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WINTER 1996

The CMTA Report

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A resource for information on Charcot-Marie-Tooth disease (Peroneal Muscular Atrophy or Hereditary Motor Sensory Neuropathy), the most common inherited neuropathy.

CMTA Email address:
CMTAssoc@aol.com

$75,000 Armington Challenge Grant Launches Research Campaign

The Evenor Armington Fund has initiated an historic $75,000 Challenge Grant to the CMTA. The grant is payable in $25,000 installments over three years and is designed to elevate fundraising efforts and accelerate CMT research activities. Board Chairman Ed Butchko remarked, "this extraordinary commitment by the Armington Fund is certain to excite our membership and I'm confident that we will not only match, but exceed, our goal."

Elizabeth Reardon, daughter of the Armingtons, said, "I'm thrilled that as a family, we are able to make this contribution, especially through an organization like the CMTA, which has helped us so much already in dealing with this disease. As I watch my little 1-year old run from room to room crowing with delight at his new-found mobility, my greatest hope is that our gift and the gifts of others will accelerate research over the next decade to preserve that mobility and keep him free from the pain and frustrations that shadow the lives of so many with CMT."

The Armington Fund became interested in CMT research because family members have CMT. A son-in-law was diagnosed at Johns Hopkins University through biopsies and electromyogram tests. One of his two children was diagnosed by Dr. Roger Lebo in one of the first prenatal testing experiments.

The Armington Challenge Grant will make it possible for the CMTA to be a major force in CMT research. Please help our efforts by giving generously to our March fundraiser.

The Evenor Armington Fund was founded two generations ago and is administered by family members. The fund supports resourceful individuals or small organizations that are of particular interest to the family. Projects are selected in which relatively small grants may significantly affect the feasibility or success of the endeavor. Family members assess whether the contribution is used wisely and whether future contributions should be made. CMT research fits well within these goals. Research is at a stage where relatively small contributions can significantly accelerate the pace of important discoveries. The Armington challenge is meant to attract attention and funding from other sources. There are a number of truly dedicated and productive researchers working in the field right now and there have been impressive advances in diagnosing CMT in the last few years.

The Armington Challenge Grant will make it possible for the CMTA to be a major force in CMT research. CMTA Board Members have pledged 100% participation toward this matching grant and will formally launch the annual Research Fund Campaign in March. The Armington Grant is a vital catalyst. Alone, it is not enough. Each member of the CMTA community must be a partner in the effort to discover causes, design therapies and find cures. Working together, we will achieve our goals.

YOU CAN REACH CMTnet ON THE INTERNET @URL<http://www.ultranet.com/~smith/CMTnet.html>

A MESSAGE FROM THE TREASURER TO OUR FOREIGN MEMBERS

We would appreciate it if you would use your Visa or Mastercard or checks drawn in American funds when sending money to the CMTA. It costs the CMTA $14.50 to collect funds from a foreign check issued in foreign currency. For example, a $100 check in Canadian funds resulted in only $56.74 for the organization. A $25 check resulted in $3.52 for the organization.

The CMTA appreciates each gift that is made to us, but we know that you want your money to be used for CMTA projects and not to be lost in banking transactions.

RESEARCH UPDATE

Summer Fellowship for Erasmo Perera, Dr. Lisa Baumbach's Laboratory

Charcot Marie Tooth (CMT) Disease is a very heterogeneous disease, with respect to the numerous genetic loci as well as the varying clinical presentations. Although significant insight has been gained into the molecular basis of CMT Type 1A, mapping to Chromosome 17p11.2, little understanding has been gained regarding the genetic and biological basis for the clinical variability evidenced within a CMT family.

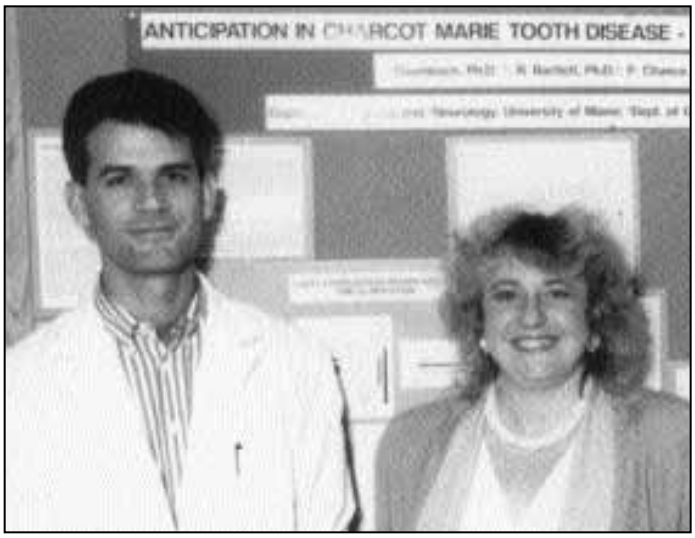
In the course of our studies at the University of Miami, we have identified a few families with CMT 1A which initially appeared to have anticipation, that is, the disease course worsened in severity and age of onset in subsequent generations. Anticipation has been documented for several other neurological/neuromuscular diseases (i.e. Myotonic Dystrophy). The molecular basis of this phenomena is being defined. However, anticipation has not been rigorously investigated nor documented in CMT families.

To test our hypothesis, a Clinical Severity Scoring System (CSS) was developed in collaboration with Dr. Walter Bradley. This system evaluates an individual's disease course over time through the assignment of a decade wise global neuropathic deficit score based on review of individual's medical records and medical history. A longitudinal profile of the CSS over decades reflects the comparative severity and clinical course of CMT 1A neuropathy among affected family members. The CSS rating is plotted against the age at which the rating occurred. Anticipation in families would be suggested by an increase in the disability rating (CSS score) per age or a decrease in age of onset for a certain disability rating. Using these criteria, the four families initially ascertained were strongly suggestive of anticipation, while other CMT families using the same criteria did not evidence anticipation.

