

1983-2003
CELEBRATING 20 YEARS
OF LIVING OUR MISSION

Funding
a Cure

Creating
Awareness

Improving
Quality of Life

WINTER 2003

The CMTA Report

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Our Mission:

To generate the resources to find a cure, to create awareness, and to improve the quality of life for those affected by Charcot-Marie-Tooth.

Our Vision:

A world without CMT.

TO GENERATE THE RESOURCES TO FUND A CURE...

2003 Grant Recipients Announced

Continuing our commitment to live our mission, the CMTA has funded four post-doctoral students for 2003 who are working on CMT research which holds promise for the future, both in knowledge about CMT and in practical applications for CMT patients.

Two of this year's recipients are continuing their research from 2002. The first recipient, Dr. Raul Perez-Olle is a foreign national working in the laboratory of Dr. Ronald Liem, an established researcher at Columbia University in New York City. His research project is entitled "Genotype-Phenotype Analysis of Mutations in the Human Neurofilament Light Gene Linked to Charcot-Marie-Tooth Neuropathy." He has been awarded a \$35,000 grant named the Carolyn Redell CMTA Fellowship in memory of one of the founders of the patient support function of the organization.

Dr. Perez-Olle will be describing the consequences of mutations in the neurofilament light gene that has recently been identified as a cause of CMT 2E. His approach is based on the production of mutated proteins in cultured cells in Petri dishes, followed by analysis of the ability of these proteins to function normally in cells and to assemble, (which is crucial for the formation of axons) and to transport mitochondria, the "power plants" of cells that produce vital energy.

His work should advance the understanding of CMT 2E, in particular, but also of all other forms of CMT.

The second recipient is Dr. Jerome Devaux who is working in the laboratory of Medical

In our anniversary year, the CMTA awarded the Carolyn Redell and Howard F. Shapiro fellowships in honor of their roles in founding the organization.

Advisory Board member Dr. Stephen Scherer at the University of Pennsylvania. His project is entitled "The Role of Potassium Channels in CMT 1." He has been awarded a \$35,000 grant named the Howard F. Shapiro CMTA Fellowship. This grant is named for the man who began the CMTA (then the National Foundation for Peroneal Muscular Atrophy) in 1983.

Dr. Devaux is investigating the function of certain channel proteins that regulate the potassium concentrations on the inside and outside

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Attendees at the groundbreaking Arden House, Second International Conference, held in 1987 at Columbia University.

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2003 GRANT RECIPIENTS ANNOUNCED

(Continued from page 1)

of cells and thus play a crucial role in the flux of the electrical current up and down the peripheral nerves. It is hoped that in the future this work might lead to the identification of certain medications that, by changing the function of these potassium channels, might improve electrical transmission and, thereby the symptoms of CMT.

The third recipient is Dr. Pauline Fraissignes from the Faculté de Medecine, Marseille, France. She is working under the mentorship of Dr. Michel Fontes. Her project is entitled "Therapy of CMT 1A: A Pharmacological Approach." She is the recipient of the James Thomas Moore Fellowship, as designated by the Moore family.

Dr. Fraissignes, working with Dr. C. Huxley in London, developed a mouse model by injecting human YAC containing the PMP22 gene into some fertilized mouse oocytes (the early ovum before it has developed completely). This mouse model will be used to test therapeutic approaches to treating CMT 1A. In preliminary studies, mice treated with a number of simple molecules have presented with less severe phenotypes than untreated animals. This molecule (called the CMT molecule in the studies) is already in use in human medicine and this grant will allow the French team to develop information leading to human clinical trials. They also hope to begin to understand the molecular basis of the correction, so they can develop modified molecules which might be even more efficient.

The fourth grant is awarded to Dr. Marie Marthe Krady working on "Skin Biopsies in CMT" at Wayne State University, under the mentorship of Medical Advisory Board member Dr. Michael Shy. This grant is named the Buuck Family Fellowship in recognition of the funding provided by the Buuck family.

Dr. Krady's study aims to optimize the techniques required for an analysis of nerves from skin biopsies in order to interpret subsequent results from CMT patients. Once the technique is refined, the study will gather skin biopsies from patients with CMT1A, CMT1B, and CMT1X. The studies will allow Dr. Krady to examine the effects of particular mutations both morphologically and at the molecular level. This information should greatly enhance genotype-phenotype correlations on patients with various forms of CMT. ★

2002 GRANT RECIPIENT REPORT:

Studying How Mutations in the Neurofilament Light Gene Cause Charcot-Marie-Tooth Disease

By **RAUL PEREZ-OLLE M.D. and RONALD K. H. LIEM Ph.D.**

The axons of a nerve cell or neuron carry the electrical impulses from the cell body to the target cells, and also send information back from the peripheral receptors to the neuronal cell bodies. These axons can be very long, up to one meter in length in the leg. To maintain and organize this highly specialized structure, a network of filamentous or threadlike structures is present in the axon. This network is called the cytoskeleton (cell skeleton). The most abundant structures in the cytoskeleton of the axon are the neuronal intermediate filaments. These filaments are 10-nm wide and made up of three different subunit proteins. These proteins are called the neurofilament heavy subunit (NFH), the neurofilament medium subunit (NFM), and the neurofilament light subunit (NFL). Recently, mutations in the NFL gene have been described in different CMT families, defining a new subtype of axonal CMT (CMT2E).

The two mutations in the NFL gene linked to CMT2 disease that were first described are located in different parts of the NFL protein. In order to characterize the effects of these two mutations on the function of NFL, we used human cells in culture to determine if these mutations resulted in changes in the ability of the mutant proteins to form filaments. For these studies, we first made the mutations in cloned DNA copies of human NFL and then compared the abilities of the normal unmutated (or wild-type) and mutant NFL proteins to form a network in filaments in cultured human cells. The wild-type NFL forms a network of filaments, but the two mutant NFL proteins formed protein aggregates. When mutant and wild-type cells were expressed together, they also formed aggregates, consistent with the observation that the mutations are dominant. These studies indicate that the mutant NFL proteins can no longer assemble into filaments and in fact inhibit the ability of the normal NFL to form filaments. For these experiments, we used human NFL without its normal partners, NFM and NFH. When normal NFL is expressed together with either of these other two proteins, a much more extensive network is seen in the cells where they are expressed. We therefore wanted to study the

effects of NFL mutations on the formation of a network of filaments composed of both NFL and NFM subunits. When we expressed the normal NFL and NFM genes in the cultured cells, we observed the formation of an extensive network of filaments. However, these normal filaments were not formed after expression of mutant NFL proteins. When we expressed NFM with one of the NFL mutants, we observed the formation of abnormal filaments. These filaments formed bundles, and were often broken and are different from the normal, extensive network of filaments that we see with the unmutated wild-type NFL and NFM. When the second NFL mutant was expressed together with the NFM subunit, the NF proteins formed aggregates rather than a filamentous network. The results were published in the December 15th, 2002 issue of *The Journal of Cell Science*.

In ongoing experiments, we are studying the mechanisms by which these abnormal bundles of filaments or aggregated NF proteins could cause CMT. One possibility, which is also supported by findings from other groups that are investigating the effects of mutations in NFL, is that the abnormal bundles of filaments and aggregates could disrupt and block the transport of proteins and organelles through the axons. In a situation analogous to a traffic jam, the blockage caused by the abnormal filament bundles and aggregates will cause the axons to be deprived of components required for its structure and activity, which in turn could lead to axonal dysfunction and, eventually, to the development of CMT neuropathy. ★

Raul Perez-Olle was supported by a post-doctoral fellowship from the CMTA (2002) and is the Carolyn Redell CMTA Fellow (2003). Research in Dr. Liem's laboratory is supported by the National Institutes of Health.

