

# The CMTA Report

WINTER 1997

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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.*

## First Armington Research Fellow Announced

**D**r. Agnes Jani of Wayne State University in Detroit, Michigan is the recipient of the first Armington Research Fellowship. She received the award in January and will work throughout 1997 with Dr. Michael Shy and Dr. John Kamholz on gene therapy in an animal model of CMT1. An outline of her winning proposal follows.

Charcot-Marie-Tooth disease (CMT) is the most common inherited disease of nerves, the structures that connect the spinal cord to muscles. The most frequent form of CMT (CMT1) is caused by genetic abnormalities in Schwann cells; the cells which make the insulation or myelin that ensheaths nerves in the peripheral

nervous system. CMT1A is caused by a duplication or doubling of a piece of chromosome 17 containing the peripheral myelin protein 22 (PMP22) gene. CMT1B is caused by mutations in the peripheral myelin protein zero (P<sub>0</sub>) gene. Both of these proteins are necessary for Schwann cells to make normal myelin in the peripheral nervous system. Recent advances in understanding the causes of CMT have not as yet led to corresponding advances in treatment.

The goal of Dr. Jani's project is to use the techniques of molecular biology to correct the genetic defect in CMT1B Schwann cells, and thus to ameliorate the clinical effects of this dis-

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*Left to right, Michael Shy, M.D., Agnes Jani, M.D. and John Kamholz, M.D., Ph.D pose in their lab at Wayne State University.*

# CMTA's Anita Harding Fellowship Report

By Dr. Peter Denton

*“Dr. Peter Denton’s work during the past year was very successful as it established a YAC contig for the first time across the CMT2A region and has allowed us to move to the next step of looking for candidate genes. The Anita Harding Fellowship came at a critical time as it allowed Peter to continue his work on CMT2A between funding sources for the project. We are very grateful to the CMTA for their support .”*

—Dr. Jeffrey Vance,  
Duke University

**CMT** has two basic forms, CMT1 and CMT2. Patients with CMT1 have slow nerve conduction velocities (NCV) due to abnormalities in the myelin covering that surrounds the nerve. Conversely, CMT2 has normal NCV but poor transmission of the nerve impulse due to a presumed abnormality of the nerve itself. Most of the previous genetic work has been on CMT1, with three genes identified that cause this type: one on chromosome 17 (PMP22); a second in the middle of chromosome 1 (P<sub>0</sub>); and a third on the X chromosome (Connexin 32). No genes have been identified so far as causing CMT2, even though it accounts for at least one third of all CMT cases.

Our laboratory is working on CMT2, looking for the gene that causes one form of CMT2. We gathered DNA from many families with CMT and, using known areas in DNA that vary from one individual to another (polymorphisms), localized one form of CMT2, CMT2A, to the very top of chromosome 1. Although this gene has been shown to cause CMT in several families, in many other families it does not. In some families the disease is caused by another CMT2 gene, CMT2D, that was recently localized by Dr. Ionasescu in Iowa and lies on chromosome 7. In at least half of the CMT2 families, we still do not know where the gene disease-causing gene is located.

Finding a chromosome location for a particular type of CMT is just the first step. Having identified the location of the CMT2A gene, our laboratory is now working on identifying the actual gene that causes the disease. To do this

we must have a great quantity of DNA from the CMT2 region so that we can do experiments which will eventually find the gene. This is too much to get from one or several individuals. Therefore, over the past year I have been working on reproducing the area that contains the CMT2A gene in large pieces of DNA called yeast artificial chromosomes (YACs). To make these YACs the DNA from a person was cut up into small pieces of about a million base pairs and then put into the fake YAC chromosomes. These can be grown in yeast like real chromosomes and allow enough copies of one piece to be studied easily. I succeeded in reproducing the CMT2A area with many YACs, so that the CMT2A gene lies on one of these YACs. This work has shown us that the area containing the CMT2A gene is very unstable and breaks a lot, (producing what are known as crossovers). The next step is to use this framework of YACs and identify genes that are important in the nerve and spinal cord. Each of these genes will be examined until the CMT2A gene is found.

I wish to thank the CMTA for the Anita Harding Fellowship. The past year has been very rewarding and important to the research. In times when the government is cutting back on research funds, it allowed work to continue on CMT2A. Because of the success of this work, Dr. Vance’s laboratory has now received a grant from the National Institutes of Health to keep this work going to identify the CMT2A gene. Hopefully, once we identify this gene, it will give us a clue to the identity of the other CMT2 genes.