Having documented these observations, we then wanted to determine if the families were type 1A or 1B (chromosome 1 gene defect). In collaboration with Dr. Phillip Chance at Children's Hospital of Pennsylvania, we have been studying the CMT 1A region (17p11.2) to first determine if these families have either the 1.5mB duplication or a pmp-22 mutation, and then to determine if novel rearrangements within this region could account for the different clinical presentations among members of these families.

The summer fellowship from the CMT Association allowed Erasmo Perera to travel to Dr. Chance's lab, and to train with his personnel for the necessary techniques to continue molecular studies in my laboratory. To date, we have confirmed that two of the four anticipation families have the 17p11.2 region. Once these studies are completed, they will be followed by extensive restriction enzyme analysis, Southern blotting and pulse field gel analysis to study extensively the DNA regions surrounding and within the duplication region, in hopes of detecting genetic rearrangements which may be associated with different clinical presentations.

The main result of the fellowship award was the transfer of all appropriate technologies, DNA probes, cell lines, etc. from Dr. Chance's laboratory to ours, so that this project can continue to be pursued throughout the year. The fellowship allowed for the dedication of personnel, time, and necessary travel to complete this goal. We are hopeful that significant insights will be achieved in the next year as to the molecular basis of anticipation in these families, furthering our understanding of genetic defects associated with clinical symptoms in CMT.



Erasmo Perera and Dr. Lisa Baumbach

Son Develops Walker for Mother with CMT

Jonathan Miller developed a walking aid for his mother who has Charcot-Marie-Tooth disorders because she had severe walking difficulties. His invention, the U-Step, is completely on wheels, so there is no need to lift it every few steps and one can keep their weight on the unit and still walk. It also has stability of design which greatly reduces people's fear of falling. Finally, it has a tension adjustment which controls the rolling speed of the unit, allowing for regulating walking speed. The tension adjustment is unique to the U-Step.

Jonathan writes, "It took many design trials to refine this feature, but without it, my mother was afraid that the unit would roll away from her even though there was a hand brake."

The Parkinson's community has already embraced the U-Step causing Jonathan's small business to struggle to fill all the orders. However, he believes that other patients with CMT might profit from its use as his own mother has. She was able to walk down the aisle at his wedding in May of 1994 with the U-Step.

The U-Step turns in place and is only 22 inches wide, allowing it to pass through narrow doorways and aisles. It also folds flat for transporting in back seats or trunks and weighs only 15 pounds. It has height adjustments for people from 4'10" to 6'6".

The U-Step Walking Stabilizer is usually covered by conventional insurance, as well as Medicare and Medicaid with proper medical documentation. Because of Jonathan's link to the CMT community, he is offering the U-Step to members of the CMTA at a $25 discount if they mention the organization. Call (800) 588-7837 with questions.

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CMTA MEMBERSHIP/ORDER FORM

Name:_____

Address:_____

_____

Phone Number: _____

If outside the US, please see Treasurer's Note on adjacent page.

	QTY	COST	TOTAL
Charcot-Marie-Tooth Disorders: A Handbook for Primary Care Physicians		*members* $15 *non-members* $20	
Membership Dues		$25	
CMT Facts I ☐ English ☐ Spanish		$3	
CMT Facts II ☐ English ☐ Spanish		$5	
CMT Facts III		$5	
VCR Tape: CMT Neurology		$15	
VCR Tape: Physical Therapy & Occupational Therapy		$15	
VCR Tape: CMT Genetics		$15	
VCR Tape: Orthopedic Surgery & CMT		$15	
CMT Informational Brochure ☐ English ☐ Spanish		FREE	*Send Self-Addressed Stamped Envelope*
Physician Referral List: States: _____ _____ _____		FREE	
Letter to Medical Professional with Drug List		FREE	
Contribution to CMT Research			
TOTAL			

☐ Checks payable to the CMTA

☐ VISA ☐ MasterCard

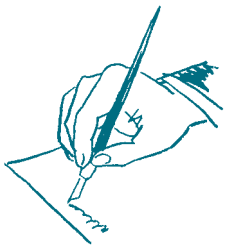
Card Number_____ Expiration Date _____

Signature _____

Mail to the CMTA, 601 Upland Ave., Upland, PA 19015

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.

Letters to the Editor



WRITE TO US!
Pat Dreibelbis, Editor
The CMTA Report
CMTA
601 Upland Ave.
Upland, PA 19015

The CMTA Report
is published by the Charcot-Marie-Tooth Association, a registered non-profit 501(C)(3) health organization.

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.

Dear CMT:

I was 27 when I was diagnosed with CMT (I'm now 43). Up until that time, I knew I didn't have the same musculature in my hands and feet as other males or as I had in the rest of my body, but I wasn't worried…I was playing golf and softball and racquetball, etc., and life was proceeding fine.

The diagnosing neurologist advised me to get braces (when I was 27) to protect my weak ankles. I waited until I was 38. Finally, after a more serious ankle turn, I consented to visiting an orthopedic brace designer "for a consultation." He scared me to death…I was informed that the continual ankle turns could have the serious effect of increasing arthritis trauma when I got older.

So I consented to the braces which turned out to be more like cement shoes/ski boots/plaster casts…Needless to say, not a pleasant experience. I was "overbraced" and have been uncomfortable for 6 years.

The major reason I am writing is this issue of being overbraced. All I needed was assistance to reduce my ankles from turning and what I received were devices that totally "locked" my ankles from any normal movement and therefore magnified the muscle deterioration in my calves and ankles (due to lack of using those muscles…very similar to the experience one has after a cast is removed).

Braces reduced my ankle "trauma" but created a very serious balance problem as the result of my calf muscles not having to work. My ability to simply stand straight, without the need of effort from my upper leg muscles has become a real challenge. The braces also reduce blood flow when I am not walking, and my lower legs constantly "fall asleep" due to the "locked" position of my ankles…The minimal foot drop I experienced has been exacerbated and when I am without bracing (in my bare feet) it is a challenge to just walk.