Help Perpetuate the CMTA's Work

You can give hope to thousands of CMT patients by extending your support of the CMTA's programs beyond your lifetime. Whether your legacy is small or large, you can support our programs of education, service, and research by remembering the CMTA in your will.

A bequest to the CMTA is fully deductible for estate tax purposes. Call the CMTA office at 1-800-606-2682 for more information. ★

2002 GRANT RECIPIENT REPORT:

Identification of Novel Genes Associated with Charcot-Marie-Tooth and Related Peripheral Neuropathies: An in silico Strategy Based on Identification of Putative Paralogs

By **GULAM MUSTAFA SAIFI, Ph.D.**

As of January 2003, seventeen genes have been associated with Charcot-Marie-Tooth (CMT) and related peripheral neuropathies. In addition, there are at least twelve CMT-linked chromosomal loci harboring potential candidate genes. Here, an in silico (bioinformatics) strategy is defined to identify these unknown potential candidates. The strategy is based on the rationale that “a gene that is structurally similar, at the amino acids level, to a known CTM gene may have a similar function. Further, if such a putative candidate maps to one of the CMT-linked loci then, it could be considered as a strong ‘positional candidate’.” The methodology is described briefly as follows: The protein sequences of known CMT genes were individually aligned against the human

non-redundant nucleic acids database. The resulting output was analyzed using a suite of programs written in PERL. In other words, the chromosomal location of each of the sequences shown by the output from tblastn was identified. From among these, a subset was identified that contained genes mapping to the twelve CMT-associated loci that harbor potential candidates. One such gene identified, alpha-internexin (INA), has been evaluated in a cohort of approximately 170 CMT cases by mutation detection methods. Two mutations, in two unrelated cases, have been identified. Segregation studies on family members from these two pedigrees did not identify any other individual, affected or unaffected, carrying the corresponding mutation. However, in the first family, the individual carrying the INA mutation is apparently the one who is most severely affected. We

THE POWER OF ONE...

Fundraising by one family



Yohan motivated his family's fundraising efforts on behalf of the CMTA.

Elizabeth Ouellette read about members of the CMTA who swam the Chesapeake and raised huge amounts of money and those who organized golf tournaments and also brought in thousands of dollars. She wanted to do something, herself, but anything as involved as a swim or golf tournament was beyond her scope at this time.

What she could do, she decided, was to celebrate her 40th birthday with a party where all the “gifts” would be contributions to the CMTA and where educating the attendees about the disease would be part of the fun. She hosted her party on December 21, 2002 in her former hometown of Burlington, Vermont, and raised a total of \$3465, which she asked to be given to the research fund.

She and her husband also took advantage of an offer from Hewlett Packard, his employer,

to match any gift made to a recognized non-profit in November. The CMTA will be the beneficiary of another \$2,000 from their family and the matching gift program. Hewlett Packard made the offer in order to stimulate charitable gifts, which have fallen off sharply in the last year because of the economy.

Elizabeth's son, Yohan, has CMT. He is nine years old and lives with his family in Los Altos, California. Now, to continue the fundraising efforts, Yohan's grandmother, Beverly Rooney, is planning to place a contribution box in her diner (Henry's Diner) in Burlington, VT, to raise money in honor of her beloved grandson.

This family demonstrates the power of one—one person, one family, one goal; to raise money to help fight a little-known disease and hopefully change the future for a child. ★

are in the process of obtaining additional clinical data on the second family.

Alpha-internexin is the first neuronal intermediate filament protein expressed in postmitotic neurons of the developing nervous system. In the adult, its expression is restricted to mature neurons in the central nervous system. Mice deficient for both INA (-/-) and NFL (-/-) exhibit no overt phenotypes, suggesting that these loss-of-function animals are not good mouse models for CMT.

To summarize, the in silico paralog-based strategy has the potential to identify candidate disease-causing genes. The above strategy was initiated when thirteen genes were associated with CMT. We are currently redoing this analysis to include the four additional, recently identified, CMT-associated genes. This analysis would also make use of the more recent build of the human genome map (build 31) as opposed to build 28 used in our initial analysis. This strategy could, thus, likely be extended to identify disease-causing genes in other human genetic disorders.

Duplication of 17p11.2-p12 and point mutations in Cx32, MPZ, and PMP22 account for approximately 85% of all CMT cases. With an additional fourteen genes already identified, one may question why one would like to search for additional CMT genes that would be rare and, hence, difficult to identify. The answer lies in the fact that every CMT gene identified would (i) help in establishing a specific diagnosis and (ii) contribute to our understanding of the peripheral nerve biology and illuminate the pathological mechanism involved in the progression of the disease. This is expected to help in better prognosis and could also potentially help in developing better molecule-based therapies.

In addition to the above, we have screened the above-mentioned cohort of nearly 170 CMT cases for mutations in LMNA, a known CMT-associated gene. This cohort has previously been screened for mutations in Cx32, MPZ, PMP22, EGR2, PRX, MTMR2, NEFL, and GDAP1 and, no mutations have been detected. Two novel mutations in LMNA have been identified. We intend to carry out segregation analysis for these two mutations in their respective family members to determine their disease-causing status. Further, we have excluded human homolog of mouse Cx29 (7q14) and SNCG (10q23) as likely candidate genes for CMT by examining for mutations in the same cohort mentioned above. A number of polymorphisms, but no mutations, were identified.

Exciting Gene Discovery Announced

An article about Dr. Valerie Street and Dr. Phillip Chance's work in discovering the gene defect for CMT Type 1C appeared in the December 31, 2002 addition of the Seattle Post-Intelligencer. The article was entitled "Scientists strike back at nerve disorder that cost them their dreams." That title refers to the fact that both Dr. Street and Dr.



Chance had dreams for vocations that were not likely to be compatible with CMT. In Dr. Street's case, she originally hoped to be a veterinarian, handling large farm animals, but knew her lack of strength would eventually make that impossible. Dr. Chance hoped to be a concert clarinetist, but knew that compromised hand dexterity would make that difficult.

Each turned to science and as University of Washington researchers, they are striking back. Their work with three Northwest families led to the new gene discovery, although it has been years in the making. Dr. Street was the CMTA's Post-doctoral fellow in 1999 and at that time, she was doing an analysis of two families who were tentatively called Type 1C because they did not have gene alterations in any of the known locations for type 1. By sifting through genetic data from blood samples, the doctors believe they have now found the gene defect and hope the discovery will lead to new treatment strategies.

Dr. Phillip Chance, a member of the CMTA's Medical Advisory Board, was previously recognized for his work in discovering the under-expression of PMP22 as the cause of hereditary neuropathy with liability to pressure palsy. Dr. Valerie Street is a past recipient of a CMTA post-doctoral fellowship. Their findings were published in the January issue of *Neurology*. ★

Expression studies of TDP1, a gene that has been recently identified in our laboratory as the disease-causing gene for individuals with spinocerebellar ataxia and axonal neuropathy (SCAN1), have been carried out. This gene is expressed at low levels in almost all tissues tested (different regions of the brain, liver, placenta, heart, kidney, lungs testis, and thymus). Expression was highest in brain tissues. Increased expression was also seen in testis and thymus.