## Supporting the CMTA

To improve our services and internal operations, we are implementing a fundraising schedule. The membership year will run from July 1 to June 30. Membership dues will be solicited in mid-June. You will receive a membership card with this summer’s membership renewal.

Two other fundraisers occur during the year. They are the Annual Appeal, scheduled for November, and the Research Appeal, which takes place in February of each year.

Membership dues support daily operating expenses: publishing this newsletter, staffing the office, and operating the toll-free telephone service. However, the annual appeal provides the additional money needed to help the organization expand and become more recognized in the medical and scientific communities. It is that growth which enables us to improve and enlarge our services to our members. The research appeal generates money specifically dedicated to funding various types of CMT research and is restricted to that alone.

We hope this information both clarifies the use of contributions and the importance of continuing member support.



## First Armington Fellow

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ease in patients. Successful gene therapy in CMT1A or CMT1B will require the development of techniques to introduce genes into Schwann cells in peripheral nerves. Developing this system is the focus of Dr. Jani's grant proposal. To introduce new genes into Schwann cells, Dr. Jani is starting with a common respiratory virus known as an adenovirus. Adenoviruses are all around us and, outside of an occasional sore throat, do not cause any pathology in humans. By genetic engineering, human adenoviruses can be altered into what are known as adenoviral vectors. These adenoviral vectors are no longer able to divide and cause an ongoing infection. However, they can be used to introduce new genes into cells whether the target cells are dividing or not, which is an important issue in the peripheral nervous system since Schwann cells in contact with their nerves are not dividing. Dr. Jani's proposal is to develop the technology to use adenoviral vectors to introduce the  $P_0$  gene into mice which do not have  $P_0$  and therefore have a disease which is similar to CMT1B.

$P_0$  knockout mice are mice which have been genetically engineered in such a way that they cannot make  $P_0$ . They therefore develop a severe demyelinating neuropathy that starts in "childhood" and in many ways mimics CMT1B. A colony of these mice is maintained at Wayne State University. Dr. Jani has generated an adenoviral vector which can introduce  $P_0$  into the cells the vector "infects". We are preparing to introduce  $P_0$  into Schwann cells of  $P_0$  knockout mice with this vector. In preliminary studies using a gene which turns infected cells blue instead of introducing  $P_0$ , Dr. Jani and other members of Drs. Shy and Kamholz's laboratories have demonstrated that adenoviral vectors can be used to introduce genes into Schwann cells in living peripheral nerves in animals. With proper manipulation of the immune system, expression of these genes can persist in the nerve for up to several months. We thus believe that replacing  $P_0$  by adenoviral vectors in  $P_0$  knockout mice has the potential to remyelinate these nerves and begin to develop the basic methodology which will ultimately lead to effective gene therapy in humans with CMT.

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Here is an excerpt from a chapter in the publication, "Current Therapy in Neurologic Disease" Fifth Edition, Edited by Richard T. Johnson, M.D. and John W. Griffin, M.D., published in October, 1996. Both Dr. Garcia and Dr. Griffin are members of the CMTA Medical Advisory Board.

# Treatment of Familial Neuropathies

By Carlos A. Garcia, M.D.

## *Clinical Features*

The phenotypes of all forms of CMT are generally similar. However, there is a wide range of variation in the clinical severity within the same genotype in unrelated individuals as well as individuals in the same family, including identical twins. The symptoms of the most frequent form, CMT1, usually appear in the first decade or early in the second decade of life. Children with the disease often walk on their toes. Adults consult a physician because of abnormalities of gait, foot deformities, or loss of balance. Tripping over objects on the floor and ankle sprains are frequent because of foot drop produced by weakness of the peroneal and anterior tibialis muscles. This leg muscle weakness and foot drop are also the cause of the steppage or equine gait. Pes cavus deformity is not seen early in the disease and when it does appear, it seems to progress with age.

Having short, high-arched feet makes it difficult for the patient to find shoes that fit. Hammer toes are a late finding and produce pain over the dorsal surface of the toes where they rub against the shoes. Atrophy of the legs may be a prominent feature in some patients, giving the stork legs or inverted champagne bottle appearance, but a thicker layer of subcutaneous fat may mask the leg muscle atrophy. Leg cramps are a frequent complaint and are worse after long walks.