I am not a big fan of serious bracing…as you can tell.

My recommendations are to use as limited a brace as possible in the early stages. Bracing should start with a simple nylon "sock boot" with laces and Velcro straps to support the ankle (a popular item with football teams as opposed to taping ankles). An alternative item or a possible next step would be to use the Air Cast (from Air Cast Company) which produces very comfortable bracing for athletes. I have been successfully wearing an Air Cast on my left ankle for two months. I tried the right ankle and felt a little unstable with both ankles in Air Casts, as my right foot drop is a bit more pronounced. I am certain the units would have worked wonderfully for both ankles had I not had muscle weakening.

By the way, my left foot no longer "falls asleep" and I feel better at the end of the day because I only have discomfort in one leg. Air Cast also has an option for foot drop and it is a very creative one. They put two holes in the top of the bracing and with an extra shoe string simply hook the string, with a small metal hook, into the lowest point on the shoe lacing. Keeps the toe up and avoids all that plastic all the way up to the knee.

I cover up my bracing with socks. I have found socks that help with not impeding blood flow. They are by Comfort Products (215-781-0300) used primarily by diabetics. Great long stretchy socks (if you like blue and it doesn't matter as these are under the braces). SAS makes a great casual shoe called Time Out that has been functional and comfortable. For dress shoes, I wear the male version of the shoe that the women wear on the TV commercial, when they are playing basketball in high heels (Easy Spirit).

Exercise: I am very focused on keeping other muscles in my body in shape. I do not have the experience where my CMT gets worse if I exercise. I do lots of push-ups and sit-ups and weights and deep knee bends and pull ups. I would not hesitate to tell CMT kids and adults to be aggressive when they exercise with the muscles that can be worked.

Golf is my love and with my skinny hands and skinny lower legs, I still can drive the ball 230-250 yards. I share this because it might let kids or another adult know that other persons with CMT can still golf as they age…). Balance is a challenge and I focus everything on not moving my head and the ball usually takes off OK (That's not a bad tip for any golfer).

I need: more shoe options and better bracing ideas, as even the fancy spiral braces my brace guy designed crack after about a year. The standard braces crack in about 6 months from the twisting and turning (primarily due to my golf swing).

I am sure my CMT is somewhat different than other's CMT, but I thought that maybe some of the above information would prove to be useful.

—Sincerely, BH, Auburn, CA

(Editor: The CMTA does not endorse any particular products. The opinions in this letter are those of the author.)

Dear Friends at CMTA,

I have been wearing modified AFO's for the past 12 years. As anyone who has to wear them knows, there are a lot of very practical problems associated with wearing them. I feel that the medical community has an "AFO mind set" in that they use AFO's for a variety of conditions and try to "modify" them for the CMT patient. I would like to see someone design an orthotic specifically for us. I have several ideas myself but do not have the knowledge of materials or the necessary tools to play with these ideas. Understandably, medical professionals do not have the incentive nor the time to devote to a project like this. I am on the verge of trying to contact a local university that has a biomedical engineering program to see if I can generate some interest in this as a student project. But before I re-invent the wheel, I wanted to find out if this has already been done. Has anyone out there designed any kind of alternative to the standard AFO specifically for the CMT patient? Or are there people out there with CMT who have discovered alternatives on

their own that they could share with the rest of us? I would also be interested in hearing any ideas, advice, suggestions, etc. from my fellow AFO wearers.

The "problems" that I would like to see eliminated or at least addressed are:

1) bruising and pain in the balls of the feet due to standing and walking all day on hard plastic that can never be adequately padded because of space restrictions in the shoe.

2) difficulty in finding women's shoes that are wide enough through the ball of the foot to accommodate the AFO yet don't look orthopedic.

3) chronic rashes and eczema on the feet and ankles due to constant enclosure in plastic.

Maybe I am being too optimistic, but I believe that an orthotic could be designed that does not place the rigid part of the support system under the ball of the foot where we carry most of our weight, that places any bulky areas of the device in places where shoes are more yielding and not in places where shoes are unyielding, that is more comfortable and kind to the skin, and that can be easily camouflaged to allow maximum freedom in clothing choices. Totally rigid support of the foot and ankle is not the answer for everyone. Comfort and freedom of movement are also important and I feel that many of us would like to find some happy medium between the two.

—Sincerely, MWH, Dayton, OH

Dear CMTA:

I am in my 70's and have CMT. I also have an arthritic right hip and have been contemplating hip replacement. In discussing the replacement with various doctors I have received conflicting opinions. Two well regarded neurologists in LA have recommended against the surgery for fear of damage to the major nerve that runs down the leg. Two well regarded orthopedic surgeons say there is no danger to the nerve in the hip replacement operation, and to proceed. So the quandary. What to do?

I am asking people with CMT who have had the hip replacement operation what their experiences have been. If you are willing to share the information, please write to me: Larry Roman c/o CMTA, 601 Upland Ave., Upland, PA 19015. Leave your phone number in the correspondence if you want me to call you. Or, phone me at: 818-766-2612. Leave your name and phone number on the answering machine and I'll get back to you.

—Larry Roman

Dear CMTA:

The *Winter 1995 Report* had an article on Good Grips gadgets. I purchased their can opener which is great when an electric opener is not available. My first opener broke after several uses so I wrote to OXO. They were polite, concerned, and sent me a replacement opener plus a paring knife. Their products are not only easy to handle, but they back them also. Thank you for your informative publication and support of CMT. I have learned more about CMT in the past 2 years from CMTA than I did in the previous 38 years.