We believe that a combination of the above-mentioned in silico approach with relevant biological data, in particular gene expression data from peripheral nerves, will be useful in identifying more CMT-associated genes. ★

2002 GRANT RECIPIENT REPORT:

A Report on the Investigation into the Role of Potassium Channels in CMT 1

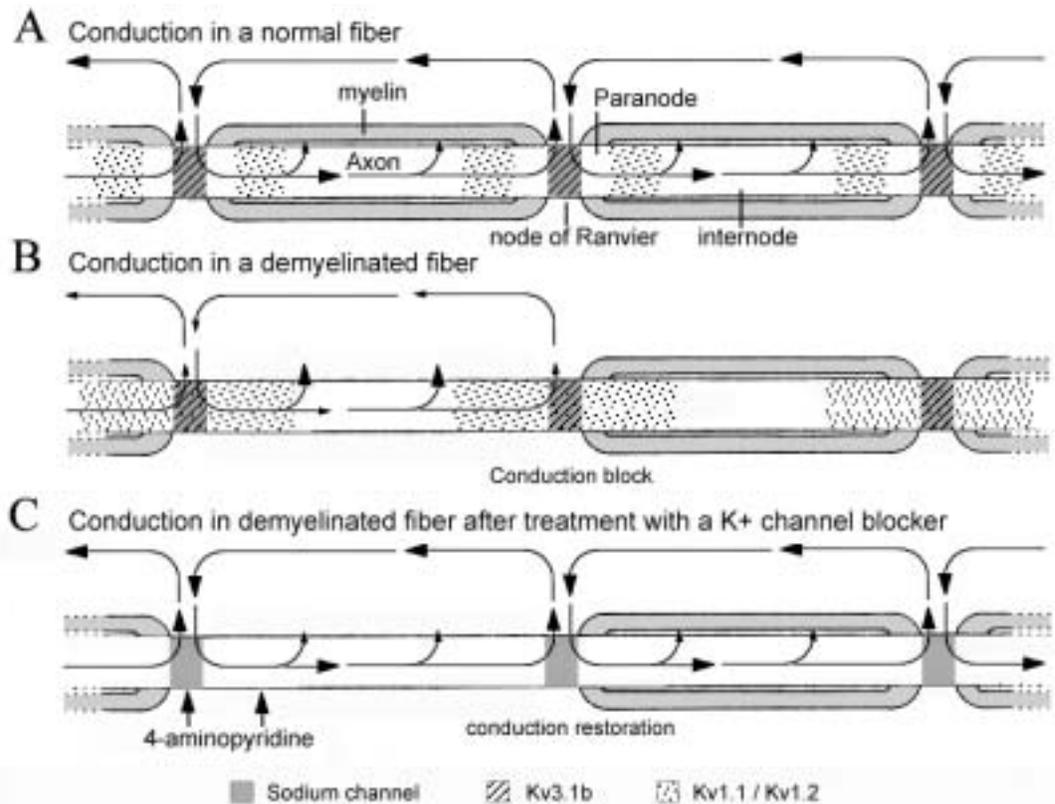
By JEROME DEVAUX, Ph.D.

Axons are the parts of neurons that are specialized to carry electrical signals. They generate and conduct electrical signals in a manner that is fundamentally different from the way electricity moves in wires (where free electrons move according to the voltage). Axons generate their electrical impulses through the tightly regulated opening of different types of ion channels in their surface. Sodium (the chemical symbol is Na^+) is the principle ion that generates bio-electricity, but potassium (the

chemical symbol is K^+) also plays a role.

The surface of all cells, and axons are no exception, is covered by a lipid membrane that is a formidable barrier to ions. Thus, the ion channels are the sole means by which Na^+ and K^+ can move across cell membranes. Na^+ is higher on the outside of cells, so when Na^+ channels open, Na^+ rushes into the axon. Because Na^+ is a charged ion, this generates a current. Na^+ channels are open very briefly—for a few milliseconds (a millisecond is 1/1000

FIGURE 1: ORGANIZATION OF THE ION CHANNELS IN NORMAL AND DEMYELINATED AXONS.



A: In normal myelinated fibers, the propagation of the action potential is saltatory: the action potential “jumps” from one node to the next. Na^+ channels and the K^+ channel Kv3.1b are localized to nodes of Ranvier, whereas the K^+ channels Kv1.1 and Kv1.2 are localized underneath the myelin sheath.

B: After demyelination, the propagation of the action may be blocked at one node due to the loss of the current in the demyelinated axon, caused in part, by the leakage of current through K^+ channels (Kv1.1, Kv1.2 and Kv3.1b).

C: Blockade of the K^+ channels may restore the conduction in the demyelinated axons.

of a second). This brief opening is long enough, however, because only a tiny amount of Na⁺ entering the axon is sufficient to generate an action potential, the bio-electric signal of axons. This is shown in Figure 1.

In myelinated axons, the Na⁺ channels are clustered in the small gaps between adjacent myelin sheaths, called nodes of Ranvier (Ranvier was the scientist who first described them). Thus, the current (carried by Na⁺) enters nodes through sodium channels and travels down the axon. The myelin sheaths reduce the loss of current as it travels down the axon (small arrows in Figure 1A), so that when the current reaches the next node, it can trigger the opening of Na⁺ channels, and the cycle repeats itself (large arrows in Figure 1A). This propagation of action potentials is called “saltatory” conduction, because the action potentials “jump” from one node to the next. For an axon of any given size, saltatory conduction is about 10 times faster than non-saltatory conduction.

The loss of a myelin sheath causes demyelination. Demyelination slows axonal conduction, because too much current gets lost as the current travels down the demyelinated part of the axon (large arrows in Figure 1B). Even worse, if the amount of current that reaches the next node is too small, there may be too little left to trigger the opening of Na⁺ channels (small arrow in Figure 1B). If this happens, then conduction is “blocked”: the axon fails to conduct the action potential even though the axon itself is still intact.

Axons also have several kinds of K⁺ chan-

nels. In normal myelinated axons, one kind (Kv1.1/Kv1.2) is found under the myelin sheath (Figure 1A). Last year, as a post-doctoral fellow in the laboratory of Dr. Steven Scherer and with the support of the CMTA, I found another K⁺ channel, Kv3.1b, at the nodes of Ranvier (Devaux et al., 2003). In normal myelinated axons, all of these K⁺ channels may serve to restore the excitability of the axon after each action potential. In demyelinated axons, however, these K⁺ channels are redistributed, and may contribute to the loss of current in the demyelinated part of the axon (Figure 1B).

Thus, blocking these K⁺ channels seems like a sound strategy for treating demyelinating diseases, including the demyelinating forms of Charcot-Marie-Tooth disease. The theoretical effect of blocking K⁺ channels in a demyelinated axon is shown in Figure 1C. K⁺ channel blockers reduce the loss of current of the demyelinated axon, thereby allowing sufficient current to reach the node of Ranvier, so that an action potential is initiated. “Broad-spectrum” K⁺ channel blockers (drugs that act on many different kinds of K⁺ channels) have been used for the treatment of another demyelinating disease, multiple sclerosis. The drugs that were used in those studies, however, can cause significant side effects, including seizures. Thus, it is important to determine which K⁺ channels are present on axons, so that more specific blockers can be developed. ★

Devaux, J, G Alcaraz, J Grinspan, V Bennett, R Joho, M Crest, SS Scherer (2003) Kv3.1b is a novel component of CNS nodes. (submitted).