Weaknesses of the intrinsic hand muscles usually occur late in the course of the disease but are not usually related to the degree of leg weakness or atrophy. In severe cases, the wasting of the intrinsic hand muscles may give the appearance of claw hands. The most frequent complaints concerning hand involvement are difficulty opening jars, turning door knobs, and holding pens and eating utensils. Patients also have difficulty using zippers, buttoning and unbuttoning clothes, and manipulating small objects with their fingers. Hand tremors are a frequent complaint and are most likely related to an essential tremor.

Muscle stretch reflexes disappear early in the ankles and later in the patella and upper limbs. The plantar reflex is frequently flexor or shows no response. Sensory involvement to any significant degree is rare, but decreased pain to pricking in stocking distribution may be seen in some patients. Vibratory sense is the most frequently affected modality.

Definitive diagnosis of CMT can frequently be made and requires the family pedigree, neurological examination, NCV (nerve conduction velocity), and DNA studies. The inheritance pattern, clinical features, electrophysiology, and progression of CMT1A, B, and C are similar except for the slightly greater clinical severity of patients with the PMP22 or MPZ9 (CMT1B) point mutations. Distinguishing between the types is only possible with DNA tests. The same rule applies for CMTX1 and CMTX2. Sporadic cases of CMT in which there is no family history can be due to an autosomal dominant spontaneous mutation, autosomal recessive inheritance, or X-linked inheritance. Spontaneous mutations are frequent in CMT1A.

## *Therapy*

The plan for a therapeutic regimen begins with an accurate diagnosis. Genetic counseling of the parents of an affected child or adult patients is important and should be based on the inheritance pattern. The young adult patient should be informed of the chances of having an affected child. However, the positive aspects of normal life expectancy, lack of involvement of the central nervous system, and the fact that most patients hold jobs, can have a family, and lead fulfilling lives should be emphasized.

## *Medications*

No medical treatment is available at the present time. However, a few reports have described steroid-responsive forms of CMT1 and HNPP. Unless PMP22 is shown in the future to be involved in the cause of immune neuropathies, there is no justification at this time for putting patients at risk for having multiple and serious side effects associated with the long-term use of this kind of medication. The tremor caused by CMT is aggravated by coffee and nicotine and responds to beta-blockers. Nonsteroidal anti-inflammatory medication and analgesics relieve lower-back pain and leg pains. Most important in considering the use of medication is the avoidance of drugs, including alcohol, that can worsen the neuropathy.

## *Nutrition*

General information for the CMT patient should include nutritional advice with instructions for maintaining a normal weight. For obese

patients, a weight-loss program is recommended to reduce the strain on weight-bearing muscles and joints. An appropriate weight for the patient's size and frame will make ambulation easier and less painful in the legs and back.

### *Physical and Occupational Therapy*

Evaluation is recommended for all patients as soon as the diagnosis is made. An adequate exercise program has to be adjusted to the patient's level of functioning and needs. The goals of the therapy should be directed toward maintaining function and comfort, ensuring safety, and protecting joints. The program should include active and resistive exercises that can help patients conserve energy, function safely, and decrease the discomfort produced by joint contractures. The patients should learn how to do their own exercises on a daily basis. Emphasis should be placed on active and resistive exercise of the dorsiflexor and plantar flexor muscles as well as the muscles that supinate and pronate the foot. It is important to keep the intrinsic muscles of the hand and the finger flexors and extensors active by using exercise putty. Hand splints may be needed during the day or night to improve function. Finally, the occupational therapist can advise the patient about the use of tools for buttoning, holding pencils or eating utensils, and zipping a zipper. Tightness of the heel cord is frequent in all patients with CMT1 but is severe in children and is the cause of toe walking when the disease manifests in early childhood. Stretching of the heel cord by daily therapy is important. Three months after intensive heel cord stretching has failed, surgical intervention needs to be considered.

### *Orthotics*

Braces should be recommended by the physician, preferably a neurologist familiar with neuromuscular disorders, with the input of the physical and occupational therapist. Early in the course of the disease, high-top shoes or boots that fit properly will be enough to hold the weak feet and improve gait. Obtaining shoe inserts that are molded to the patient's feet is the next step. Custom-made devices that are properly designed, fabricated, and fitted are very important for the patient. The braces need to be easy to put on, comfortable, and cosmetically pleasing. Leg braces such as molded ankle-foot

orthoses (AFOs) are the most frequently prescribed braces used to minimize an abnormal steppage gait. The brace needs to be used with appropriate shoes, such as laced or Velcro-fastened sneakers. Dynamic AFOs that allow mobility to the ankle can be prescribed in patients that have not developed heel varus. Once the brace is fitted, the patient needs to examine the skin daily to check for pressure areas. AFO braces need to be adjusted periodically in children who are growing.