—Sincerely, ET, York, PA

Dear CMTA:

I am one of the four in my family that has CMT—the only female with it. I am 43 and already I've had over thirty surgeries, but am still very independent—I can drive and work part-time at Walmart with the help of a scooter. I do walk, but not long distances. I have considerable pain, but there truly is a new drug that has helped me amazingly. ULTRAM I take 250 mg a day and I am doing things I haven't done in years. It is non-addictive. Please share this information with others who suffer with chronic pain. They tried everything with me. Nothing worked. But this has.

—Thank you kindly, WW, Cartersville,GA

Editor: A call to the local pharmacy reveals that McNeil Consumer Products Company is marketing a new medication, Ultram. It is a pain killer that is a synthetic analgesic but non addicting. It is distributed in 50 mg. tablets. people tend to react to it in extremes—it either works well, or produces side effects within five days. Ask your physician for more information.

Dear CMTA,

The new image of *The CMTA Report* is a first class make-over from cover to cover! The colors and the graphics are great and the layout is so easy to read. To all those responsible, THANKS A BUNCH!!! *The CMTA Report* is a valuable resource. I appreciate the pertinent and up to date information that is made available to us through *The Report*. Keep up the good work!

I also want to take this opportunity to thank you for *The Physician's Handbook*. I've made my doctors aware of this new resource and have sent them the information needed to order it.

I would like to share with others a treatment that I have greatly benefitted from. It is massage therapy. In the last five years I've had much progression in my CMT. I'm 56 years old, and as they say, things always go faster down hill. Seriously, I have had much pain in my upper and middle back. I also have Scoliosis. Two years ago, at the end of my rope with pain and not wanting to live my life on pain pills, I went to a massage therapist. The therapist I receive treatment from does Integrative Holistic Massage. It is my understanding that there are many types of massage therapy. I have therapy on a regular basis, and I've received a great amount of relief from the pain. It is a new lease on life! Yes, it does cost money. But, what was the pain costing me? Pain put extra stress on my body, my attitude, and my relationships. No, it is not a cure for CMT or for Scoliosis. But, it sure makes everyday living more enjoyable! I wonder if anyone else has benefitted from massage therapy? I would be interested in hearing from others on this subject.

—Sincerely, MB, Orlando, FL

GIFTS WERE MADE TO CMTA IN MEMORY OF

Irene Arend
Sharon Arend

Miron Canady, Jr.
Bobbi McElroy and friends

Mrs. James Carter
Opal Mae Mosby
Lucile Dendinger
Charlene Leistner

Esther Day
Dollie Day
Retha Schlais

Louis Charles Giancola
Diane Kline

Grace Hawkes
Robert Hawkes

Dorothea Nielsen
Mr. and Mrs. Gilbert Stucker

Rebecca Sand
Rhoda and Stephen Sand

Chester Sporka
Julia Sporka

Ellen Wall
Michael Wall

GIFTS WERE MADE TO CMTA IN HONOR OF

Dr. Rebecca Brezel
Bonnie and Melvin Hirshowitz
Lauren and Emily Julian
Charles and Helen Lynch

Mr.and Mrs. Henry Eldredge
Mr. and Mrs. Douglas Moody

Her brother
Brynhild Housch

The Lynch Family
Helen Lynch

Cecilia Thorp
Leonore Smith

George Smith
Leonore Smith

Christina Schwab
Gisela Schwab

Bill Westerfer
Catherine Westerfer

The CMTA Awards Its Firs

OF INTEREST

Genetic Discrimination: Several federal legislators have introduced legislation to prohibit genetic discrimination by insurance companies and/or employers. Senator Tom Harkin (D-IA) tried to amend Senator Kassebaum's *Health Insurance Reform Act of 1995* when it was marked up in the Senate Labor committee, but the amendment to prohibit insurance discrimination failed to pass. However, he did succeed in inserting some language in the committee's report showing that it was the committee's intention to prevent genetic discrimination. On the other hand, such "report language" does not have the force of law. Senator Mark Hatfield (R-OR) introduced the *Genetic Privacy Act of 1995*, cosponsored by Senator Connie Mack (R-FL). Representative Louise Slaughter (D-NY) introduced the *Genetic Information Nondiscrimination in Health Insurance Act.* Senator Diane Feinstein (D-CA) announced that she, too, is drafting similar legislation and expects to introduce it soon in the Senate. However, none of these bills are expected to pass because the influential insurance lobby opposes the non-discrimination concept. *(From NORD ONLINE, December 1995.)*

Dr. Peter Denton of Duke University was unanimously awarded the Anita Harding Charcot-Marie-Tooth Association Postdoctoral Fellowship by the CMTA Board of Directors on the recommendation of a seven member selection committee of the Medical Advisory Board. This fellowship is named, this year, for Dr. Anita Harding of the Institute of Neurology, London, and the post graduate medical institute and hospital of Hammersmith, London. Anita was a member of the CMTA's Medical Advisory Board who passed away this past summer.

Dr. Denton will work under Dr. Jeffrey Vance, a previous CMTA awardee for his ground breaking work on describing the gene for the most common form of CMT—CMT 1a and the reduplicating sequence of DNA on chromosome 17.

CMT II is the second commonest form and is the neuronal form in which the axon of the nerve is affected, rather than the myelin sheath, as in CMT 1a. Peter Denton's work will be in mapping and identification of the CMT 2a gene.

Dr. Peter Denton

Dr. Denton is a graduate of Sienna College, Loudenville, NY, with a BS in chemistry in 1986. He was awarded his doctorate in 1991 by the University of North Carolina, Chapel Hill, in microbiology and immunology. He is a talented and dedicated research scientist with original work in nearly a score of articles in journals. A recent one in 1993 has already described genetic linkage of a locus(CMT 4a) to chromosome 8q for the autosomal recessive form of CMT and is published in human molecular genetics, representing an international collaboration of Dr. Vance's group with the North African Tunisian neuroscientists, Drs. Ben Othmane and Ben Hamida.