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CREATING AWARENESS

Looking Back: Two People Who Started It All

Carolyn Redell and Dr. Howard Shapiro had the foresight back in the early 1980s to recognize the need for an organization that would work on a cure for the disorder they shared and who were willing to work, without thanks or recognition, to form a support side of the group and to raise the funds to further research interests. Thus began the National Foundation for Peroneal Muscular Atrophy, now the Charcot-Marie-Tooth Association.

Carolyn Wohl Redell is credited with starting the first support group specifically dedicated to patients and families with CMT, or peroneal muscular atrophy, as it was more commonly known then.



Carolyn Redell started the first support group for CMT patients and families.

Carolyn and her sister, Eleanor Wohl, were both born in Missouri in the late 1800's and early 1900's and came to New York City in 1910. The family initially thought that only Eleanor had a physical problem and she was diagnosed with Parkinson's after many trips throughout the country for consultations. For many years, the Parkinson's disease masked the fact that something else was wrong with her as well. In her 50's, she found out she also had CMT after a muscle biopsy. Subsequently, her sister, Carolyn, and their children were all diagnosed with CMT.

Eleanor passed away in 1970, but her family remained interested in the disorder that plagued them. In 1982, Carolyn

Redell organized the first support group meeting in her own apartment in the Lincoln Center section of New York City. At that first meeting were Dr. Robert Lovelace, Dr. Howard Shapiro, and her nephews, George and Frank Crohn. Together they formulated plans for an organization which initially hoped to raise money for research, but which also recognized the need for a patient self-help component.

The group grew through word of mouth and networking to about 20-30 members and remained under Carolyn's leadership. Patients were found through Dr. Lovelace at Columbia Presbyterian and through the Institute of Rehabilitative Medicine (now the Rusk Institute), where many patients with CMT were seen and where their progression was watched and monitored. Over the years, the Crohns donated several pieces of equipment to the Institute. The family also organized a fundraising dinner at the Hilton Hotel in New York City to help start the National Foundation for Peroneal Muscular Atrophy.

For her leadership in starting the first support group for CMT patients and for her efforts

(continued on page 10)



Dr. Howard Shapiro now works in the laboratory of Dr. Michael Selzer at the University of Pennsylvania.

LOOKING BACK

(Continued from page 9)

and those of her family in beginning the national organization, the CMTA has proudly awarded a year-long fellowship in her memory to Dr. Raul Perez-Olle at Columbia University for 2003.

The second person who was instrumental in creating a national organization devoted to Charcot-Marie-Tooth disease or peroneal muscular atrophy, was Dr. Howard Shapiro. As is so often the case with rare-disease organizations, it is a patient or a family member who decides to work on bringing the disease to the attention of the public and the medical research world. Such was the situation for Dr. Shapiro, who established the CMTA in 1983 under its original name the National Foundation for Peroneal Muscular Atrophy to provide an administrative financial mechanism for supporting the medical research he was doing at the University of Pennsylvania Medical School from 1980-1985.

At that time, the Board of Directors believed that a more broadly defined program was needed, so Dr. Shapiro's efforts from 1985-1989 addressed the issues of a newsletter, the estab-

lishment of a medical professional's database, a series of regional patient/family educational seminars, starting local family support groups and a videotape program of seminar lectures made available, then, as a lending library. One of his greatest accomplishments was the organization of the Second International CMT Conference with Dr. Robert Lovelace. This conference was held at Arden House (the Columbia University conference center) and resulted in the publication of a textbook based on the lectures given at the Columbia meeting.

These years were not easy ones because of a lack of financial support. An office was provided by the University City Science Center of the University of Pennsylvania and they helped with organization and administrative details. But the day-to-day operations of the foundation were run from Dr. Shapiro's home in Narberth, PA. It was, at best, a small and struggling operation.

The first patient/family mailing list had 24 names on it, most of whom were members of the Crohn family of New York or Dr. Shapiro's own family. By the time he stepped down in mid-1989, the database had, perhaps, 1,200 names of patients and medical professionals. Those were the pre-Internet days and the best mechanism for contacting CMT families was through medical specialists, such as neurologists, orthopaedic surgeons, and physical therapists.

The program has grown quite a bit since those days, but all of Dr. Shapiro's initial ideas of support groups, a newsletter, patient/family seminars, and research symposia remain vital to the CMTA as we know it. In recognition of Dr. Howard Shapiro's lasting impact on the CMTA, the organization, in celebration of its twentieth anniversary, proudly named a grant in his honor which was awarded to Dr. Jerome Devaux at the University of Pennsylvania.

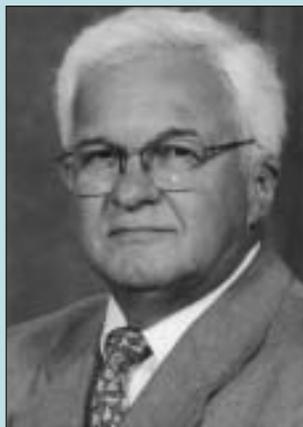
Dr. Shapiro continued to work in medical research, following his time with the organization, and has subsequently filed six domestic patent applications and four in foreign countries. His first US patent disclosed ideas for improved treatment of neurodegenerative diseases, including CMT. From 1999-2000 he worked in a gene therapy program doing analytical protein chemical studies related to the development of adult donor-derived stem cells as future therapeutic agents. Currently, he is working on research related to amyotrophic lateral sclerosis (ALS) in the laboratory of Dr. Michael Selzer at the University of Pennsylvania. Dr. Shapiro remains a dedicated member of the medical research community, the characteristic that first encouraged his establishment of this organization. ★

National Peripheral Neuropathy Conference Scheduled

The 2nd Annual Conference of the NPNC will be held in Dallas, Texas, on May 16-19, 2003 at the Wyndham Dallas North, 4801 LBJ Freeway. The conference is designed for anyone who has peripheral neuropathy and for those who provide their care.

This year, Dr. Carlos Garcia, a member of the CMTA's Medical Advisory Board, will be doing a general session on hereditary neuropathies. He will use two people on stage with him to show the difference between a CMT diagnosis and a non-CMT one. He will also conduct a breakout session with an update on CMT research, along with pain issues.

For further information or to register, call NPNC at 503-591-9412. The cost of registration is \$150 before April 1st. The organizer of this conference is Jeanne Porter, who is the Oregon support group leader. ★



Dr. Carlos Garcia

The CMTA Celebrates Twenty Years of Working to Improve the Quality of Life for People with CMT

The National Foundation for Peroneal Muscular Atrophy (NFPMA) was incorporated in 1983 in Pennsylvania as a 501(c)(3) federally recognized charity. The original founder, Dr. Howard Shapiro, is, himself, a patient with CMT and when he began the organization, he hoped to create interest in the disorder within the medical community while also providing support to patients and families dealing with the little-known problem. From its inception, the NFPMA, now the CMTA, has continued that twofold concern by supporting research on the causes and possible cures for CMT and by focusing on patient education and support.