### *Surgical Options*

Surgical procedures should be considered and the different options should be discussed with the patient, the treating physician (preferably a neurologist), the orthopaedic doctor who will perform the surgery, and the physical therapist. The orthopaedic surgeon who is consulted to perform the procedure needs to be familiar with the disease process and understand the nature of the progressive disorder. Timing of the surgery is an important factor in deciding the type of surgery and is also an important factor in a successful procedure. There are three areas that may need surgical interventions: the hip joint, the feet, and the hands. Severe hip dysplasia in children with CMT may be asymptomatic or minimally symptomatic and can go undetected until early adolescence. The signs of hip dysplasia are limping on the affected side, mild hip pain aggravated by ambulation, or mild weakness of hip abductors. The lesion is frequently bilateral and needs to be surgically corrected. Surgery of the feet is directed toward correcting the pes cavus, the heel varus, and the hammer toes. Different types of procedures are used depending on the foot deformity. Fasciotomies or plantar releases can be done early in the disease to correct the high arch of the foot. Bony deformities are treated by osteotomies. Hammer toes are corrected by tendon transfers or fusion of interphalangeal joints. Triple arthrodesis of the ankle may be necessary in some patients. Surgical procedures of the hands are directed toward restoring the strength of weak fingers and are accomplished by transfer of tendons from strong to weak muscles. Hand surgery can restore strength to the thumb to repair pinching with the index or middle finger. Finally, knowledge of the molecular mechanisms of this group of disorders may eventually open new avenues for treatment.



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Gregory Carter, M.D. is a Clinical Assistant Professor in the Department of Rehabilitative Medicine at the University of Washington and is co-director of Muscular Dystrophy Association Clinics in Olympia and Tacoma, Washington. He was a National Institute of Disability and Rehabilitation Research post-doctoral fellow at the University of California, Davis, where he also earned a Masters degree in physiology. He has authored more than 20 peer-reviewed publications in the field of neuromuscular diseases and muscle biology.

## RESEARCH EXCERPT

# Phrenic Nerves and Pulmonary Function in Charcot-Marie-Tooth Disease

By Gregory Carter, M.D., Department of Rehabilitative Medicine, University of Washington

There have been numerous case reports of respiratory failure in people with Charcot-Marie-Tooth Disease (CMT), the etiology of which has remained elusive. To further investigate this, we studied phrenic nerve (the nerve controlling the diaphragm, which is the main breathing muscle) and pulmonary (breathing) function in CMT patients over a 10-year period as part of a National Institute of Disability and Rehabilitation Research grant. Pulmonary function tests (PFTs) were performed on 40 subjects with CMT. These are tests that measure your lung volumes and capacity and how much pressure you can generate in your airways when you inhale and exhale. The results are measured against normal predicted values. The average forced vital capacity (FVC) for the group was  $92 \pm 22\%$  of the predicted value, with average forced expiratory volume (FEV) at 1 second being  $76 \pm 25\%$  of predicted value. The average total lung capacity (TLC) was  $97 \pm 38\%$  and the maximum voluntary ventilation (MVV) was  $109 \pm 38\%$  of the predicted value. The average residual volume (RV) was  $77 \pm 14\%$  of the predicted value. Ten of the subjects with spinal deformity had PFTs. There was no significant difference in FVC between those with and without spinal deformity (i.e., spine deformity does not affect breathing in CMT). Analysis of both one-time and longitudinal PFTs in five individuals with 3 or more years duration did not show a significant age or disease duration effect and there was no correlation with the frequency of pulmonary complications. Using the American Medical Association guidelines, only one subject had severe restrictive lung disease (RLD), with a FVC of 47% of predicted value. Three subjects (8%) had moderate RLD and eight (20%) had mild RLD.

In addition, 25 patients had maximal inspiratory and expiratory (MIP/MEP) airway pressures measured along with bilateral phrenic nerve conduction studies. Phrenic nerve latency was abnormally prolonged in 22 of the 23 subjects (96%) in whom a response was obtained. Eight (32%) had abnormally low

MIP values and 19 (76%) had abnormally low MEP values. The MEP/MIP ratio from 22 patients was  $1.1 \pm 0.3$ . None of the PFT parameters (FVC, MIP, or MEP) correlated with phrenic nerve latencies.