In a testimonial for Dr. Denton, the Chairman of the Division of Neurology, Dr. Allen D. Roses, describes this young scientist as being dedicated to mapping and identifying the CMT genes. He stated that Dr. Denton is innovative in devising new techniques and methods, one of which is pulse-field gel electrophoresis PCR and that already he has reduced the candidate region of the CMT 2a gene from over 10 centimorgans chromosome length to less than one cm. As well as his work on CMT 4, he has also helped to map the region on chromosome 13 for Duchenne-like muscular dystrophy. He is a mature individual who has worked for a year with a commercial firm designing new techniques for genetic analysis after this PhD and then applied these techniques when he joined the faculty at Duke as a research assistant.

RESEARCH REPORT

Strength Training in Patients with Myotonic Dystrophy and Hereditary Motor and Sensory Neuropathy: A Randomized Clinical Trial. E. Lindeman, et.al.

From: *Archives of Physical Medical Rehabilitation*, July, 1995

A randomized clinical trial on the effects of strength training was performed in myotonic dystrophy(MyD) patients and patients with hereditary motor and sensory neuropathy (HMSN,CMT). Training and most measurement tools involved the proximal lower extremity muscles. The participants trained 3 times a week for 24 weeks with weights adapted to their force. Strength was evaluated by isokinetically measured knee torque. Fatiguability was assessed by the time an isometric contraction could be sustained. Functional performance was measured by timed motor performance and by questionnaires on functional performance. Serum myoglobin levels were determined to detect changes in muscle fiber membrane permeability. The MyD group included 33 participants, and the HMSN group included 29 participants. Within each diagnostic group, patients were individually matched and subsequently randomized for treatment allocation. In the MyD patients, none of the measurement techniques showed any training effect. Neither were there signs of deterioration caused by the training. In the HMSN group, knee torques increased. Timed motor performance did not change, although the questionnaires showed an improvement on items related to upper-leg function. Mb levels did not change

st Postdoctoral Fellowship

From earlier work it appears that the area of chromosome 1 where the CMT 2a gene is located is p35036, which is quite unstable and can be further mapped using YAC and PAC technology. The first YAC is a megabase bridge of DNA fragments and the PAC is a smaller portion of recombinant DNA and they can be used separately or in combination with flanking markers to mark the suspected area. In this way, candidate genes can be defined and assessed for compatibility. These are the techniques Dr. Denton is using to narrow down the area of search, and this fellowship will enable him to move into the final phase of this investigation.

He has available five large families of CMT 2a immediately for this study, and will have access to 24 more families including several provided by another international board member (CMTA Medical Advisory Board), Dr. Lefkos Middleton of Cyprus. Some of studies of this type were reported in the journal Genomics in 1993 in which Dr. Middleton collaborated with Dr. Anita Harding, for whom this fellowship is named.

Dr. Denton submitted an extremely well-referenced research protocol with five specific aims. He indicated how he would proceed and the rationale as to why his method should be successful. He is already near the point of narrowing the candidate gene to 500 kb or less and the genes expected to be involved in the neuropathy will be preferentially selected. If this does not work, he mentions several other techniques, including the direct selection technique of Lovett. Dr. Denton's present state of investigation and his rate of progress lead the reviewers to believe that he stands an excellent chance of finding the gene during his fellowship tenure.

The importance of this research to the CMT community is well defined. One advantage will be the ability to more correctly separate the second commonest form of CMT from a host of other more difficult to diagnose acquired axonal neuropathies (toxic, alcoholic, senescent, and even subclinical diabetic) so that diagnosis of the disorder is an immediate gain. Secondarily, defining the gene will bring us nearer to discovering the gene product, a step that traditionally should lead to a rational form of therapy. As a spin-off, it will enable us to undertake prenatal diagnosis in already defined families with CMT 2a after the appropriate development of techniques. I am sure it will also demonstrate the rich genetic heterogeneity which we have already seen in CMT 1a.

The Medical Advisory Board wishes Peter Denton great success.

Robert Lovelace, MD,
Professor of Neurology, Columbia University,
Chairman, Medical Advisory Board, CMTA

Dr. Jeffrey Vance serves as Peter Denton's mentor.

GIFTS TO CMT RESEARCH

Steve Khosrova has found a way of making his contributions to the CMT Research Fund go even further. By investigating the matching program with his employer, Salomon Brothers Inc., Steve found out his contributions are matched by The Salomon Foundation Inc., a philanthropic arm of Salomon Brothers Inc. His donations to CMT research are, therefore, automatically increased.

significantly as a result of the training. In conclusion, the MyD group showed neither positive nor negative effects of the training protocol, whereas the training produced a moderate increase in strength and leg-related functional performance in the HMSN group.

From the syndrome of Charcot, Marie, and Tooth to disorders of the peripheral myelin proteins. Anita Harding

From: *Brain*, June 1995

The description of the peroneal muscular atrophy syndrome in 1886 by Charcot, Marie and Tooth was followed by an era of nosological confusion. This was partly clarified by the advent of nerve conduction studies and the definition of the most common, but heterogeneous, disorders underlying this syndrome, hereditary motor and sensory neuropathies (HMSN) types I and II. The classification of HMSN is now changing as a result of the identification of underlying mutations in genes encoding myelin proteins. Abnormalities of peripheral myelin protein 22 (PMP-22) account for dominantly inherited HMSN type I in approximately 90% of families. The commonest genetic defect is a duplication of this gene and the surrounding region of chromosome 17, although point mutations also occur. A deletion of the same region causes hereditary neuropathy with liability to pressure palsies. Point mutations of the P0 gene cause HMSN I in a small number of families. The x-linked type of HMSN is associated with defects of the connexin 32 gene, which encodes a gap junction protein. These molecular genetic advances can be translated into clinical practice, leading to improved diagnosis and genetic counseling.

