental research on growth factors and models to test them," said Dr. Donald Price, a neuroscientist at the Johns Hopkins School of Medicine in Baltimore and who is not associated with the companies developing such factors. "But we shoot ourselves in the foot when we prematurely rush them." The biological relevance of neurotrophic factors, he said, was "hyped too early."

Neurotrophic factors have a wide variety of functions in the human body. During the development of the embryo they help

NEUROTROPHIC DRUGS.... A Hope for the Future?

guide the formation of the developing nervous system. Some of these factors cease functioning after birth, and others are activated during infancy and childhood and function throughout life. These factors are often produced after nerve cell injury. The action of neurotrophic factors is exceedingly complex and not well understood. Again quoting the Times article, "...it was becoming increasingly clear that neurotrophic factors acted through complicated biological cascades and signal networks, whose inner workings are still unknown."

Neurotrophic growth factors are being tested using animal models, but as one scientist said, there is no real relationship between an animal model and actual human physiology. It is essential to use animal models for preliminary investigations, but the possibility exists that there may be no relevance to humans. Recently, the testing in ALS patients of one neurotrophic drug factor had to be stopped because of adverse patient reactions to the drug.

However, some researchers are very optimistic about the use of neurotrophic growth factors and, in particular, about their use with peripheral neuropathies (CMT is a peripheral neuropathy). The CMTA is following the progress of several companies who are studying nerve growth factors. We will report any future developments concerning possible CMT therapies and a particularly about neurotrophic growth factors. §

pictures, the book fosters positive attitudes toward differences in all kinds of people. Other books in the catalogue are geared to helping to build self-esteem in children. To order a catalogue, you can call between 9am and 5pm (Pacific Time), 1-800-992-6657.

Item 7: One of our readers recommends a wheelchair called the *Breezy* manufactured by Sunrise Medical of Fresno, California. The *Breezy* is described as "stronger, lighter and more reliable than any other chair in its class." It is lightweight, averaging around 29 pounds. The retail cost is \$890.00. To inquire about the location of the dealer in your

area, call Sunrise Medical at 1(800) 456-8168.

Item 8: Prenatal testing for CMT1A (the gene on chromosome 17) is available at the University of Pennsylvania Medical School's diagnostic laboratories. Also available is prenatal testing for CMTX as well as a diagnostic test for CMTX. For information about these procedures, contact: Lynn Godmilow at 215-573-9161.

Item 9: Indexes for CMT Facts I & II are now available. If you own these publications and wish to have an index, send your request along with a SASE to the CMTA office.

(cont'd on p. 10)

THE PHYSICIAN'S HANDBOOK

A Great Resource

Diane Publishing Company announces the publication of the book **CHARCOT-MARIE-TOOTH DISORDERS: A Handbook for Primary Care Physicians**. The book, edited by Gareth J. Parry, MD, FRACP and consisting of ten chapters, was written by CMT experts for the use of primary care physicians (family care physicians, internists, and pediatricians).

Dr. Parry, a professor of neurology at the University of Minnesota, is the author of the chapter entitled "Electrodiagnostic Studies in Charcot-Marie-Tooth Disorders". The other authors and chapter titles are "Charcot-Marie-Tooth Disorders - Historical Perspective and Overview", P.K. Thomas, MD, FRCP, DSC; "The Clinical Features of Charcot-Marie-Tooth Disorders", Carlos A. Garcia, MD; "Pathological Changes in Charcot-Marie-Tooth Disorders", John W. Griffin, MD; "The Genetics of Charcot-Marie-Tooth Disorders", Jeffrey M. Vance, MD, PhD; "Charcot-Marie-Tooth Disorders in Children", Harold Marks, MD; "Orthopedic Care For Charcot-Marie-Tooth Patients", John D. Hsu, MD, CM, FACS; "Foot and Leg Manifestations of Charcot-Marie-Tooth Disorders", Gerald A. Weber, DPM; "The Role of Conservative Management of the Care of Patients with Charcot-Marie-Tooth Disorders", Carol A. Oatis, PT, PhD, Deborah Sundberg, Christine Oliver, Pamela Yerkes; and "Additional Strategies and Care Options for Charcot-Marie-Tooth Patients", Lowell L. Williams, MD. The book also includes a list of resources for the CMT patient and the primary care physician, as well as the neurotoxic drug list.

This long awaited publication is the only comprehensive work specifically about Charcot-Marie-Tooth disorders giving an overview of CMT. The primary care physician will find this book provides easily read, technically correct information about managing the care of CMT patients. This three year project was undertaken by the authors, all of whom are members of the Medical Advisory Board of the CMTA. They recognized the profound need for this resource and willingly contributed their considerable knowledge to this publication. Their gifts are great and we thank them for their efforts.

CMTA Announces The Retirement of its President



Karol Hitt

by Pat Dreibelbis

Karol B. Hitt has served as the volunteer president/executive director of the CMTA since 1989. Under her leadership, the organization has grown from 1851 members in 1989 to over 7200 members as of this writing. Karol has been instrumental in establishing the organization's credibility in the medical and research communities, and this summer marks the first time that the CMTA has awarded grants to summer interns working on CMT research. In an effort to make the CMTA a known commodity to doctors, Karol has attended every American Academy of Neurology and American Neurological Association meeting since her election to the presidency of the organization.

If you've ever called the office of the CMTA, you might have spoken to Karol and received her unfailingly compassionate counsel. In an effort to further help the patients and their families, Karol began the doctor referral program and enlarged and improved the information in The CMTA Report. The three publications, CMT Facts I, II and III, which contain the information from previous

To order the book, send a check or money order for \$15 (includes postage and handling) payable to DIANE Publishing. Mail to: DIANE Publishing/CMT Division, 601 Upland Avenue, Upland, PA 19015. Foreign orders are \$22 payable in American funds. The book may be ordered now but will not be available until July 15. §

newsletters, were her idea. They enable new members to "catch up" on all the hard news that appeared in print prior to their finding the organization.

Karol is also known to those of you who have attended a conference hosted by the CMTA and held at a major medical center in this country. Karol expanded the number of affordable conferences and increased the geographic areas they served, informing patients about current research and state of the art therapies. The further philosophy which underlies the regional conferences is to make patients aware of the best medical care available in their geographical area. To date, Karol has scheduled and hosted 20 such regional conferences.

Karol's work for the CMTA has covered ten years, six of them in the office of President. Her contributions to the medical community and the patients and families who daily deal with the little known and often over-looked disorder, CMT, have been incomparable.

It is with consummate regret that we announce Karol's retirement from the presidency and her withdrawal from the day to day operations of the organization. All of the patients, families, clinicians and research scientists who have known Karol personally will miss her intelligence, her common sense, her passion for making CMT a household name, and her commitment to this organization's growth and prestige. §

POST-DOCTORAL GRANT TO BE AWARDED

The CMTA Board of Directors has established a one year, post-doctoral, CMT fellowship; the amount of the grant is \$35,000.00. Applicants must possess an MD and/or a PhD and the year must be spent in CMT related research. Applications for the post-doc fellowship have been sent to CMT research centers worldwide. Qualified individuals who are interested in applying for this grant should contact Dr. Robert Lovelace, Neurological Institute, Box 157, 710 West 168th Street, New York, NY 10032. This fellowship will be awarded in the late Fall of 1995.