Of 86 total patients, including the 40 who had PFTs and 25 who had phrenic nerve conduction studies, only 12 (14%) had a history of clinically significant breathing problems, and none had acute or chronic respiratory problems requiring mechanical ventilation. On one time-event analysis, there was no significant disease duration or spine deformity effect on respiratory complications. Moreover, although phrenic nerve latencies are markedly prolonged in CMT, they are not useful in predicting respiratory dysfunction.

It may be useful to study a more select, symptomatic set of CMT patients using more sensitive, quantitative measures of diaphragmatic function to better elucidate the causes of respiratory dysfunction in CMT. My colleagues at the University of California, Davis, are doing some of these studies now, but the results have not yet been analyzed.

In closing, my advice to those with CMT: keep as fit as possible by doing gentle aerobic exercise such as pool aerobics, swimming, stationary cycling, and low-resistance weight lifting. Don't become overweight. If you are overweight, go on a diet and start to exercise. Don't start smoking. If you already smoke, do whatever it takes to quit. (It isn't easy. I suggest formal addiction recovery programs.) If you live with someone who smokes, get him or her to quit because the second-hand smoke is harmful to your health. If you must have surgery requiring a general anesthetic, make sure your anesthesiologist knows you have CMT and that it can affect your breathing.



## CONFERENCE ALERT

# A 1-Day Family Conference on CMT

A conference on Charcot-Marie-Tooth Disorders will be held on April 5, 1997 at the Shriners Hospital for Crippled Children, 2001 S. Lindbergh Blvd., St. Louis, Missouri.

The conference will begin with registration and coffee from 8:00 to 9:00 a.m. Welcoming remarks by CMTA Board President Diane Freaney will be followed by a presentation on "Clinical Features of CMT and Medical Research Updates" by Dr. Michael Shy, researcher and clinician at Wayne State University, Detroit, Michigan and co-researcher with Dr. Agnes Jani, Armington Research Grant recipient. Morning workshop sessions will begin at 10:45 a.m., followed by lunch at noon.

Three morning and afternoon workshops will begin with panel discussions and leave ample time for questions.

### Workshops:

Pain Management and Medical Alerts  
Parenting Challenges  
Therapy and Adaptive Helpers  
Information Exchange Chat Room  
(Afternoon only)

At 1:00 p.m. Dr. Perry Schoenecker will discuss "Orthopaedic Surgery," followed by a coffee break, with workshops from 2:15 to 3:30 p.m. After the workshops, doctors, therapists, and workshop reporters will summarize the conference.

The maximum registration number is 150. Facilities are barrier free with ample parking. This conference will address all age groups, not children only.

If you wish to stay in St. Louis, the nearest hotel is the Frontenac Hilton (with shuttle service). Other lower-cost hotels and motels are in the area. The St. Louis Airport/Lambert Field is nearby. Hotel information will be furnished with confirmation.

On Friday evening, April 4, from 7:00 to 9:00 p.m., a hospitality suite will be hosted by the CMTA, Athena Diagnostics, and the Kansas City, Missouri support group at the Frontenac Hilton, 1330 S. Lindbergh Blvd. St. Louis, Missouri.

The cost of the conference is \$25.00 per person for members of the CMTA and \$40.00 per person for non-members. Space permitting, registration at the door on Saturday, April 5th will also be \$40.00 per person.

*Clip this form  
and mail to  
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register for the  
St. Louis Family  
Conference in  
April.*

## REGISTRATION FORM FOR ST. LOUIS CONFERENCE

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*Cost: \$25 per person for CMTA members, \$40 per person for non-members.*

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*Return registration form to CMTA, 601 Upland Ave., Upland, PA, 19015.*

# Charcot-Marie-Tooth Disease: A Primer for Patients

By Michael Shy, M.D., Wayne State University

Dr. Michael Shy is a researcher and clinician at Wayne State University in Detroit, Michigan and a member of the CMTA's Medical Advisory Board.

Charcot-Marie-Tooth disease (CMT), named for the three physicians who first described this disorder more than 100 years ago, is one of the most common inherited neurological disorders. Affecting one in 2,500 individuals, CMT is similar in prevalence to multiple sclerosis. The genetic abnormality causing CMT disease affects the peripheral nerves. These structures carry signals from the brain and spinal cord to the muscles, activating muscle contraction and producing movement. They also carry sensory information from the skin and joints back into the spinal cord and brain. For this reason, patients with CMT have both muscle weakness and sensory abnormalities. Onset of CMT usually begins within the first two decades of life and is slowly progressive. Life expectancy and intelligence, however, are not affected. There is currently no cure for CMT, although physical and occupational therapy, orthopaedic surgery, appropriate splinting and bracing, and supportive footwear all help to alleviate symptoms.