Only four years after founding the NFPMA, Dr. Shapiro raised the funds and organized the groundbreaking Second International Research Conference at Arden House, the Conference Center of Columbia University. When Arden House was convened, it was known that there were several types and subtypes of CMT, but not all had been identified. In 1987, although gene mapping was in its infancy, genetic research was taking place in two types of CMT, and it was believed that a genetic defect on chromosome 1 was responsible in the majority of CMT families. However, the specific genes had not been identified. At the same time, researchers were working hard to map the location of the gene in x-linked CMT. Following this significant conference, research and journal articles on the disease increased dramatically. A number of significant breakthroughs occurred, the majority of them in type 1 CMT.

Over the next nine years:

- CMT1A was mapped to Chromosome 17.
- The PMP22 (peripheral myelin protein) gene was identified.
- It was found that CMT1A was caused by a duplication of PMP22.
- The cause of HNPP or hereditary neuropathy with liability to pressure palsies was discovered and shown to be a deletion of the same region on chromosome 17 as in Type 1A.

- It was found that point mutations in the Krox 20 or EGR-2 gene, a transcription factor which can turn genes on and off, lead to a previously unknown, and less common, form of CMT, CMT1D. Transcription factors may be extremely important, not only in the future of genetic research, but also in research strategies in affected patients.
- CMT researchers found that a mutation in the MPZ gene is responsible for CMT1B.
- CMT1X, a dominant disorder, is caused by point mutations in the Connexin 32 gene.

Another important breakthrough during this time was the discovery that the degeneration that takes place in CMT1 is due not to demyelination, as was previously believed, but to secondary axonal involvement. This is what gives rise to the disabling atrophy and muscle weakness occurring progressively as affected patients age.

The above insights paved the way for the development of diagnostic blood tests for several types of CMT1A, HNPP, and CMTX, thus providing the definitive answer for many to what type of CMT they have, and also for their families, knowledge of the pattern of inheritance.

Thanks to the generosity of a number of donors, in the summer of 1995 we began awarding research grants and issued our first

(continued on page 12)

President/Chairman of the Board of Directors, Ann Lee Beyer, creates awareness by answering questions and giving out materials about the CMTA at medical conventions.



■ YOU CAN MAKE A DIFFERENCE!

Help us help you, by completing the North American CMT Database Survey. Call the office to receive your copy by mail, at 1-800-606-2682.



The Third International Conference was held in Quebec, Canada in 1998.

OUR FIRST 20 YEARS

(Continued from page 11)

full-year grant of \$35,000 in 1996. Since then, we have awarded 36 grants and fellowships and continue to encourage researchers to investigate topics specific to the unique problems associated with CMT.

Like its predecessor, the Third International Conference on CMT Disorders was a defining moment in the history of CMT research. The conference focused on the latest developments in research and clinical aspects of CMT. There was a special emphasis on the “cross-fertilization” of ideas and perspectives between clinicians, geneticists, molecular biologists, morphologists, and physiologists. A strong effort was made to integrate basic and clinical research and to highlight important areas for future research and collaboration. It put CMT on the international research map as a disease worthy of research interest.

Since the Third International Conference, thirteen new CMT genes have been identified, the last one in January 2003. In addition, we now have diagnostic tests for CMT1B, CMT1D, CMT2E, and CMT4F, bringing the total number of diagnostic tests for CMT up to eight.

To help speed up the pace of CMT research, in 2001, we established a North American CMT Database in conjunction with Wayne State University. Housed at Indiana University School of Medicine, the database provides researchers with ready access to families categorized by their various types and subtypes of CMT. This database is

an exciting accomplishment which will provide physicians and researchers with a more thorough understanding of all the clinical symptoms that accompany the various types and subtypes of CMT, thus allowing them to say with certainty, “THIS IS CMT!”

The database will also provide clinicians and researchers with a better picture of the severity and progression of the disease. In addition, this knowledge will make it easier to diagnose patients, providing a blessing for those who have lived, sometimes for years, with the uncertainty of whether or not they have CMT. The prevalence of CMT will be more easily measured and direction of CMT research may change as a result of the information provided on the surveys. Certainly, the pace of CMT research will be increased by making the information available to qualified researchers. The ease of accessing information may actually stimulate research interest and attract more research funds.

Throughout the years, our major strength has been arranging conferences and bringing researchers together, so following the Third International Conference on CMT Disorders, we made a decision to establish a North American CMT Consortium of clinicians and researchers similar to the very successful European Consortium. The purpose of the symposium is to expand knowledge of CMT by fostering communication and collaboration among researchers. North American CMT investigators with expertise in molecular biology, genetics, neurophysiology, and clinical medicine will be participating. Practical presentations on pain in HMSN1, gait laboratory findings, and urological



dysfunction in patients with CMT will address some of the issues patients ask about each day.

To provide patient education and support, the CMTA began publishing a newsletter in 1987. The goal then, as now, was to provide research information to its readers and to provide patients with the knowledge and understanding to deal effectively with the disease. Beginning with four issues a year, The CMTA Report is now published bi-monthly and has gone from a ten-page publication to one of 24 pages. In addition, the organization publishes a booklet called CMT Facts every 1½ to 2 years which includes useful articles from previous issues of the newsletter and serves as a permanent library of information on CMT.

In 1995, the CMTA published the first text specifically dedicated to Charcot-Marie-Tooth disorders intended to help physicians understand and recognize the disorder. The text was written by members of the CMTA's Medical Advisory Board and edited by Dr. Gareth Parry. The text is currently being rewritten to include new information and updated chapters. In 2000, A Guide About Genetics for Patients was written by Karen Krajewski and Ann Greb to provide information on inheritance patterns for patients and families.

CMT support groups are another important way in which the association serves its members. Support groups are run by caring individuals who provide other CMT patients in their general area a means by which they can interact with others dealing with the same problems and listen to specialists who discuss topics such as surgeries, physical therapy, shoe fitting, and bracing. Support groups are currently located in approximately 15 different areas of the country.

Over the years, patient family conferences have been a useful means of introducing patients to medical specialists in their area who treat CMT and are familiar with the disorder. Conferences have been held in Philadelphia, Wilmington, Detroit, New Orleans, Miami, San Francisco, Los Angeles, Dallas, and Akron. These conferences are typically attended by 75-150 patients and family members.

The CMTA is run by a board of volunteers who establish policy and procedures and who are "hands on" in spearheading fundraising activities such as golf tournaments and "swims for the cure." They generate tens of thousands of dollars earmarked for research on CMT each year.

The Charcot-Marie-Tooth Association's greatest successes have been in accomplishing their twofold goals of supporting, encouraging, and funding CMT research and of providing information and education to its members



Presenter Eddy Fuentes at St. Louis conference in 1997 conducted a small-group workshop.

through conferences, newsletters, publications, and support groups. From an organization of only a few hundred persons, the association has grown to be known throughout the medical world and to serve over 15,000 persons who make inquiries through the Internet, by phone calls, and with letters asking for our information and publications. The first twenty years have been marked by incredible advances in CMT research and knowledge. ★

CMT in the News

Dr. James R. Lupski was the 2002 recipient of the Curt Stern Award, presented to a scientist for major scientific achievement in human genetics that has occurred in the last ten years. The award honors the memory of Curt Stern, an outstanding pioneer in human genetics and a president of the American Society of Human Genetics.