Medical Advisory Board

- Shukuro Araki, M.D.*
Kumamoto Medical School, Kumamoto, Japan
- Barry Arnason, M.D.*
University of Chicago, Chicago, IL
- Pierre Bouche, M.D.*
Neurologic Hospital of the Salpetriere, Paris, France
- Thomas Bird, M.D.*
VA Medical Center, Seattle, WA
- Walter Bradley, M.D., F.R.C.P.*
University of Miami, Miami, FL
- Phillip Chance, M.D.*
University of Utah, Salt Lake City, UT
- J.S. Chopra, D.C.H., F.R.C.P., Ph.D., F.A.M.S.,*
Post Graduate Institute of Medical Education and Research,
Chandigarh, India
- Michael Conneally, M.D.*
Indiana University, Indianapolis, IN
- Peter Dyck, M.D.*
Mayo Medical School & Foundation, Rochester, MN
- Francis Dyro, M.D., F.A.A.N.*
VA Medical Center, Boston, MA
- King Engel, M.D.*
University of Southern California, Los Angeles CA
- Kenneth Fischbeck, M.D.*
University of Pennsylvania, Philadelphia, PA
- Carlos Garcia, M.D.*
Louisiana State University Medical School, New Orleans, LA
- Hans Goebel, Ph.D.*
University of Mainz, Mainz, West Germany
- John Griffin, M.D.*
Johns Hopkins University, Baltimore, MD
- Ludwig Gutmann, M.D.*
University of West Virginia, Morgantown, WV
- Anita Harding, M.D., F.R.C.P.*
University of London, London, England
- Linton Hopkins, M.D.*
Emory University, Atlanta, GA
- John Hsu, M.D.*
University of Southern California, Downey, CA
- Victor Ionasescu, M.D.*
University of Iowa, Iowa City, IA
- Jan Korthals, M.D., Ph.D.*
University Of South Florida, Tampa, FL
- Roger Lebo, Ph.D.*
University of California, San Francisco, CA
- Robert Lovelace, M.D., F.R.C.P.*
Columbia University, New York, NY
- James Lupski, M.D., Ph.D.*
Baylor College of Medicine, Houston, TX
- Kieran T. Mahan, D.P.M., F.A.C.F.S.*
PA College Podiatric Medicine, Philadelphia, PA
- Harold Marks, M.D., F.A.A.N., F.A.A.P.*
A.I. duPont Institute, Wilmington, DE
- Richard Mayer, M.D.*
University of Maryland, Baltimore, MD
- James Mcleod, M.D.*
University of Sydney, Sydney, Australia
- Lefkos Middletown, M.D.*
The Cyprus Institute of Neurology & Genetics
Nicosia, Cyprus
- Robert Miller, M.D.*
University of California, San Francisco, CA
- Stanley Meyers, M.D.*
Columbia University, New York, NY
- Carol Oatis, P.T., Ph.D.*
Philadelphia Institute of Physical Therapy
Philadelphia, PA
- Shin Oh, M.D.*
University of Alabama, Birmingham, AL
- Gareth Parry, M.D., F.R.A.C.P.*
University of Minnesota, Minneapolis, MN
- Jack Petajan, M.D., Ph.D.*
University of Utah, Salt Lake City, UT
- Irena Hausmanowa Petruszewicz, M.D., Ph.D.*
Warsaw Medical Academy, Warsaw, Poland
- Roger Rosenberg, M.D.*
University of Texas, Dallas, TX
- Marvin Rozear, M.D.*
Duke University, Durham, NC
- George Serratrice, M.D.*
University of Marsielle, Marseille, France
- Ding Guo Shen, M.D.*
Chinese PLA General Hospital, Beijing, China
- Thomas Swift, M.D.*
Medical College of Georgia, Augusta, GA
- P.K. Thomas, M.D., D.Sc.*
Royal Free Hospital, London, England
- Jeffrey M. Vance, M.D., Ph.D.*
Duke University Medical Center, Durham, NC
- Gerald Weber, D.P.M.*
New York College of Podiatric Medicine, NY, NY
- Lowell Williams, M.D., retired*
Children's Hospital, Columbus, OH
- Hitsoshi Yasuda, M.D.*
Shiga University of Medical Science, Shiga, Japan

Research Update

Preimplantation Diagnosis

The technique of prenatal testing has been available for a substantial time period and has been widely reported by the media. Currently, CMTX and CMT 1A are the two forms of CMT for which there is prenatal testing available. (See "Items of Interest" #8) There is a new technique being developed which allows diagnosis for genetic disorders at the very beginning of the development of the embryo. This procedure is called preimplantation diagnosis and, for this procedure, in vitro fertilization is preferable to in vivo fertilization. (In vitro fertilization means the egg is fertilized by the sperm in a container in the laboratory. In vivo fertilization means the egg is fertilized in the body.)

The embryo is the result of the fusion of the female egg and the male sperm and unites to form a single cell. This cell divides into a two cell embryo, then a four cell embryo, an eight cell embryo, sixteen cell embryo, etc. In preimplantation diagnosis, a single cell from the embryo at the 8 - 16 cell stage is teased out and then analyzed for a specific genetic trait. This technology has been used successfully at least once and a healthy baby resulted. That embryo was tested for cystic fibrosis.

Dr. Roger Lebo at the University of California at San Francisco is interested in preimplantation diagnosis and has been doing research in the area. In a recent issue of *Fetal Medicine*, Dr. Lebo co-authored an article on this topic. (Goldberg JD, Martin MC, Lebo RV, Pedersen RA: Preimplantation diagnosis, In *Fetal Medicine [Special Issue]*, West J Med 1993; 159:301-307) This article is for the scientific community, but the first paragraph gives a very good analysis of the concept of preimplantation. It reads, "The prenatal diagnosis of genetic disease currently allows at-risk couples the option of having only unaffected offspring. To achieve this goal, they are faced with terminating a pregnancy if an affected offspring is diagnosed. Traditional prenatal diagnosis is performed by midtrimester amniocentesis at 15 to 16 weeks' gestation and provides a diagnosis from one to five weeks after the procedure. This necessitates a second-trimester termination procedure if a couple wishes to abort an affected fetus. Because of this, chorionic villus sampling was devised as an earlier prenatal diagnostic procedure (10 to 12

weeks' gestation). Although the possibility of a first-trimester termination procedure is more acceptable to some couples, to others neither approach provides a good option. The availability of preimplantation prenatal diagnosis would avoid the issue of pregnancy termination for many couples. With this approach, a biopsy specimen is taken of the early embryo after fertilization in vitro. This is then analyzed for the specific disorder the couple is at risk for, and only unaffected embryos are transferred."

If you are interested in a reprint of this article write James D. Goldberg, MD, Department of Obstetrics, Gynecology and Reproductive Sciences, UCSF School of Medicine, San Francisco, CA 94143-0132.

Identical Twins Studied

Dr. James Lupski, of Baylor College of Medicine, Houston Texas, recently sent us a report of a study done on two sets of identical twins who have CMT. The authors report a significant difference in the severity of CMT between identical twins. The abstract of the article reads, "We report two pairs of male homozygotic twins in two unrelated families with the Charcot-Marie-Tooth disease type 1A duplication. Homozygosity was supported by DNA analysis. There was remarkable congruity of conduction velocities between the left and right side of each twin and between twin brothers. The similarity and symmetry of the electrophysiologic deficit contrast with the variable and asymmetric clinical presentations. Variability of clinical expression in these patients with identical mutations suggests the action of modifier genes, stochastic factors or environmental modulation of disease severity." The concluding paragraph of the article states, "The two sets of CMT1A twins in this report were electrophysiologically and genetically identical but they had significant differences in clinical severity regarding age of onset, functional weakness and degree of nerve hypertrophy. These findings suggest that unknown environmental or other endogenous factors may be involved in the clinical manifestations and progression of CMT1A. Identifying some of these factors may reveal therapeutic modalities to delay progression of the disease."§

This article will appear in a future issue of *NEUROLOGY* and is entitled, "Clinical Variability in Two Pairs of Identical Twins with the Charcot-Marie-Tooth disease Type 1A Duplication". The authors are CA Garcia, MD; RE Malamute, MD; J England, MD; G Parry, MD; L Paint, Mc.; and JR Lupski, MD, PhD. Address correspondence and reprint requests to Dr. Carlos A. Garcia, Louisiana State University Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112-2811.