A normal peripheral nerve consists of axons, long extensions of neurons, cells located in the spinal cord and brain, which act as the wiring of the nerve, carrying the signals from the brain to muscle and back again. Most axons in the nerve are covered with myelin, an insulating substance produced by Schwann cells located along the length of the axons. In CMT disease, abnormalities of nerve function are caused by genetic defects affecting the axons, called CMT type 2 (CMT2), as well as genetic defects affecting the structure of the myelin sheath, called CMT type 1 (CMT1). Patients with either form of CMT have muscle weakness and sensory abnormalities. Patients with CMT1, however, have slowed nerve conduction velocities because of their abnormal myelin, while patients with CMT2 do not. Over two thirds of patients with CMT have CMT1, associated with slowed nerve conduction velocities.

During the past 5 years, three mutations causing CMT1 have been identified which account for most patients with this disorder. Each mutation affects the myelin sheath and produces abnormal nerve function, muscle weakness, and sensory abnormalities because of damage to peripheral nerve myelin. CMT1A, the

most common form of CMT1, is caused by a duplication, or doubling, of a portion of chromosome 17 containing the gene encoding the myelin protein, peripheral myelin protein 22 (PMP22), necessary for normal myelination. CMTX, the next most common form of CMT1, is caused by mutations in the protein connexin 32, also important for maintaining the integrity of the myelin sheath or nerve insulation. CMT1B, the least common form of CMT1, is caused by mutations in another important myelin protein, myelin protein zero (P<sub>0</sub> or MPZ). The gene or genes that cause CMT2, however, have not yet been identified.

We evaluate CMT patients at Wayne State University in the Department of Neurology in the context of our multidisciplinary neuromuscular clinic. This clinic is directed by Drs. Michael Shy and Richard Lewis, both of whom have training in the care of patients with diseases of peripheral nerve and myelin. The clinic is also staffed by two neurogeneticists, Drs. John Kamholz and James Garbern. Dr. Kamholz has extensive experience in caring for patients with diseases of myelin in both the peripheral and central nervous systems. Dr. Garbern is also the head of the Neurogenetics clinic at Wayne State University. The Neuromuscular Clinic also contains a physiatrist, or doctor of physical medicine, Dr. Steven Hinderer, and a genetic counselor, Ann Greb. Specialists in pulmonary disease, nutrition, and psychiatric counseling are also available at the clinic.

At the Neuromuscular Clinic at Wayne State University, we have begun a clinical research project to describe the natural history or progression of patients with CMT1. This project is important, since identification of therapies for CMT will require understanding the timing and rate of progression of this disorder in order to judge the effectiveness of medication. This study will use computerized systems to measure the strength of the patient's muscles, their ability to feel sensory stimuli, and the number of functioning motor neurons. Patients will be evaluated three times in a 1 year period for evidence of disease progression. These studies will then form the basis for patient evaluation procedures in future clinical trials for the treatment of CMT.

Our interest in CMT at Wayne State University Department of Neurology is not limited to either patient care or clinical research. Both Drs. Shy and Kamholz and their laboratories are involved in projects, funded by the Charcot-Marie-Tooth Association and the Muscular Dystrophy Association, to develop gene therapy approaches for the treatment of CMT. This approach to the treatment of CMT involves introducing genes into Schwann cells, the cell producing the myelin sheath or nerve insulation, using a genetically modified cold virus. In this way, we hope to replace the defective genes in the peripheral nerves of patients with CMT1, thus repairing their damaged myelin. These studies are ongoing, however, and this approach is not ready for use in patients at this time.

We believe that our combination of clinical and basic research, as well as the multidisciplinary nature of our clinical approach, enable us to be uniquely qualified to understand, study, and care for patients with CMT.