At least 1 of every 1000 births arises "de novo" (a first case) due to a genomic disorder, a term established by the pioneer of this field of research, James R. Lupski. Genomic disorders arise from structural rearrangements of chromosomes and altered dosage of a gene or genes. Dr. Lupski provided the first details of this mechanism in 1991 for Charcot-Marie-Tooth disease type 1A and later made contributions to work in hereditary neuropathy with liability to pressure palsies. Both diseases arise from dosage imbalance of the PMP22 gene. He was awarded for his insight and body of work illuminating the importance of genomic disorders.

The Prudential Spirit of Community Awards singled out Pennsylvania youths for their volunteer efforts. Among those recognized was Lisa Thomas, 17, of Hollsopple, a senior at Conemaugh Township High School in Davidsville, PA, who organized a volleyball tournament in memory of Marah Griffith and raised \$3,000 for patient care and research for the CMTA. ★

Membership and the CMTA

By **CHARLES HAGINS, Executive Director**

The Charcot-Marie-Tooth Association (CMTA) was founded in 1983 to provide a focal point for those involved with CMT—patients, families, medical professionals, research scientists, and anyone who had a need to learn more about the disease.

It is estimated that approximately 150,000 Americans have CMT, but we believe that the reality may be even greater.

The mission of the CMTA is to generate the resources to find a cure, to create awareness, and to improve the quality of life for those affected by Charcot-Marie-Tooth. We cannot fulfill our mission if we do not reach out to a greater number of people suffering from the disease. We need your help. We are asking current members to help us reach out. Every current member knows at least one other person who has the disease and would benefit from a membership. YOU can make a difference by encouraging one new person to join the CMTA.

With additional members the CMTA will represent a greater number of people who share in our mission and that can translate into greater influence that will advance our cause on many fronts. It will also help us average the cost of providing ongoing benefits over a greater number of people.

Each issue of the newsletter has a membership form. Please give it to potential new members or have them contact the CMTA today.

Beginning July 1, 2003, annual membership fees must be increased to \$40.00. We believe that this is necessary in order to continue providing the following benefits to our members:

- Bimonthly newsletter subscription
- Patient-family conferences
- Professional symposiums and published research findings
- Website and discussion forum
- An 800 number for personal information (1-800-606-2682)
- A support group network
- Physician referral lists
- Patient advocacy
- Direct funding of CMT-specific research

We regret that this increase must be implemented, but costs continue to rise as we continue to provide an increasing number of benefits to the people we serve.

We appreciate your continuing support of this organization and we know that as we increase our membership, we will attract greater attention from the medical community. There is strength in numbers! ★

Board Sets Ambitious Goals for the New Year

The CMTA Board of Directors held their first meeting of the new year on January 9th and 10th in Syosset, Long Island, NY. The board discussed and voted to:

- Fund four CMT Post-Doc fellows for 2003
- Come up with a plan to raise money to fund more research grants
- Put out a call to CMT researchers to contact us about ideas for research
- Ask researchers about projects currently “in progress” that need more funding to complete, that we might consider funding.
- Establish more CMTA support groups.
- Initiate a membership drive to reach more patients and their families
- Formulate a plan to improve the CMTA web site
- Create a contact list of media in metropolitan areas and periodically send them press releases ★

Details of these plans will be discussed in upcoming newsletters.



IMPROVING LIFE

Keeping a Medical History for Your Children

By PAT DREIBELBIS

Parents are an essential part of their child's healthcare team. When medical personnel ask for vital facts, an accurate record of the child's history of illness, medications, and surgeries can be impossible to remember, but having a written record of all those facts can literally be life-saving. For that reason, investing a little time from the beginning can make a notebook of useful medical facts a viable way to keep everyone informed about your child's medical health.

Usually, a looseleaf notebook is an easy way to start. Much like you might keep a "baby" book of important milestones and events, you simply keep a record of all his/her pertinent medical history.

You might begin with a title page that includes the child's name, social security number, and medical insurance information (identification number and group name, etc.). The first page would be just like the one in baby books where you list all the immunizations they have received with the dates the shots were given. If your child had any adverse reaction, list it here.

The second page might list all drugs your child has been given and, again, any adverse reactions to those drugs. Also list here any allergies your child has. These could be allergies to specific drugs or seasonal allergies, or asthma. If your child had a reaction to any medication, give the date and the nature of the reaction.

Next, list all the medical problems your child is dealing with. You might begin with the diagnosis of CMT and then consider each specific problem, such as ADHD or scoliosis or any other diagnosed problem. Because you will use this notebook with non-medical personnel as well as doctors (such as school counselors or gym teachers), you should include a brochure about CMT as well as any other simple explanations of the limitations the diagnosis places on your child's performance.

If your child takes medication on a daily basis, you should create a page discussing the medications, the times they are taken, and the dosage strength. If your child goes to camp, is hospitalized, or just stays with friends or relatives for a weekend, this page will be invaluable.

Medical treatments should be recorded next. A history of any tests that have been administered, any surgeries performed, and any therapy programs your child has participated in will help medical personnel decide what to do next. With surgeries, include the date performed, the name of the procedure (tendon transfer, tendon lengthening), the name of the doctor who performed the surgery, and any other relevant information. The more information you provide, the less likelihood that tests will be duplicated for no real reason.

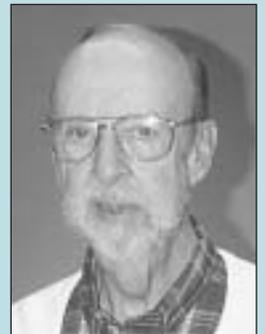
Finally, you should have a list of all doctors who have treated your child. List their names, medical specialties, address, phone number, fax number, email address, and any other contact information. Not only is this information helpful while your child is young, but it can follow your child all through his life and provide the history of care and treatment that he might need to recall when he is older and beginning his own family.

A medical history requires some work to assemble, but it is easy to maintain and in an emergency, it is crucial to have accurate information readily available. ★

SUPPORT GROUP LIAISON ANNOUNCED

Bob Budde, former leader of the Kentucky support group for four years, has agreed to be the liaison between the support groups and the CMT Association. He will serve in this capacity for 2003. Bob can be reached by telephone at 859-255-7471 or email at rebudde@aol.com. He will contact the support groups regularly to see how the groups are doing and how the organization can help and support them more effectively. As Bob said, "The CMTA mission statement in a few words defines what we are all working to achieve. My job will be to find out what the support groups need and to provide it, when possible. Different groups work in different ways and I look forward to talking about how you each perform." We are all working toward the vision of a "world without CMT!"

The CMTA has also arranged for Athena Diagnostics to make their area representatives available to speak to support groups on the genetics of CMT and the availability of the DNA tests. ★



Statins Can Cause Nerve and Muscle Problems

from Quest October, 2002

(Editor's note: Because of the volume of mail regarding this subject, we are presenting the article regarding the problems in the use of statins and the abstract of the study that prompted the article.)

Medications used to lower blood cholesterol levels are associated with a somewhat increased risk of damage to nerves and muscles, studies say.

The so-called statin drugs, with names like atorvastatin (Lipitor), fluvastatin (Lescol), lovastatin (Mevacor), pravastatin (Pravachol), and simvastatin (Zocor), are taken by millions of middle-aged and elderly people and are considered highly beneficial in protecting against cardiovascular disease when dietary and other lifestyle measures fail.

However, several studies, including a large Danish study reported by David Gaist and colleagues in the May 14 issue of *Neurology* (see abstract below), suggest a needed increase in awareness of potential side effects of these popular drugs.