CMTX Test Available This Summer

Athena Diagnostics, Inc. (formerly Genica), who in July 1993 made available the DNA-based diagnostic test for CMT1A, is expanding its CMT testing services to include a definitive test for CMTX. This test, scheduled for release this summer, can be analyzed on an individual's DNA, extracted from whole blood.

A change in the sequence of the DNA, comprising the CMTX gene called connexin-32, indicates the presence of a mutation associated with the disorder. The connexin-32 gene is located on the X chromosome. However, unlike most X-linked disorders, the clinical features appear in both males and females. The clinical symptoms of CMTX are similar to those found in individuals with CMT1A and therefore, it is often difficult to distinguish them based on clinical exam only.

Incorporating both CMT1A and CMTX analysis into the workup of an individual symptomatic for CMT increases the possibility of making a definitive diagnosis by an estimated 50%, based on experience at Athena Diagnostics. Distinguishing between two forms of CMT is important to the affected individual and to his/her family. With the definitive diagnosis comes a more accurate clinical prognosis as well as an accurate recurrence risk for subsequent offspring.

More information about the availability of the CMTX test will be available in the summer newsletter, or call Athena Diagnostics' Client Services Representatives at 1-800-394-4493 for assistance. §



Ask the Doctor



Dear Doctor:

The CMTA literature mentioned the possibility of partial vision/hearing loss due to CMT in one type of the disorder. I am particularly interested in finding information about vision and CMT as I have been experiencing vision difficulties, diagnosed as a problem with nerves or muscles, for the past five years. What vision difficulties can be experienced by CMT patients?

A second patient wrote:

In the beginning of December I became aware of a vision disturbance in my left eye. So far, glaucoma, macular edema, retinal tear, and optic neuritis have been eliminated. I have had an angiography and visual fields as well as numerous exams by optometric and ophthalmologists. Next comes a cranial MRI and visits with a neurologist and neuroophthalmologist. The symptoms are double vision, vision of 20/50 in my left eye, corrected and disturbing light patterns at night. It is agreed that these are cataract symptoms, but no cataract is visible.

My doctor asked me to contact the CMTA to see if vision is affected by CMT.

(Editor's note: These questions were forwarded to an expert in both ophthalmology and genetic disorders. His reply follows.)

The Doctor Replies:

Thank you for your intriguing letter and the two challenging questions which you presented. Before I answer each question, we must agree with a fundamental premise: vision disorders of any type are no different among people or families with CMT than they are in anyone else without CMT in the population. Unusual reports of families with two different diseases, such as neurofibromatosis, cystic fibrosis, asthma, and a whole variety of other things that have nothing to do with CMT, have been allegedly associated. The associations, however, are quite coincidental. Some diseases are common in the population, and some are not. If you have a relatively common disorder like CMT, and you are human, it is possible that you will have another common human disease as well. If everyone begins

with that idea, then answering the two challenges may be straightforward.

1. Information about vision and CMT: "What vision difficulties can be experienced by CMT patients?"

As mentioned, individuals with CMT may be nearsighted or farsighted, may have crossed eyes, may have color vision deficiencies, may have a whole range of common eye problems, merely because they are human. Just because someone has CMT does not increase his/her risk for glasses, cataracts, glaucoma, retinal blood vessel damage from diabetes, or any other common eye disorder. Merely because you have a problem with vision does not necessarily mean the CMT caused it or that the CMT is associated with it. There are no specific nerve or muscle problems related to the eyes exclusively or uniquely related to CMT.

2. A patient of unknown age became aware of vision disturbance in her left eye, with vision of 20/50, "double vision", and disturbing light patterns at night. A number of optometric and ophthalmologic examinations have been performed allegedly with an abnormal result, and special diagnostic studies including apparently a fluorescein angiogram and visual fields were all normal. What's going on?

This is a much more difficult problem. Clearly, the writer has a problem which affects one eye only. There is a real complaint: double vision and blurred vision. I infer, perhaps not correctly, that the "double vision" is in one eye only; that is, closing that eye eliminates the double image, while closing the other eye leaves it exactly the same. That the physician asked the patient to contact the CMTA to see if vision is affected by CMT suggests that the physician is not aware that CMT is a disorder that has no effect on vision. Therefore, the simple analysis is still the correct one: Look at the patient, examine the patient carefully, and decide what is the problem with vision. In this situation, we have an additional advantage: the vision problem exists in only one eye. Many diseases that affect the brain, the visual pathways in the brain, the portions of the visual system at the base of the brain behind where the two optic nerves come together, and the muscles of the eyes can be eliminated from further consideration. If the patient has normal pupil function when examined appropriately by an ophthalmologist,

and a normal vision field, it is highly unlikely that this represents an intracranial or optic nerve problem. Therefore, consultation with a neuro-ophthalmologist and a neurologist, and the cranial MRI scan are all probably unnecessary. Glaucoma, optic neuritis, retinal tears, and "macular edema" are unlikely explanations as well, since they do not create "double vision" in only one eye.

The most likely explanations are either an error of refraction (glasses or a corrective lens problem) not adequately investigated at this point, or a cataract, or rarely, a cornea problem. If this is purely a problem of "focusing light", such as a mild cataract, especially a cataract in the central portion of the lens called the nucleus, the patient may be asked to read the eye chart through a pinhole. A pinhole eliminates the refractive error of the eye, by allowing only the very central rays of light to pass through the pupil to the retina. In essence, this is the same phenomenon that we all do when we "squint" our eyes into a little slit, except that the pinhole is a little slit in all directions. If the "pinhole vision" is improvable to considerably above 20/50, and closer to 20/20, and the "double image" improves, then the problem is a refractive error or a lens problem and should be correctable (or improvable) by glasses. This possibility is even more likely depending on the age of the patient, particularly if someone is over 45.

In summary, this should be a straightforward problem to analyze and to solve, and the examinations that have already been conducted should be sufficient to clarify the issue. A few other similar symptoms, such as keratoconus (a conical steepening of the cornea), intermittent intraocular pressure elevations (except that vision is not described as being fluctuating), and some unusual retinal problems, which again are unlikely if this problem has persisted unchanged since December, might be responsible, but are very unlikely.

I look forward to hearing the final outcome of this story.

Richard A. Lewis, M.D., M.S.

Departments of Ophthalmology,
Medicine, Pediatrics, and Molecular &
Human Genetics
Cullen Eye Institute
Baylor College of Medicine, Houston

Letters to the Editor



Dear CMTA,

I was very grateful to receive the packet you sent me and in such a timely manner! Not only did you respond to my request, but at the same time you opened the door to a very dark room that was full of mystery for a long time. I have been a CMT patient since 1966 when there was no information. I certainly didn't learn much over the years, either! I'm so grateful there is your association. I would appreciate your sending me the CMTA Report and the dates for any conferences in 1995. I have lived in and around Frederick, MD, for the last 10 1/2 years. We are about an hour away from Baltimore. We are in Western Maryland, and there is a distinction!