## STUDY VOLUNTEERS NEEDED

We are seeking adult volunteers to participate in a research project to investigate the relationship between activity and strength. We are looking for subjects between the ages of 18 and 80 with CMTI disorders. Participants must have some complaints of hand involvement with no history of hand surgery, arthritis in the hands, or any recent hand injuries. Participants will be evaluated in the Physical Therapy Department of Beaver College. The tests will be performed in a single session which will last approximately 1 to 2 hours. If you are interested in helping with this study, please contact:

Carol Oatis, P.T., Ph.D.  
Associate Professor  
Department of Physical Therapy  
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## OF INTEREST

### WAYNE STATE UNIVERSITY SCHOOL OF MEDICINE



## Symposium on the Gene Therapy of Neuromuscular Diseases

*Friday, March 21, 1997*

*Scott Hall*

*Wayne State University*

*Detroit, Michigan*

This symposium will focus on the use of viral and non-viral methods of gene transfer into muscle and peripheral nerve and their potential use in the treatment of Duchenne muscular dystrophy, Charcot-Marie-Tooth disease, and motor neuron disease.

### SPEAKERS

**George Karpatt**

McGill University

**Paula Clemens**

University of Pittsburgh School of Medicine

**Hansel Sledman**

University of Pennsylvania School of Medicine

**Jon Wolff**

University of Wisconsin School of Medicine

**John Kamholz**

Wayne State University School of Medicine

**Michael Shy**

Wayne State University School of Medicine

**Gyual Acsadi**

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*This symposium is sponsored by the Department of Neurology and the Center for Molecular Medicine and Genetics, Wayne State University School of Medicine. For information, call Izabella Gavric at 313-577-1689.*

# Defining Life and Individual Worth

By Dale O'Reilly

This article first appeared in the *Philadelphia Inquirer* on Sunday, January 5, 1997. Dale O'Reilly is my friend and I marvel at her inner strength. Six years ago I introduced Dale to Elyn Phillips. Elyn lost her husband to ALS. After his death, Elyn became President of the Greater Philadelphia Chapter of the ALS Association. Elyn received all the records and funds of the chapter in a shoebox when she took over.

Today, Elyn presides over a chapter that contributes more money to ALS research than the CMTA's entire budget. In 1997, Elyn expects six clinical trials on ALS drugs to begin.

Researchers into the causes of CMT have reason to believe that drugs which are effective for ALS patients might also be effective for CMT patients. Dr. Michael Shy and other researchers at Wayne State are working to prove that clinical trials on CMT are possible and can yield significant results.

We salute our friends at the ALS Association. We hope to ride on your coat-tails and replicate your success.

—Diane Freaney,  
President

**M**y first grandchild was born a few days ago. This was not a big deal to the world at large. After all, approximately 11,000 children are born every day in the United States alone.

There is nothing exceptional about this child, Elena, except for her utter and complete normalcy. She is a child born into the American dream. Her parents are college educated, employed as a bank officer and an engineer. They own their own home and are happily married to each other.

Elena also will know five of her great-grandparents and all four of her grandparents. While not people of great wealth, they will have much to share with her.

One grandmother is a classical violinist who plays in a chamber ensemble. Her husband is a chemist and accomplished sailor. The other grandfather, a successful business executive, was quite an athlete in his youth. He can teach her to pitch, hit or kick any kind of ball. His wife (me) has published several books and numerous articles. But what will I be able to teach this perfect child?

I lied when I said there was nothing exceptional about Elena because to me she is a miracle, the child I was never supposed to know.

Six years ago, I was told I have an incurable disease and wouldn't live five years. Twenty months later, the disease (amyotrophic lateral sclerosis—ALS—or Lou Gehrig's disease) had progressed to the point where I could no longer breathe sufficient air or swallow enough food to sustain life. I had already lost the use of my arms and legs and the ability to articulate coherently.

This is the point when most people with ALS die. Several over the last few years have availed themselves of the services of Dr. Jack Kevorkian.

I was not yet ready to die. When my doctors offered me an alternative, as frightening as it sounded, I took it. Three and a half years later I'm still here, kept alive by a ventilator that does my breathing for me and a feeding tube in my abdomen that delivers liquid nutrition directly into my stomach. I cannot move or speak, but I am still very much alive in my head. I access the computer by blinking my eye, go out to the theater, read books I always meant to read, talk with people who can read lips. And now, I will get to know my granddaughter.

What will she make of me? Hopefully, in her innocence, she will accept me for what I am—someone who loves her, just her grandmother. That may be difficult since society as a whole has a hard time accepting people who are disabled—other than “normal.”

Despite the fact that each American citizen is promised the “right to life, liberty and the pursuit of happiness,” we as a people are very conflicted when it comes to valuing life. Nowhere is this more obvious than in our government where the same people who are anti-abortion are for stronger enforcement of the death penalty, vote billions for a new fighter plane but want to cut Medicare.