CMTA Disability Survey

OF INTEREST

Physical Therapy:
MDA will assist with the payment for one consultation annually to (a) evaluate the need for physical therapy and (b) instruct family members and others on how to administer prescribed exercises. Physical therapy can neither arrest the disease process nor restore affected muscle tissue. It may, however, help keep still healthy muscles functioning and may delay the onset of contractures. Contact your local MDA clinic doctor to receive a prescription.

The Right Fit
If your right foot isn't the same size as your left, there's a solution on the horizon. More than 50% of people have different size feet because their bodies are asymmetrical. Athlete's Foot franchises in Delaware and Pennsylvania in cooperation with New Balance are offering the New Balance 800 walking shoe in individual sizes so a left 9 can happily coexist with a right size 10. The New Balance 800 sells for about $80. Each shoe will come in its own box, but the shoes will be sold in pairs. Wilmington podiatrist Raymond DiPretoro says that a poorly fitting shoe puts tremendous force on the foot's ligament structure and can contribute to foot deformity.

Again, a big thank you goes out to all of you who participated in the disability survey that I conducted in November, 1993. Of 1,027 surveys mailed out, I received 485 responses, a 47% response rate, which is an incredibly good response for a mailed survey.

To summarize, persons with CMT were chosen at random from our database and were asked questions on the types of disabilities that they experience. It is important to note that ALL persons selected for the survey were encouraged to reply: "Even if you are mildly affected and have few or none of the problems questioned in this survey your participation is very important." This statement was added to the survey introduction to eliminate skewing of the data toward the more disabled.

The Stanford Health Assessment Questionnaire (HAQ)

The bulk of the survey, that which will be reported below, was taken from the Stanford Health Assessment Questionnaire (HAQ) developed by J.F. Fries et. al. in 1980(J. Fries et. al., Arthritis and Rheumatism, 1980; 23:2). Although the original HAQ assesses four aspects of disease: disability, pain and discomfort, economic and drug side effects, I chose to focus on the first two aspects, disability and pain.

Most widely used is the disability section of the HAQ which represents a functional disability test. The purpose of a functional disability test is to assess how a disease, such as CMT, impacts upon a person's daily activities, in contrast to a neurological evaluation in which a physician quantitates the disease based on how strong the muscle groups appear on a few repetitions of manual muscle testing.

Although used initially for the measurement of patient outcome in arthritis, the HAQ was developed for use in all illnesses. Since 1980 the disability section of the HAQ has been used to quantitate disability in diseases such as scleroderma, lupus, fibromyalgia, gout, Paget's Disease, low back pain, HIV and normal aging (J. Fries et al, Arthritis Care and Research, 1992; 5).

The disability survey (printed below with results) is composed of 8 categories of daily living: Dressing and Grooming, Arising, Eating, Walking, Hygiene, Reach, Grip and Activities, each of which has at least two component questions. For each of these categories the participants were asked to record the amount of difficulty they have using the four choices: Without ANY difficulty, With SOME difficulty, with MUCH difficulty, or UNABLE to do. The higher the level of difficulty the higher the score for the question.

SCORING	
Without ANY difficulty	= 0
With SOME difficulty	= 1
With MUCH difficulty	= 2
UNABLE to do	= 3

The highest score for any component question determines the score for that category.

The questionnaire also asks participants to indicate their use of any aids or devices or if they need help from another person for any of these activities. If either devices and/or help from another person is checked for a category, the score for the category = 2.

Standard Disability Index (SDI)

The Standard Disability Index (SDI) is calculated by adding the scores for each of the categories and dividing by the number of categories, 8.This gives a score in the 0 to 3.0 range. A SDI of 0.0 indicates a completely normal functional ability; a SDI of greater than 1.0 indicates moderate impairment in at least one Activity of Daily Living category and a SDI of greater than 2.0 indicates severe impairment in at least one Activity of Daily Living category. A SDI of 3.0 would indicate severe impairment in all categories.

—Diana Eline, M.A.

* For CMTA Disability Survey Results- Part I see the *Summer 1995 CMTA Report.*

Results — Part II*

HAQ Functional Disability Questionnaire Results

1. DRESSING AND GROOMING
Average score = 1.02
(for all participants)
Are you able to:
a. Dress yourself, including tying shoelaces and doing buttons?
b. Shampoo your hair?

2. ARISING
Average score = .88
Are you able to:
a. Stand up from a straight chair?
b. Get in and out of bed?

3. EATING
Average score = .91
Are you able to:
a. Cut up your meat?
b. Lift a full cup or glass to your mouth?
c. Open a new milk carton?

4. WALKING
Average score = 1.59
Are you able to:
a. Walk outdoors on flat ground?
b. Climb up five steps?

5. HYGIENE
Average score = 1.07
Are you able to:
a. Wash and dry your body?
b. Take a tub bath?
c. Get on and off a toilet?

6. REACH
Average score = 1.16
Are you able to:
a. Reach and get a 5 pound object (such as a bag of sugar) from just above your head?
b. Bend down to pick up clothing from the floor?

7. GRIP
Average score = 1.36
Are you able to:
a. Open car doors?
b. Open jars which have been previously opened?
c. Turn faucets on and off?

8. ACTIVITIES
Average score = 1.30
Are you able to:
a. Run errands and shop?
b. Get in and out of a car?
c. Do chores such as vacuuming or yardwork?

SUMMARY
Number of respondents: 377
Males: 160 (42.4%)
Females: 217 (57.6%)
Average age: 50.3 years (11 - 89)

Note: Although I received 485 responses, some surveys were incomplete in certain sections of the functional disability test and had to be eliminated, respondents younger than age 10 were also eliminated.