I am an R.N. and do have some access to our medical community in this part of the world and I think it would be nice to educate certain professionals to this mysterious disease and to the inheritance factor.

K.H. MD

Dear CMTA,

I have been receiving your newsletter for some time and I have found it very informative and interesting.

I am 53 years old and was diagnosed with CMT about 15 years ago. I had known for years that something was wrong. I just didn't know what. I have pain in my legs and feet and cramps that are bad at night in my legs. I do stumble and fall often and have very little sensation in my fingers. I'm also especially tired late in the day or afternoon.

I'm fortunate enough, however, to still be able to work full time, 6 am to 2:30 pm as a licensed practical nurse at an institution for physically and mentally handicapped children. I'm on my feet most of the day, so by 6 or 7 pm, I'm ready to retire to bed. I get no special favors at work and still carry my load, just a little slower, maybe.

Two of my three children also have CMT and one of my six grandchildren has been diagnosed, also. There are many in my family...brother, sister, nieces, and nephews, also with CMT.

I was delighted to attend the CMTA support group meeting in Jackson, MS, in March and hear the speaker, Dr. Philip Chance. Everyone came away understanding CMT much more. I would like to be a contact person for southern Mis-

issippi and I'm looking forward to more great newsletters!

M.B. MS

Dear CMTA,

I am trying to gather information regarding trauma or injury exacerbating symptoms of CMT or triggering this disease from a plateau. I am asking anyone with a similar story to write to me. I am fighting a lawsuit against a car insurance company which is trying to blame all of my problems on the disease.

I believe this might be happening to many people with CMT and printing this letter could help us prove otherwise and help CMT patients in similar situations receive benefits to which they are entitled.

I was a 28 year old man in perfect health, working in a foundry that required hard labor under high heat conditions. I worked long hours, sometimes four to five 16 hour shifts a week. I thoroughly enjoyed an active life, having no symptoms that were noticeably CMT.

I was hit by a car in the fall of 1990, pinching me between two cars at hip level. Immediately after the accident, many things began happening. A CAT scan showed a slight herniations of a disc at L4 and L5. My legs started to weaken; fatigue set in and an EMG diagnosed me with CMT. I now have a chronic sleep disorder due to back pain and restless leg syndrome. I have continually worsened since the accident took place.

I believe that this accident triggered my CMT, exacerbating the CMT at an alarming rate. I feel the CMT would not have affected me at this early age, otherwise. It is vital that I receive as much information as possible to prove my case.

If you can help, please write to me in care of the CMTA. Address your response to Wayne Collee, CMTA, 601 Upland Ave. Upland, PA, 19015.

Wayne Collee, Niagara Falls, Ontario

Dear CMTA,

I was very pleased to learn of your association and definitely surprised at some of the information presented in the State Journal-Register, Springfield, IL, Health and Fitness Section. I found the statement that CMT is the most common inherited disease of the nerves almost unbeliev-

able. My father (age 72) and I (age 43) have both been diagnosed as having a variant or abnormal strain of this disease. Neither of us have been diagnosed by the genetic blood tests mentioned in the article. Both of our diagnoses have been made by different teams of doctors, and all by the process of elimination of other diseases or conditions.

My father had always been active in the Boy Scouts, including being a member of the Order of the Arrow and receiving the Silver Beaver award. His profession was a photo-retoucher for 37 years. He, of course, is now retired. I was semi-professional in ballet by the age of 13. A knee injury ended that career and after high school, I went on to college, and became a Registered Respiratory Therapist. Later, in my off hours as Assistant Manager of a home Respiratory care company in Las Vegas, I also was a Firefighter/ EMT II with the volunteer fire department in Goodsprings, NV. A car accident followed a year later by a fall that fractured my left arm and leg and dislocated my left knee which ended my active lifestyle. Now I am a receptionist at a produce warehouse and in danger of losing that position due to the increasing difficulty in climbing the stairs.

My father is now permanently wheelchair bound with no use of his legs below the knees. He is experiencing increasing pain and decreasing dexterity in his hands and lower arms. My symptoms are no where near as advanced. Much of the time I use a cane and if I need to be walking for long distances especially in combination with periods of standing in one place for extended periods of time, I will also use a wheelchair. I am experiencing constant pain in both my arms and legs, as well as muscle twitching, spasms and prolonged cramping predominately in my legs. Both of us experience something we find very difficult to explain to others. That is, the sensations caused by external stimuli are exaggerated while the sensations we perceive and the control we have when we attempt a task are decreased. For example, pin pricks, hot and cold items seem much more intense than normal. A normal handshake or gentle massage can be extremely painful. On the other hand, if we are holding something in our hands, we cannot sense the tightness of our grip. We can be holding a glass and suddenly drop it. If my father is not looking at the object he is

(continued on next page)

Letters - cont'd from p.9

touching, he cannot identify it simply by touch.

I would certainly appreciate receiving any information you may have regarding all phases of this disease as much of the information we have been given is contradictory, confusing and in many ways, frightening. We have found that even our various physicians disagree about treatment methods, prognosis, and even the accuracy of the diagnosis. It seems the only points they do agree on are - that it is rare, little is known about it, and it is progressively degenerating, with no cure. Thank you for any help you can give us.

Sincerely,
C.K. IL

Dear CMTA,

Enclosed is a check as a memorial to my mother, Leona M. Thyer, who died March 29, 1995. My mother had CMT type II, as did her mother, grandfather, great-grandfather, great-great and great-great-great grandfathers and many of their descendants. My mother had five children - three of us have been diagnosed with CMT and the other two are showing symptoms of it. Mother had used a wheelchair the past few years when a walker no longer provided enough support. Her sister (the only sibling) also uses a wheelchair now at age 87. Several cousins use either a wheelchair or a walker. Younger ones can still get by with a cane. Some wear braces; some do not. Some are finding their arms and hands are affected, too.

I appreciate your CMTA Report very much and always look forward to the next issue, hoping to learn all I can about the Type II that is so prevalent in our family. Keep up the wonderful work!

Sincerely,
K.S. KS

Dear CMTA,

I can't express how grateful I am for the support of the CMTA. The two women who work in the office there in Upland have truly kept me pushing forward.

My birth certificate said "baby born perfect", except at fifty four, I've found out that I wasn't. I was born with CMT and at seventeen I had a hammer toe on the big toe of my left foot. The tendon was removed. I walked; I worked on cement floors as a sales clerk. I finished school at the University of Arizona. I played tennis. When I had physical exams I was able to do everything.

In 1983, I was told I had arthritis in my ankle. Two bones were rubbing and my heel was being pushed over. I needed a triple arthrodesis. Believing that was what I needed, I had the operation performed. In the cast, my foot kept swelling, but eventually when I was out of the cast, I was again going at full speed. I need a qualified medical expert to help me prove that trauma from a car accident has activated my CMT. The car rear-ended me and slammed my feet into the floor boards. I also hit my face on the steering wheel causing TMJ. During therapy for my jaw, the therapist noted how my toes were curling. I was sent to a neurologist and a neurosurgeon. Both said I have CMT. That was in 1994. The accident seems to have aggravated and activated my CMT. The doctor here feels that CMT is so new and so unknown that no one wants to come forward.

I have suffered like any one with CMT..a lot. Sometimes it is extremely hard to walk. I'm in therapy and my therapist is patient and helping. With ultrasound and heat, I'm walking better. If a support group is ever started out here, I certainly will help. In the meantime, if anyone out there can recommend a medical expert who could examine me and testify, please call collect.