The Danish study found a slightly increased risk of nerve damage, while other studies (such as one in the September 2001 issue of *Annals of*

Pharmacotherapy and one in the September 2001 issue of *Journal Epidemiology*) have concentrated on muscle damage. All studies so far have been done in patients without any underlying neuromuscular disease.

It isn't clear that people with neuromuscular diseases are unusually susceptible to the nerve- or muscle-damaging effects of statins. However, a worsening neuromuscular disease in someone taking a statin medication could be a warning. Unusual muscle pain or cola-colored urine in someone on a statin may indicate acute muscle destruction and should prompt an immediate call to a physician.

"Statins need to be added to the list of potentially contraindicated medications in patients with any type of neuropathy [nerve problem] or any type of muscle disorder, but especially in patients with Charcot-Marie-Tooth disease," noted Carlos Garcia, a specialist in nerve and muscle diseases who heads the MDA clinic at Our Lady of Lourdes Hospital in Lafayette, LA. ★

From *Neurology*
May 2002 (Volume 58, Number 9)

STATINS AND RISK OF POLYNEUROPATHY: A CASE-CONTROL STUDY

Statin treatment has emerged as a popular therapy for the primary and secondary prevention of coronary artery disease. In addition, recent evidence has suggested that it may also help reduce the risk of stroke. Although the benefits appear substantial, the agents have been associated with some damaging effects including the development of myopathy and polyneuropathy. Gaist and colleagues conducted a nested case control study to estimate the relative risk of idiopathic polyneuropathy in statin users.

The study population was obtained from the county of Funen, Denmark (465,000 inhabitants; 9% of the Danish population), and the cases were identified from a patient registry. In order to determine exposure to statin therapy, the investigators reviewed a prescription registry. All of the cases were assigned an index date that corresponded to the earliest of the following events: date of first contact with the hospital or date on which the patient's physician made the diagnosis of polyneuropathy. The control group

(n = 25) was randomly chosen among the residents of Funen and matched for age, sex, and calendar time (index date).

Investigators identified 166 cases of idiopathic polyneuropathy. The group consisted of 35 definite cases, 54 probable, and 77 possible cases. The results revealed that statin users were at a 4- to 14-fold higher risk of developing idiopathic polyneuropathy than the background population. The odds ratio relating idiopathic polyneuropathy with statin use was 3.7 (95% CI 1.8-7.6) for all cases and 14.2 (5.3-38.0) for definite cases. The relative risk estimates (odds ratio) of polyneuropathy in current statin users were 4.6 (2.1-10.0) if all cases were included, 8.0 (3.4-18.2) in probable and definite cases, and 16.1 (5.7-45.4) in definite cases only. For those who had used statins for 2 or more years, the odds ratio of definite idiopathic polyneuropathy was 26.4 (7.8-45.4).

Although the results of the study demonstrated a risk of developing polyneuropathy, particularly with long-term statin exposure, further investigation is needed to determine the cause of the polyneuropathy from statin use and what factors are associated with its development. ★

Gaist D, Jeppesen U, Andersen M, Garcia Rodriguez LA, Hallas J, Sindrup SH *Neurology*. 2002;58(9):1333-1337

CMTA Support Groups

Arkansas—Northwest Area

Place: Varies, Call for locations
Meeting: Quarterly
Contact: Libby Bond, 501-795-2240
E-mail: charnicoma57@yahoo.com

California—Berkeley Area

Place: Albany Library, Albany, CA
Meeting: Quarterly
Contact: Gail Whitehouse
E-mail: gwhite@earthlink.net

California—Northern Coast Counties (Marin, Mendocino, Solano, Sonoma)

Place: 300 Sovereign Lane,
Santa Rosa
Meeting: Quarterly, Saturday, 1 PM
Contact: Freda Brown, 707-573-0181
E-mail: pcmobley@mac.com

Colorado—Denver Area

Place: Glory of God Lutheran Church
Wheat Ridge
Meeting: Quarterly
Contact: Marilyn Munn Strand,
303-403-8318
E-mail: mmstrand@aol.com

Kentucky/Southern Indiana/ Southern Ohio

Place: Lexington Public Library,
Northside Branch
Meeting: Quarterly
Contact: Martha Hall,
502-695-3338
E-mail: marteye@mis.net

Massachusetts—Boston Area

Place: Lahey-Hitchcock Clinic,
Burlington, MA
Meeting: Call for schedule
Contact: David Prince, 978-667-9008
E-mail: baseball@ma.ultranet.com

Michigan—Flint

Place: University of Michigan,
Health Services
Meeting: Quarterly
Contact: Debbie Newberger/
Brenda Kehoe, 810-762-3456

Minnesota—Benson

Place: St. Mark's Lutheran Church
Meeting: Quarterly
Contact: Rosemary Mills, 320-567-2156

Mississippi/Louisiana

Place: Clinton Library, Clinton, MS
Meeting: Quarterly
Contact: Flora Jones, 601-825-2258
E-mail: flojo4@aol.com

Missouri/Eastern Kansas

Place: Mid-America Rehab Hospital,
Overland Park, KS
Meeting: First Saturday bimonthly
Contact: Lee Ann Borberg, 816-229-2614

Missouri—St. Louis Area

Place: Saint Louis University
Hospital
Meeting: Quarterly
Contact: Carole Haislip,
314-644-1664
E-mail: c.haislip@att.net

New York—Greater New York

Place: NYU Medical Center/
Rusk Institute, 400 E. 34th St.
Meeting: 2nd Thursday of each month
Contact: Dr. David Younger,
212-535-4314,
Fax 212-535-6392
Website: www.cmtnyc.org

New York—Horseheads

Place: Horseheads Free Library on
Main Street, Horseheads, NY
Meeting: Quarterly
Contact: Angela Piersimoni,
607-562-8823

New York (Westchester County)/ Connecticut (Fairfield)

Place: Blythedale Hospital
Meeting: 3rd Saturday of each
month, excluding July &
August
Contacts: Diane Kosik, 914-937-2013,
Beverly Wurzel,
845-783-2815
E-mail: DianeK319@optonline.net or
cranomat@frontiernet.net

North Carolina—Archdale/Triad

Place: Archdale Public Library
Meeting: Quarterly
Contact: Ellen (Nora) Burrow,
336-434-2383

North Carolina—Triangle Area (Raleigh, Durham, Chapel Hill)

Place: Church of the Reconciliation,
Chapel Hill
Meeting: Quarterly
Contact: Susan Salzberg,
919-967-3118 (evenings)

Ohio—Greenville

Place: Church of the Brethren
Meeting: Fourth Thursday,
April–October
Contact: Dot Cain,
937-548-3963
E-mail: Greenville-Ohio-CMT@
woh.rr.com

Oregon/Pacific NW

Place: Portland, Legacy Good Sam
Hospital, odd months
Brooks, Assembly of God
Church, even months
Meeting: 3rd Saturday of the month
(except June and Dec.)
Contact: Jeanie Porter,
503-591-9412
Darlene Weston,
503-245-8444
E-mail: jeanie4211@attbi.com or
blzerbabe@aol.com

Pennsylvania—Philadelphia Area

Place: University of PA, Founders
Building, Plaza Room A
Meeting: Bimonthly
Contact: Amanda Young,
215-222-6513
E-mail: stary1@bellatlantic.net

Pennsylvania—Johnstown Area

Place: Crichton Center for Advanced
Rehabilitation
Meeting: Bimonthly
Contact: J. D. Griffith,
814-539-2341
E-mail: jdgriffith@mail.charter.net



WRITE TO US!