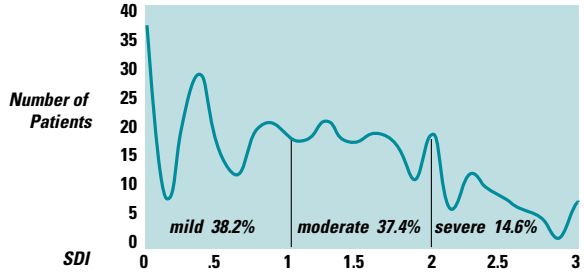
The results show that the on the average the participants in this study had an Standard Disability Index (SDI) of 1.16 (Standard Deviation = 0.80), which is in the low range of moderate disability, however there was considerable variability.

The CMT patients can be divided into 4 groups based on their SDI scores (J. Fries et al, The Journal of Rheumatology 1988; 15:10).

9.8% had completely normal functional ability, SDI = 0.0 , average age 44.5 (12-76)
38.2% had mild impairment, SDI = 0.01 - 1.0, average age 46.1 (11-82)
37.4% had moderate impairment, SDI = 1.01 - 2.0, average age 53.0 (11-87)
14.6% had severe impairment, SDI = 2.01 - 3.0, average age 57.9 (14-89)
On average, the level of disability appears to increase with increasing age.

The activity of daily living that had the highest average score (and therefore representing the greatest disability) was WALKING (1.59), followed by GRIP (1.36), ACTIVITIES (1.30), REACH (1.16) and HYGIENE (1.09). All were in the range of moderate disability. EATING (.91) and ARISING (.88) showed average values in the range of mild disability.

DEGREE OF IMPAIRMENT PERCENTAGES

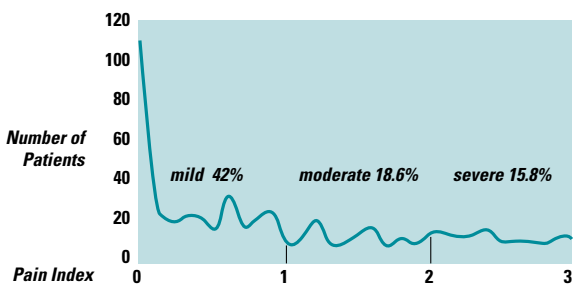


HAQ Pain Questionnaire Results

How much pain have you had because of CMT in the past week?
Place a mark on the line to indicate the severity of the pain.

Pain — Severe Pain
0_____100

DEGREE OF PAIN IN SURVEY RESPONDENTS



A score from 0 to 3.0 was determined based on the location of the respondent's mark.

SUMMARY
number of respondents: 431
males: 189 (43.9%)
females: 242 (56.1%)
average age: 49.2 years (10 - 87)

Average score = 0.89
(Standard Deviation = 0.89), again, there was considerable variability.

23.7% had no pain, Pain = 0.0
42.0% had mild pain, Pain = 0.01 - 1.0
18.6% had moderate pain, Pain = 1.01 - 2.0
15.8% had severe pain, Pain = 2.01 - 3.0

If you have any questions about this survey, please feel free to contact me through the CMTA office or over the Internet at eline@ix.netcom.com.

Summer Grant Results Announced

The study entitled, "Moderate Resistance Exercise: Its Effect on Patients with Charcot-Marie-Tooth Disease" which was run from June to October 1995 by Steve Sepel, a graduate student in physical therapy at Beaver College and Carol A. Oatis, PT, PhD, his faculty advisor, is now complete. Since some more statistical analysis needs to be done prior to sending the paper for publication, limited amounts of information can be released at the present time.

The literature on the effects of exercise for people with progressive neuromuscular disorders is controversial. Some papers report a degenerative effect of exercise on muscles weakened by a neuromuscular disease, while others describe the benefits of it. There have been very few group studies done to measure the change in strength in patients with neuromuscular disorders and none looking specifically at patients with Charcot-Marie-Tooth disease (CMT). Therefore, there is a need to research specifically the possibility of improving, without neuromuscular damage, the functional capacities and the strength of people with CMT using mild or moderate exercise.

Carol A. Oatis and Steve Sepel

Due to the fear of more neuronal degradation, physicians have warned patients with CMT about the ill effects of exercising. The result is a general deconditioning and a decrease in strength of the involved muscles caused by the sedentary lifestyle of these patients. In order to give moderate exercises to patients with CMT, without resulting in overwork, it is important to recondition them through exercising their uninvolved muscles.

The purpose of the present study was to specifically examine the above issues. Sixteen subjects with mild to moderate CMT took part in the study...nine of them as the study group (exercising) and seven of them as the control group (not exercising). Both groups were initially evaluated. The evaluation consisted of: 1) a hands-on manual muscle test to record the strength of the individual muscles of the legs, feet, arms, and fingers, 2) specific tools recording strength to assess pinch, grasp, and ankle strength, 3) two different types of non-invasive electrical stimulation tests to monitor any nerve damage,and 4) functional tests of legs, feet, hands and fingers (mounting and descending stairs, walking, grasping small and large objects, etc.). The study group followed a daily, individualized exercise program that was developed according to each patient's status. Each subject in both groups was reevaluated eight weeks after his/her initial evaluation to identify any change in strength, function, and nerve conductivity.

The method and design of the following research project was previously used by Dr. Oatis' research group on one subject. However, studying one individual is quite different from studying a group, and the differences did bring unexpected problems that overshadowed the results. The primary problem was the difficulty in getting enough subjects which led to a disparity between the study and control group. Hence, for many of the tests, a comparison could not be made between the two groups.

Some subjects, who took part in the exercise regimen, reported no changes in their daily life even though they showed some mild improvement such as being able to make a circle with the thumb and each of the other fingers. Others reported an increase in balance (being able to put on pants while standing without losing one's balance), walking capacity, hand dexterity (opening small bottles) endurance (using scissors more effectively), and an overall better sense of well-being. A complete review of the results will be made available to the CMTA after the study has undergone the appropriate peer review process within the medical and scientific communities.

This was a good initial study which can serve as the basis for further research. The study should be repeated with some changes in the design to increase the validity of the results.