Carole Hannah
520-795-6815

Referrals Available

The CMTA has compiled a list of neurologists, orthopedists, physiatrists (a physiatrist is a physician trained in physical medicine and rehabilitation) and podiatrists who have a special interest in CMT. We can also access respiratory specialists. Additionally, we have listings for pedorthists. A pedorthist is a practitioner who provides care to the patient by fitting orthopedic shoes and devices, at the direction of and in consultation with physicians.

To receive any of these referrals send a stamped self-addressed business-sized envelope indicating the geographic areas needed to: CMTA, 601 Upland Avenue, Upland, PA 19015.

For hand surgeon referrals contact the American Society for Surgery of the Hand, 6060 Greenwood Plaza Blvd., Suite 100, Englewood, CO 80111-4801, Ph.303/771-9236. §

Items of Interest - cont'd from p. 4

Item 10: What do AT&T, the Gore Family Memorial Foundation Trust, the American Society of Composers, Authors and Publishers Foundation, and the Easter Seal Society have in common? All provide scholarships to youth with disabilities. And ACCESS Foundation provides information on all these scholarships on the Internet. If you would like additional information, please contact ACCESS Nuz-Clips at danyaon@savvy.com. You can still get information if you're not on the Internet. Contact: Foundation for the Disabled, P.O. Box 356, Malverne, NY 11565-0356. §

We Are Looking For A Few Good Men And Women

The military's slogan is very applicable to the CMTA. The Board of Directors of the CMTA needs additional members. Currently, the Board consists of fourteen men and women, and we have vacancies we would like to fill with interested, capable people.

If you have experience with public relations, fund raising, corporate relations, administration, writing, or any other applicable talent/experience and are interested in serving on the Board of Directors, please contact the CMTA.

The Board's usual meeting place is in New Jersey. Historically, we have tried to secure a location that is convenient for the majority of members. However, as this organization grows, it is obvious that other geographic areas of the country need to be represented. Board members are financially responsible for their own transportation to attend meetings. However, attendance by telephone conference call is possible.

For consideration for Board membership please submit a letter citing your background, including work experience, and your interest in CMT. Many of our current members represent CMT families, however, this certainly is not a requirement for Board membership. Please send your letter to Karol Hitt, CMTA, 601 Upland Avenue, PA 19015. §

Honoraria & Memorials

| In Memory of: | by |
|--------------------------|--------------------------|
| Elmer Publitz | Anthony Savage |
| Albert "Bruddy" Krause | Salamancas Class of 1972 |
| Patrick Haptonstall | Louise Phippen |
| Patrick Haptonstall | Loren and Christy Entz |
| Patrick Haptonstall | Leonard Gruenberg, Jr. |
| Joseph Rust | Michele Weissman |
| Agnes McTernan | Robert Christensen |
| Beloved Father | Reeva Sterling |
| Leo K. Breeden | Drucilla Lake |
| Leona M. Thyer | Kathryn Simms |
| William Sloan | Shirley Hubbard |
| Mason Gross | Shirley Hubbard |
| Murray Winters | Marvin Greenwald |
| Massimino (John) Picconi | MM Joseph DiPilla |

| In Honor of: | by |
|-------------------|------------------------|
| Darin Palmer | Patsy Furey |
| Chris Buck | Michael Buck |
| Sara Wainwright | Barbara Cook Bernstein |
| Christy Wagner | Pam Gatfield |
| Keith Petersen | Barbra Griffin |
| Marjorie Bradwick | R. Gordon Bradwick |

Neuromuscular Diseases

Editor's note: The following article is taken from Rehab Brief, Vol. XI, No. 9, a publication of the National Institute on Disability and Rehabilitation Research. The article surveys the findings of the University of California at Davis' 5-year study of progressive neuromuscular diseases.

When Lou Gehrig delivered his farewell-to-baseball speech in 1939, before 60,000 fans packed into Yankee stadium and millions more who listened, he made the public painfully aware of amyotrophic lateral sclerosis (ALS), now commonly called "Lou Gehrig's disease."

ALS is one of over 200 neuromuscular diseases (NMD's) that affect approximately 500,000 children and adults in the United States. ALS, an adult onset disease, and Duchenne muscular dystrophy, which disables children at young ages and leads to death in the mid-twenties, are the most commonly known of the 200.

The media and celebrities have helped to generate millions of dollars for research by making the public aware of the need to find a cure for ALS and the muscular dystrophies. They have also given the general public- including many health care providers, rehabilitation counselors, and teachers- the view that all NMDs are rapidly progressive and fatal. Some experts blame this opinion for the lack of research into medical management.

During the last decade, recognition has grown that most of the NMDs are slowly progressive or even static over a relatively normal lifespan. "Incurable" is not synonymous with "untreatable," and the National Institute on Disability and Rehabilitation Research (NIDRR) provided a 5-year grant to fund a Rehabilitation Research and Training Center (RRTC) in Progressive Neuromuscular Diseases in 1983, to the University of California at Davis (UCD). The grant was extended in 1987. The RRTC's goal is to conduct a broadly based multidisciplinary program of research in the area of comprehensive rehabilitation management of neuromuscular diseases. Currently, it focuses on identifying factors that prevent or limit successful rehabilitation outcomes and on developing intervention strategies to modify these limiting factors.

Characteristics of the Disease

The neuromuscular organ system includes the anterior horn cells in the spinal

cord, the peripheral nerves, the myoneural junctions (MNJs), and the muscles. Acting as a single functional unit, this neurologic system is also called the "motor unit" or "lower motor neuron." The anterior horn cells are connected to both the pathways to the brain and the peripheral nerves. The axons-electric wires- in the peripheral nerves are connected to the muscles via the myoneural junctions.

NMDs affect all of the components of this unit and may be either acquired or hereditary. The major results produced by these disorders are weakness and muscle atrophy. Examples of neuromuscular diseases are summarized in the following table.

| AFFECTED COMPONENT | ETIOLOGY | |
|--|---|---|
| | ACQUIRED | HEREDITARY |
| Anterior horn cell | Amyotrophic lateral sclerosis Poliomyelitis and post polio muscular atrophy syndrome | Spinal muscular atrophy |
| Peripheral nerve and motor nerve roots | Physical injury Toxic and toxins Guillain-Barré syndrome | Charcot-Marie-Tooth syndrome |
| Myoneural junction | Myasthenia gravis Botulism | Hereditary myasthenia gravis |
| Muscle | Polymyostis | Muscular dystrophies Congenital and metabolic myopathies |

The RRTC's research focuses on the following 10 neuromuscular diseases: Duchenne muscular dystrophy (DMD), amyotrophic lateral sclerosis, (ALS) facio-scapulo-humeral dystrophy (FSH), limb-girdle dystrophy (LGD), chronic spinal muscular atrophy (C-SMA), Charcot-Marie-Tooth syndrome (CMT), Becker muscular dystrophy (BMD), congenital myopathy (CM), myotonic muscular dystrophy (MMD), and Friedrich's ataxia (FA).

The characteristics identified as common to the 10 include 1) weakness (all NMDs), 2) limb contractures (DMD, C-SMA, CMT), 3) spinal deformity (DMD, FA, CM, C-SMA), 4) restrictive lung

disease (all NMDs, but rapidly progressive in DMD and ALS), 5) cardiac dysfunction, and 6) cognitive deficits and/or personality changes (DMD, MMD, FA).