Pat Dreibelbis, Editor

The CMTA Report

CMTA

2700 Chestnut Pkwy.

Chester, PA 19013

The CMTA reserves the right to edit letters for space.

The CMTA Report

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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.

Letters to the Editor

Dear CMTA:

On page 15 of your Fall 2000 CMTA Report you had an item about Albuterol possibly helping with CMT. I started using an inhaler (I don't have asthma) and feel it has helped a lot with balance. I use Maxair, which is *Perbuterol*, but works in the same way as *Albuterol*.

—M.B.

Dear CMTA:

I just finished reading Mitch Warner's article on the Helios braces and I just had to write you of my recent visit to his office in Las Vegas. I learned of Mitch through the other CMT periodical, the CMT Today, so I called him after reading his web pages on treating CMT. He had me follow to the letter what he says in the article. He does what he says he will do and more. I have CMT type 2 and have fallen arches to the extent that my left foot is deformed. He detected this from the go. He has made me a brace for the left foot that corrects that deformity. The right foot took less work. I immediately was able to stand alone without finding something to touch or hold on to. I took off walking faster and with less effort and more naturally than before. My wife who accompanied me to his office had tears in her eyes when she witnessed the restoration of balance and vigorous walking with little effort. I am having some discomfort with my feet being tender, but was assured that my feet would become accustomed to the correction. It has taken me a couple of weeks to get my skin toughened up until I can wear them all day long. I received them on December 6, 2002. I just wanted to assure your readers that these are the ultimate in braces that can be found. I have tried 4 different types of braces from 3 different orthotists and I can speak from experience that Mitch knows what he is doing and whatever he tells you it will be the truth. Sure, they are more expensive than any of the other braces that I have tried, but these are made to last where my others would break after 3 months of wear. I can be reached by e-mail at foxclu@ameritech.net if anyone wishes to question my experience with Mitch's Helios braces.

Dear CMTA,

I have found a wonderful gadget. It's a device to make anything you plug into electrical outlets remote controlled. They are sold in Target after Christmas for about \$6.00 each. They

normally cost about \$20. I use them on all my lamps, fans and even the air conditioner. Anyone with a disability could definitely use them. The manufacturer is NCC, Inc. (1-800-730-3703) Model #PT-TX01P. They are made for outdoor and indoor Xmas decorations and seem to be available only during the holidays. They come in single and double base units. Black and Decker also makes them, but they sell for about \$25.

—Angh from the Internet

Dear CMTA,

Two of the helpful things my husband has done for me are to replace all the round door knobs with lever style handles and all of our small round lamp switches with the key style. These small changes make it easier for me to remain independent around the house.

—Note in contribution envelope

Dear CMTA,

From my picture, I hope you can see that the pen point comes out between my index and middle fingers. The pen's weight and control are helped by removing the cap from the end. I use permanent roller ball/Gel-writer pens on regular paper and ultra-fine Sharpies on photos. They do not require pressure for dark smooth lines.

—J.I., MD



Dear CMTA,

I am so grateful that someone is getting the word out. So far, all of my 2nd cousins have this disease and one of my uncles. I don't know if any of my first cousins have this disease yet, but it is a constant fear in all of us. I don't totally understand this disease or what causes it or all that it might affect. But at least the name is out there now. Five years ago, very few had ever heard of it and I'm sure there are still some who haven't heard of it, but at least you have helped make progress in that area. Thanks.

—T.L.

Ask the Doctor

Dear Doctor,

I'm wondering if there is an association between CMT and diabetes. There seem to be many people with CMT who are also Type 2 diabetics. Or, is it that we often are not able to exercise easily and that puts us more at risk of acquiring diabetes?

The Doctor Answers:

There is no recognized relationship between CMT and diabetes. Diabetes is a very common disease. An estimated 12-15 million Americans have diabetes and there are perhaps as many as 200,000 people with CMT. That means there are going to be a lot of coincidental associations.

Dear CMTA,

Can seizures be caused by CMT?

The Doctor Answers:

CMT and seizures don't usually go together. If someone has CMT and seizures, it is either an unrelated coincidence (seizures are not rare) or some very unusual disease and not typical CMT. Also, petit mal is a very specific neurological diagnosis that requires EEG confirma-

tion and does not refer to people who simply feel queasy while seeing flashing lights.

Dear Doctor:

Is it safe to take Avelox antibiotics if someone has CMT type 2? I have heard that Cipro is not good and I would like to know if Avelox has the same effect.

The Doctor Answers:

Otherwise known by the generic name of moxifloxacin (it is a "relative" of Cipro), it was approved by the Food and Drug Administration in December, 1999 to treat bacterial infections of the upper respiratory tract, as well as skin infections. In patients with certain cardiac conditions, those with what is called prolonged QT intervals (on electrocardiograms), the medication should be avoided; this would also apply to patients receiving cardiac medications, e.g., quinidine; procainamide (Pronestyl); and amiodarone (Cordarone). Caution should be employed if patients are taking: cisapride (Propulsid) and certain psychiatric medications like amitriptyline (Elavil). ★

Support Group News

■ Minnesota - Benson

The group met on September 28th and was attended by six people with CMT and five family members who support them. Everyone went away from the meeting with some knowledge they didn't have when they came (which is always the goal.) The topic for discussion was "The Many Feet of CMT."

The next meeting will be on April 5, 2003, and the guest speaker will be Medical Advisory Board member, Dr. Gareth Parry. The group is excited to have such a noteworthy guest to answer questions about CMT.

■ New York - Horseheads

The meeting location for the Horseheads CMT Support Group has been changed to the Horseheads Free Library on Main Street in

Horseheads, NY. The group will continue to meet quarterly. The group is encouraged that CMT is being publicized at medical conventions. The group has expressed a wish that the doctors in their area become more up-to-date and interested in CMT. To that end, the group intends to invite them regularly to attend the support group meetings.

**The CMTA lives its mission
so that the vision of
a world without CMT
can be achieved.**

MEDICAL ALERT:

These drugs are toxic to the peripheral nervous system and can be harmful to the CMT patient.

Adriamycin
Alcohol
Amiodarone
Chloramphenicol
Cisplatin
Dapsone
Diphenylhydantoin (Dilantin)
Disulfiram (Antabuse)
Glutethimide (Doriden)
Gold
Hydralazine (Apresoline)
Isoniazid (INH)
Megadose of vitamin A*
Megadose of vitamin D*
Megadose 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.

*A megadose is defined as ten or more times the recommended daily allowance.



What is CMT?

- ... is the most common inherited neuropathy, affecting approximately 150,000 Americans.
- ... 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 also known as peroneal muscular atrophy and hereditary motor sensory neuropathy.
- ... is slowly progressive, causing deterioration of peripheral nerves that 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).
- ... 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, which means if one parent has CMT, there is a 50% chance of passing it on to each child.
- ... Types 1A, 1B, 1D (EGR2), 1X, HNPP, 2E, 4E, and 4F can now be diagnosed by a blood test.
- ... is the focus of significant genetic research, bringing us closer to answering the CMT enigma.

The CMTA Report

Information on Charcot-Marie-Tooth Disorders from the Charcot-Marie-Tooth Association



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