—Steve Sepel and Carol Oatis, PT, PhD

GIFTS TO CMT RESEARCH

The Beyer Family of Upper Saddle River, New Jersey, all gathered together at Christmas time and came to the decision to make a joint contribution to CMT Type II research since that version of the disorder is the one which affects their family. This is another example of the way in which people can support research and the ultimate goal of curing CMT.

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, fax 1-610-499-7487, or call the office at 1-610-499-7486. This page will appear in the newsletter whenever space permits.

Alabama/Greater Tennessee Valley
* Bill Porter 205/386-6579 work
205/767-4181 home

Arizona
Lavon Little 602/516-0539

California
* Janice Hagadorn 805/985-7332 after 5
(Oxnard/Thousand Oaks)
* Sheila Levitch 805/254-5322
* Denise Miller 805/251-4537
(Canyon County/Saugus)
* Freda K. Brown 707/573-0181
(Santa Rosa)
Gary Oleze 619/944-0550 after 6
Eda Adams 916/677-6460
Jeanne Amour 408/749-1661
Sandra Huntley 310/597-3728
Felice Gail Viggers 805/492-2840
Verna M. Sabo 818/892-6706
Mary Micalizzi 619/441-2432 after 6
Bob Hedge 310/645-2761 9-5

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

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

District of Columbia
* Lorraine Middleton202/362-4617 6-9p.m.

Florida
William Brady 904/443-6271
Mary Beeler 407/295-6215 9a.m.-8p.m.
Harold Wilson 407/465-3656
Pat Ports 407/965-3691 M-W-F 4-9p.m.
Joe Ellenbogen 305/921-4660
Edward Carhart305/567-1066 9:30-5:30
Beatrice Bannister 407/737-3267
Robyn Cohen 407/622-5829
M-F 8-9:30 p.m. anytime weekends
Erika Stilwell 305/232-9066
* Walter Sawyer 407/335-8624

Georgia
Nancy Lee McCutchen 404/925-1020

Kansas
* Ardith Fetterholf 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 Kight 410/668/3054

Massachusetts
Wayne Cardillo 413/298-3156
* Donald Hay 617/444-1627 9a.m.-7p.m.
(Boston)
Jim Lawrences 508/460-6928
Jennifer Brelsford 413/538-9579

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

Mississippi
* Julia Prevost 601/885-6482
* Henry/Brenda Herran 601/885-6503
(Jackson)
Mae Blackledge 601/763-5151

Minnesota
Grace Wangaard 612-496-0255

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

New Hampshire
Mary Nightly 603/598-5451

New Jersey
* Janet Saleh 908/281-6289
(Sommerville)
Linda Muhlig 609/327-4392
Gary Orson 609/584-9025
M-F 6-10 p.m. & weekends
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 9 p.m.
(New York City)
* Abby Wakefield 212/722-8052
* Lauren Ugell 515/433-5116
(Long Island)
* Bernice Roll 716/584-3585
(Rochester)
* Kay Flynn 914/793-4710
(Westchester County)
Amy Gander 518/373-9907
Angela Piersimoni 607/562-8823 after 2
Sharon McAvey 718/380-3792
afternoon & evening
William Carrington 718/486-6953
4-11 p.m.

North Carolina
Diane Rodden 910/584-3655
* Susan Salzberg 919/967-3118 5-9 p.m.
(Durham)
Raymond Woodie 910/838-3221

Ohio
Roger Emmons 216/286-6485
Suzanne Lammi 513/339/4312
Norma Markowitz 215/247-8785

Oklahoma
Leah Holden 405/255-4491

Pennsylvania
Dennis Devlin 215/269-2600 Work
610/566-1882 Home
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
Tony Petre 412/647-8324

Rhode Island
Robert Matteucci 401/647-9154 in p.m.

Texas
Karen Edelson, DPM 214/542-0048
214/542-0122
M-T-Th 8:30-5
Tony Collette 713/699-8432 1-8 p.m.

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

West Virginia
* Joan Plant 304/636-7152 after 6 p.m.
(Central)
Barbara Compton 304/636-5456 24 hrs.

New Support Group Meets

The Western Pennsylvania support group held its first meeting on January 20,1996. Over 30 people attended the first meeting which featured a neurologist who described the aspects of CMT to the audience. Representatives from the departments of Physical Medicine and Rehabilitation, Orthopaedics and Physical Therapy were also in attendance to answer questions. Future meetings will feature speakers on foot and ankle problems and genetic counseling.

The support group is sponsored by the University of Pittsburgh Medical Center and was started by Dr. Stephen Conti, an orthopaedic surgeon who specializes in foot and ankle problems. The next meeting will take place on April 27, 1996, at 9:00 am in the Conference Center, Room 1104 at the University of Pittsburgh Medical Center. Anyone interested in more information can contact Tony Detre at 412-647-8324.

OF INTEREST

Airline Accessibility
When you book your flight, mention to the travel agent or the airlines person that you are handicapped and would like a seat as near to the airplane entrance as possible. Also, request boarding passes with your ticket. When you arrive at the airport, check your luggage at the curb, if possible. This may permit you to go directly to the gate. If you are taking a wheelchair, do not check it through with your luggage. Use it to take you to the gate. It should be tagged for storage on the plane, so that it will be available to you upon arrival at your destination. If you have to change planes enroute, it is especially important that you have it available to go from one gate to another. The magazine *Access to the Skies* reports that new 777 will have one lavatory that is accessible from an on-board chair, either with or without an attendant. United is already using these new planes.

* Denotes support group leader

MEDICAL ALERT:

These Drugs Are Toxic to the Peripheral Nervous System and can be harmful to the CMT patient.

Adriamycin
Alcohol
Amiodarone
Chtoramphenicol
Cis-platinum
Dapsone
Diphenylhydantoin (Dilantin)
Disulfirarn (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, Macrodantin)
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.

What is 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 and CMTX 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