General Principles of Disease Management

Current approaches to management of neuromuscular disorders are more aggressive and future oriented than in the past. Most physicians and therapists now believe that it is important to preserve maximal physical capacity and maintain useful function as long as possible so that optimal function will be present when specific treatments become available. Treatment is not limited to palliation- ideally it is prospective, inhibits the de-

formities, prolongs independent ambulation, and maximizes functional capabilities and quality of life.

Management is best carried out by multidisciplinary comprehensive care and considers all the needs of each individual. Major goals include:

- early diagnosis and establishment of a rehabilitation plan,
- maintenance of activities of daily living and ambulation as long as possible,
- anticipation of complications and development of a program of prevention, and

- supportive counseling to both patient and family.

Managing musculoskeletal complications requires understanding the natural evolution of patterns of weakness and the development of contractures and deformities. Knowledge of pathokinetics is essential to proper timing of therapy, bracing and surgery. Treatment goals take into account whether symptoms are rapidly progressive, static, or temporary. Implementation is carried out by utilizing various therapeutic modalities, bracing, assistive devices, and surgery, and requires attention to cardiovascular, pulmonary, and other complications as well as psychosocial care.

The primary advances in clinical research have occurred in the management of musculoskeletal complications and in descriptive studies of the natural course of Duchenne dystrophy. The efficacy of exercise in progressive muscular diseases remains controversial. Exercise therapy does not appear to have short-term deleterious effects if started early and if carried out at submaximal levels. Stretching alone has not been found to be very effective, but stretching combined with braces has resulted in significant reduction in the progression of lower extremity contractures. There is no question that lower extremity bracing and surgery reduce progression of contractures and spinal deformity, and prolong mobility, but there remains considerable doubt whether the mobility is functional. While spinal orthosis may slow the progression of minor curvatures, bracing has little or no effect on severe scoliosis. Early surgical spinal stabilization is the only effective means of controlling scoliosis in rapidly progressive neuromuscular diseases.

In the past, rehabilitation management was based primarily on clinical observations. Most investigations of treatment were retrospective and failed to follow sound research techniques. In addition to using improved methodology, two parallel categories of research are desirable: 1) longitudinal investigations of the natural history of each disease and 2) prospective studies of treatment outcomes including adequate treatment-group samples, control subjects matched for duration or severity of disease, supervised therapy sessions, and appropriate, objective, valid, reliable measurement criteria against which to assess outcomes.

Current Research

UCD researchers are investigating successful rehabilitation strategies and evaluating the outcomes of selected physical therapeutic interventions.

Natural History Profiles

A comprehensive disability natural history profile has been developed and is in use at the UCD RRTC. In addition to the physical disability components, this profile includes data from a comprehensive battery of neuropsychological tests. The physical disability profile consists of 1) qualitative and quantitative measures of muscle strength, endurance, fatigue, upper and lower extremity motor function (timed motor performance tests), limb contractures, spinal deformity, restrictive lung disease, cardiac dysfunction, and cardiopulmonary fitness; and 2) functional evaluation scales. This profile, all or in part, is currently being used to 1) develop natural history profiles for 10 NMDs; 2) evaluate outcomes of physical and pharmacological interventions; and 3) assist in educational, vocational, and independent living planning. Significant findings include:

- * Loss of strength in Duchenne muscular dystrophy and amyotrophic lateral sclerosis is rapid and decreases in a linear fashion without periods of plateau or accelerated loss. The linearity of the progression of weakness suggests that the motor neuron loss in amyotrophic lateral sclerosis or the muscle fiber loss in Duchenne dystrophy may actually slow as the disease progresses. In both diseases, longitudinal measurements of strength permit predictions as to the further course of the disease such as loss of ambulation. In the other NMDs, loss of strength is usually much slower and there are marked fluctuations of the progression of weakness with periods of plateaus.

- * Limb contractures and spinal deformities are relatively rare in all of the NMDs except Duchenne dystrophy, early onset chronic spinal muscular atrophy, and some of the congenital myopathies. (In the latter, a detailed analysis of the epidemiology and pathokinetic mechanisms is in progress.)

- * The incidence of pulmonary infection and acute respiratory failure is high in amyotrophic lateral sclerosis and in Duchenne dystrophy, but is low in the other NMDs. In the former, the major cause of death is acute respiratory dis-



West Palm Beach Support Group Meeting

In the last issue of the newsletter, we noted the resignation of Robyn Cohen as support group leader in West Palm Beach, FL. A member of her group, Walter Sawyer, has agreed to fill in as her replacement. He has contacted the Medical Center of Port St. Lucie and has scheduled a support group meeting for September 9, 1995 from noon to 3 pm. The hospital has donated soft drinks, coffee, and pastries for the meeting. A local doctor will be the speaker. For members of the CMTA who would be interested in attending the meeting, Walter has provided the following directions: From I-95 exit 63C, Saint Lucie West Blvd. leads to Prima Vista Blvd.; continue east to Rt. 1 (three miles) turn right, go south on Route US Federal Hwy. 1, follow the "H" sign for about 4 traffic lights and turn left on to Tiffany. The hospital will be on the right. Enter the front parking lot. The meeting will be held in the education trailer in the rear of the hospital.

stress. In Duchenne dystrophy and amyotrophic lateral sclerosis, impaired pulmonary function is homogeneously progressive and strongly correlated with disease duration. In the other NMDs there is not correlation between pulmonary function measurements and disease duration. These findings are important for the proper timing of treatment, such as spinal stabilization for scoliosis.

- * While the incidence of abnormal EKGs and Echocardiograms is very high in most of the NMDs, the prevalence of clinical evidence of cardiac disease is very low.

Quantitative Measurements

Validated measures of static and dynamic strength, endurance, and fatigue are being developed and tested for use in both natural history profiles and treatment outcome evaluations. Quantitative measurements of cardiopulmonary function also have been developed. Results to date suggest:

- * Comparison studies between manual muscle tests (MMTs) and quantitative testing show 1) widely variant strength values occur among persons graded normal or near normal by MMTs; 2) MMTs overestimate the extent to which an individual is normal, or fail to detect strength differences when muscle groups present almost equal strength; and 3) MMT grades remain at relatively normal values among disabled individuals who exhibit the most clinical improvement.

(continued on p. 14)

CMTA Contacts

Following is a list of CMTA contact persons and support group leaders. There are many CMTA support groups, but more groups are needed. The CMTA will help you set up a group in your area. For information about forming a group or being a local contact person please inform the CMTA by mail or call 610-499-7486.

*denotes support group leader

Alabama / Greater Tennessee Valley

*Bill Porter 205/386-6579W
205/767-4181

California

*Janice Hagadorn 805/985-7332 after 5
(Oxnard/Thousand Oaks)
*Sheila Levitch 805/254-5322
*Denise Miller 805/251-44537
(Canyon Country/Saugus)
*Freda K. Brown 707/573-0181
(Santa Rosa)
Gary Oleze 619/944-0550 after 6pm
Eda Adams, will return calls
916/677-6460
Jeanne Amour 408/749-1661(Sunnyvale)
Clair Bumgarner 209/874-4963
Felice Gail Viggers, 805/492-2840
Verna M. Sabo, 818/892-6706
Mary Micalizzi, after 6pm
619/441-2432
Bob Hedge, 9am-5pm 310/645-2761

Colorado:

*Dr. Gregory Stilwell 719/594-9920
(Denver area)
Roberta Cummings, 719/846-5611

Connecticut:

Mary Rehm 203/744-2786
(Danbury)
*Kay Flynn 914/793-4710
(Fairfield)

District Of Columbia:

*Lorraine Middleton, 6pm-9pm
202/362-4617

Florida:

William Brady 904/443-6271
Mary Beeler, 9am-8pm 407/295-6215
Harold Wilson 407/465-3656
Pat Ports, M,W, F, 4pm-9pm,
407/965-3691
Joe Ellenbogen 305/921-4660
Edward Carhart, 9:30am-5:30pm
305/567-1066
Beatrice Bannister 407/737-3267
Robyn Cohen 407/622-5829
8pm-9:30pm M-F, weekends anytime
Erika Stilwell 305/232-9066

Georgia:

Nancy Lee McCutchen 404/925-1020

Kansas:

*Ardith Fetterhoff (Eastern Kansas)
816/763-2176
voice mail 816/756-2020

Louisiana

Bobbie Marberry 504/872-0895

Maryland

Jean Iler 410/987-5432
Linda Ember Miller 410/882-4019
Robert Right 410/668-3054

Massachusetts

Wayne Cardillo 413/298-3156
*Donald Hay 9am-7pm, 617/444-1627
(Boston)
Jim Lawrence 508/460-6928
Jennifer Brelsford 413/538-9579

Michigan

Robert D. Allard 517/592-5351
Debbie Clements 616/956-1910
(Grand Rapids)
*Suzanne Tarpinian 313/883-1123
(Detroit)
Laurie Vasquez 517/893-4125

Mississippi

*Julia Prevost 601/885-6482
*Henry & Brenda Herren 601/885-6503
(Jackson)
Mae Blackledge 601/763-5151 (Southern)

Minnesota

Grace Wangaard 612/496-0255

Missouri

*Ardith Fetterhoff 816/763-2176
voice mail 816/756-2020
Allan Degenhardt 816/942-1817

New Hampshire

Mary Nightly 603/598-5451

New Jersey

*Janet Saleh 908/281-6289
(Somerville)
Linda Muhlig 609/327-4392
Gary Orson, Mon-Fri 6pm-10pm
& weekends 609/584-9025
Russell Weiss 908/536-6700

New Mexico

Jesse Hostetler 505/536-2890

New York

Joe Ehman 716-442-4123
Internet:KOLOB@Multicom.Org
*Diana Eline 201/861-0425 before 9pm
(New York City)
*Abby Wakefield 212/722-8052 (NY)
*Lauren Ugell 516/433-5116
(Long Island)
*Bernice Roll 716/584-3585 (Rochester)
*Kay Flynn 914/793-4710
(Westchester County)
Amy Gander 518/373-9907

Angela Piersimoni, after 2pm
607/562-8823

Sharon McAvey, afternoon & evening
718/380-3792
William Carrington, 4pm-11pm
718/486-6953

North Carolina

Diane Rodden 910/584-3655
*Susan Salzberg (Durham)
5pm-9pm 919/967-3118
Raymond Woodie 910/838-3221

Ohio

Roger Emmons 216/286-6485
Suzanne Lammi 513/339-4312
Norma Markowitz 216/247-8785
(Cleveland)

Oklahoma

Leah Holden 405/255-4491

Oregon

*Mary Elizabeth York 503/246-4939
(Portland)

Pennsylvania

*Dennis Devlin 215/269-2600 work
610/566-1882 home
(Delaware Valley)
Patricia Zelenowski 717/457-7067
Camille Walsh 215-747-5321
Janet Fierst 412/487-0757
Mary MacMinn 215/322-1073
Carol Henderson 215/424-1176

Rhode Island:

Robert Matteucci 401/647-9154 PM

Texas

Dr. Karen Edelson, D.P.M.
214/542-0048
M,T,Th, 8:30am-5pm, 214/542-0122
Tony Collette, 1pm-8pm, 713/699-8432
Ken Kerby 817/282-9329

Virginia

*Mary Jane King 804/591-0516
(Tidewater)

West Virginia

*Joan Plant 304/636-7152 after 6pm
(central)
L. Ben Simmers 304/693-7731
Beverly Simmers 304/364-5309
Ronald & Rebecca Sampson,
304/636-7449 24 hours
Barbara Compton 24 hours
304/636-5456



* Individuals with myotonic muscular dystrophy show increased resistance to fatigue while persons with other types of NMDs show greater fatigability. (Editor's note: The question of fatigue in CMT patients is often asked. Here is verified proof that the tendency to fatigue is present in patients with CMT.)

* Among nondisabled subjects, strength is significantly greater on the dominant side. In individuals with NMDs, there is no difference between the dominant and nondominant sides, indicating the possibility of secondary overwork weakness.

* In all types of NMDs, especially those which are rapidly progressive, exercise performance is limited by reduced cardiorespiratory capacity and peripheral oxygen utilization. Even a few minutes of passive exercise can result in increased cardiac cost. Progressive loss of muscle mass may lead to reduced cardiopulmonary maximum work capacity and endurance as well as muscle weakness and fatigue.

Cognitive Function and Psychological Patterns

In Duchenne dystrophy, there is early, nonprogressive impairment of verbal intelligence. Nonverbal deficits occur at an early age also, while verbal scale IQs among older males are often "normal." In myotonic dystrophy, cognitive deficits are primarily restricted to men and women of maternal inheritance and congenital onset. In facio-scapulo-humeral, limb-girdle, and myotonic dystrophies, high levels of depressive features have been found, especially in the latter. While there is no correlation with disease duration and severity or employment status, higher levels of depression occur among individuals with progressive NMDs than non-progressively disabled paraplegics. Depression is not an intrinsic characteristic of the NMDs, but concern about progression may produce depressed feelings.

Physical and Pharmacological Treatment Interventions

Studies are currently in progress to evaluate 1) effects of strengthening exercise programs among individuals with slowly or rapidly progressive NMDs, 2) the effects of aerobic exercise programs on metabolic performance and well-being, 3) the effects of comprehensive rehabilitation programs on the course of restrictive lung disease and the prevention of respiratory infections and acute

respiratory failure, and 4) pharmacological interventions.

Basic and Applied Research of Clinical Significance

Experimental studies using animal models have greatly expanded knowledge of the effects of exercise on muscle and overwork weakness. Exercises of various types have been shown to result in increased muscle fiber degeneration when 1) weakness is severe and/or rapidly progressive and 2) exercise is of high intensity.

Other interventions such as immobilization, low-frequency electrical stimulation, and passive continuous stretch of muscles have been shown to reduce muscle degeneration if carried out early in the course of the disease.

Implications for Practitioners

More research regarding neuromuscular diseases has been done in the past 10 years than in the preceding 50. These findings have major implications for rehabilitation.

Historically, the educational and vocational rehabilitation needs of people with NMDs have been undocumented and unmet, probably due to the tendency to focus on medical aspects of dramatically disabling conditions. The establishment of RRTCs in neuromuscular diseases by NIDRR in 1983 was a major corrective step.

A RRTC-initiated review of the California Department of Rehabilitation District showed that a very limited number of people with NMDs had entered that program during the past five years. Meetings with involved medical students and residents indicated that they only occasionally refer potential clients to the Department of Rehabilitation. The major reason given was their belief that the agency was not interested in clients with progressive diseases.

Pilot surveys and meetings with district counselors and administrators indicated that both they and their employer contacts considered "neuromuscular disability" to be synonymous with fatal and rapidly progressive disorders that hold

In our December 1994 fundraising letter, an article featuring Dr. Howard Shapiro was included. Please note that any inference that Dr. Shapiro was then affiliated with the CMTA was erroneous. Dr. Shapiro has not been affiliated with the CMTA since May, 1992.

little promise for vocational rehabilitation.

Interviews with a small group of individuals with NMDs showed that they, too, believed the Department of Rehabilitation and potential employers to be uninterested in people with progressive disorders.

Discussions with counselors showed two major bases for client rejection: 1) counselor rejection based on personal misunderstandings regarding individuals with NMDs and 2) rejection based on their perceptions of employer attitudes and beliefs regarding the employability of people with NMDs.

A pilot program to cross-train vocational rehabilitation counselors and medical residents is being implemented at the UCD RRTC, which will evaluate pre- and post-exchange attitudes about the target population. In addition, vocational needs and success rates among NMD clients are being reviewed in another district.

Rehabilitation practitioners' attention to the psycho-social, educational, and vocational aspects is as critical as the treatment of physical complications. Early educational and vocational "diagnosis" and planning are important, too, and tentative, target rehabilitation goals should be established as early as possible.

Vocational rehabilitation practitioners can participate in the ongoing research as they accept these clients and help keep them active. Few of these diseases are the direct causes of death; clients often die from complications of inactivity or bed rest.

Call for Participants

Dr. Francis X. Palermo, a physiatrist (a physician trained in rehabilitation and physical medicine), is conducting a study of the effect of electric stimulation on CMT patients. The procedure is patterned electric stimulation of the legs and is gentle and non-painful. The electric stimulation unit is placed in the participant's home, although some professional monitoring will be required. Dr. Palermo is looking for patients with either type 1 or type 2 CMT. Results from CMT patients currently in the study indicate some restoration of function, greater endurance, and increased balance. There is some cost to the participant, as well as, minimal travel to New Haven, CT. For more information contact: Dr. Francis Palermo, Gaylord/Yale Rehabilitation, One Long Wharf, New Haven, CT 06511, phone 203-624-3140.

The CMTA Report is published by the Charcot-Marie-Tooth Association, a registered non-profit 501 (C)(3) health organization. Copyright 1994 The CMTA. All rights reserved under International and Pan American Copyright conventions. No part of this newsletter may be reproduced in any form or by any electronic or mechanical means, including information storage and retrieval systems, without permission in writing from the publisher. The newsletter is co-edited by Karol Hitt and Pat Dreibelus. The layout is by Chesapeake Bay Design, 17 S. Longpoint Lane, Media, PA 19063.

The opinions expressed in the newsletter are not necessarily those of the Charcot-Marie-Tooth Association. The material is presented for educational purposes only and is not meant to diagnose or prescribe. While there is no substitute for professional medical care for CMT disorders, these briefs offer current medical opinion that the reader may use to aid and supplement a doctor's treatment.

Ask the Doctor - cont'd from p.

Dear Doctor,

In patients with CMT and collagen disease, is it possible for a Treponema pallidum fluorescent antibody test (the test for syphilis) to result in a false positive?

The Doctor replies:

The test would not be affected by CMT, but it might be by some collagen diseases.

Dear Doctor:

A 29 year old CMT patient had surgery on the ball of his foot. The incision failed to heal and he is receiving intravenous antibiotics several times a day. Do CMT patients have healing problems?

The Doctor replies:

The circulation problems in CMT and decreased sensory loss could slightly affect healing.

Dear Doctor:

My son, otherwise healthy, has an abnormally high bilirubin. Is this in any way connected to his CMT?

The Doctor replies:

There is no connection between high bilirubin and CMT.

Membership/Order Form

Name: _____

Address: _____

Phone Number: _____

Tell us about yourself:

- CMT Patient
- Interested Supporter
- Medical Professional
- CMT Family Member

Enclosed is:

- \$25
- \$100
- \$50
- other

for my membership in the CMTA (newsletter included in membership)

- At this time I cannot contribute to the CMTA but would like to receive mailings.

Publications and Tapes available from the CMTA

(Check to order)

- VCR Tape - CMT Neurology (\$15)
- VCR Tape - Physical Therapy & Occupational Therapy (\$15)
- VCR Tape - CMT Genetics (\$15)
- VCR Tape - Orthopedic Surgery & CMT (\$15)
- Handbook (16 pp.) - CMT FACTS I (\$3)
- Handbook (24 pp.) - CMT FACTS II (\$5)
- Handbook (24 pp.) - CMT FACTS III (\$5)
- Transcript - San Francisco CMT Conference (\$5)
- Letter - to Medical Professionals regarding the drug list (free to members with self addressed stamped business envelope)
- List - Physician Referrals (by state) (please send SASE) please list states: _____
- CMT Informational Brochure (gray brochure) (one copy free with self addressed stamped business envelope)
- CMT Informational Brochure (gray brochure) in Spanish (one copy free with self addressed stamped business envelope)

Total amount enclosed: _____

Contributions are tax deductible. Please make checks payable to the CMTA.

A copy of the official registration and financial information may be obtained from the Pennsylvania Department of State by calling, toll-free, within Pennsylvania, 1-800-732-0999. Registration does not imply endorsement.

MEDICAL ALERT

Certain Drugs Toxic to the Peripheral Nervous System



This is a list of neurotoxic drugs which could be harmful to the CMT patient.

Adriamycin
Alcohol
Amiodarone
Chloramphenicol
Cis-platinum
Dapsone
Diphenylhydantoin
(Dilantin)
Disulfiram (Antabuse)
Glutethimide (Doriden)
Gold
Hydralazine (Apresoline)
Isoniazid (INH)
Mega Dose of Vitamin A
Mega Dose of Vitamin D
Mega Dose of Vitamin B₆
(Pyridoxine)
Metronidazole (Flagyl)
Nitrofurantoin
(Furadantin, Macrochantin)
Nitrous Oxide
(chronic repeated inhalation)
Penicillin
(Large IV doses only)
Perhexiline (Pexid)
Taxol
Vincristine

Lithium, Misomidazole, and Zoloft
can be used with caution

**Before taking any medication please
discuss it fully with your doctor for
possible side effects.**

5/94

Blood Test Available

The blood test for diagnosing CMT Type 1A found on chromosome 17 is available from Athena Diagnostics. They can be reached by calling 1-800-394-4493, ext. 106. Ask for Sarah Quiry, customer service representative. A physician must order the shipping kit. The cost of the test is \$395.00. §

CMT...

- is the most common inherited neuropathy, affecting approximately 125,000 Americans.
- is also known as peroneal muscular atrophy and hereditary motor sensory neuropathy.
- is slowly progressive, causing deterioration of peripheral nerves which control sensory information and muscle function of the foot/lower leg and hand/forearm.
- causes degeneration of peroneal muscles (located on the front of the leg below the knee).
- causes foot-drop walking gait, foot bone abnormalities, high arches and hammer toes, problems with balance, problems with hand function, occasional lower leg and forearm muscle cramping, loss of some normal reflexes, and scoliosis (curvature of the spine) is sometimes present.
- does not affect life expectancy.
- has no effective treatment, although physical therapy, occupational therapy and moderate physical activity are beneficial.
- is sometimes surgically treated.
- is usually inherited in an autosomal dominant pattern.
- may become worse if certain neurotoxic drugs are taken.
- can vary greatly in severity, even within the same family.
- can, in rare instances, cause severe disability.
- is the focus of significant genetic research, bringing us closer to answering the CMT enigma.
- Type IA can now be diagnosed by a blood test.



THE CMTA REPORT

*information on Charcot-Marie-Tooth Disorders
from the*

Charcot-Marie-Tooth Association

Crozer Mills Enterprise Center
601 Upland Avenue
Upland, PA 19015

TO:

**Non-Profit Org.
U.S. Postage Paid
Glen Mills, PA
Permit #10**