The same attitude is seen as medical care becomes more of a business. When I was first diagnosed with ALS, my insurer was a nationally known HMO. We had no problem with the HMO up to that point, but as soon as the word “terminal” appeared, so did rejections of requests for services and equipment.

Finally, after arguing back and forth, we were told that if my doctor would certify, in

*Dale holds her 18-hour-old granddaughter Elena in the hospital after her birth.*



writing, that I would be dead in six months, the equipment would be approved. Otherwise, we were on our own. What kind of message does that send to someone who is fighting for life?

How much is a life worth? No one doubts the worth of my perfectly healthy grandchild, but what about the disabled child?

Michael Berube, who teaches African American literature at the University of Illinois, has written a book on life with a Down syndrome child, *Life as We Know It*. In it, he challenges lazy attitudes about individual worth. He asks us to “determine what kind of ‘individuality’ we will value, on what terms, and why.”

If we do value the individual, able and disabled, what are our obligations to each other? Berube writes, “I cannot say why it is that we possess the capacity to imagine that we might have obligations to others, nor do I know why, if we possess such things, we habitually act as if we do not. But I do know (my son) has compelled me to ask these questions anew, just as I know how crucial it is that we collectively cultivate our capacities to imagine our obligations to each other.”

Berube tries to imagine his son as a type, a child with Down syndrome, but it doesn't work—the child remains Jamie, an individual.

In the same way, I will not be someone with ALS—I am an individual with rights and obligations. I vote, pay taxes, purchase goods and services. My granddaughter gives me one more reason to live. I won't be the grandparent who teaches her to play a musical instrument, or catch a ball, or know the incredible joy of sailing. But there are things I can promise to do for and with her.

- I will never be too busy for her...out, away, or on the telephone.
- I will always listen and never interrupt.
- I will try, by example, to teach her the intrinsic value of life.

During the holiday season—and this year's was typical—there is always much talk of giving and of miracles. But if we as a people would seriously address the questions Berube raises, and come to some life-affirming answers, that would be a true miracle.

## GIFTS WERE MADE TO CMTA IN MEMORY OF

**Ms. Louise Bessey**  
Cicely L. Zeppa

**Brian A. Bruder**  
Ground Warfare  
Assessment Division

**Lois Cashman**  
Mrs. Carl E. Touhey

**Sydney Dicker**  
Margaret A. Traub

**Bruce Gates**  
Mary and Bob Williams

**Anita Harding**  
Karol B. Hitt

**Ann Kerrigan**  
Michael L. Schwartz

**Ashley and Krystal**  
Ruth Stefanovich

**David P. Leahy**  
Mary Rehm

**Edward Nash**  
Kay Flynn

**Merrill Bliss Park**  
John and Margarth Hardy

**George F. Phy**  
Elizabeth Oliver

**Rebecca Sand**  
Rhoda and Stephen Sand

**Mollye Schwartz**  
Michael L. Schwartz

**Florence Spooner Vinson**  
Sam and Joan Spooner

**Catherine Wiesner**  
The Koenigs

**Miriam Van Huss**  
The Physical Medicine and  
Rehab Department and Social  
Services Department of  
Harris Methodist Hospital  
Bedford, Texas

**Eugene D. Zichichi**  
Mr. and Mrs. Linly Zichichi

**Gene Zichichi**  
Alice Rew

## GIFTS WERE MADE TO CMTA IN HONOR OF

**Irv Bank's Birthday**  
Jerry and Debra Banks

**Dann Caldwell (Christmas)**  
Beth Caldwell

**Ruby Egnew**  
Vickie Egnew

**Mr. and Mrs. Henry P. Eldredge**  
Mr. and Mrs. Douglas H. Moody

**Henry Friedmann's Birthday**  
Pete Friedmann

**Charles and Helen Lynch**  
J. C. Julian

**Leo and Bernice Sermersheim  
(Christmas)**  
Beverly and Henry Sermersheim

**Samantha Lynn Sheriff**  
Paul F. Hall

**Mr. and Mrs. B.E. Smith's  
Wedding**  
Georgett Smith

**Camille Thomas (Christmas)**  
Martha Troup Mayforth

**Cecilia Thorp**  
George and Lenore Smith

# Charitable Medical Air Transport System in Place



By Edward R. Boyer, President, Mercy Medical Airlift

**M**ultiple sources of charitable medical air transportation are now available in the United States. There is no guarantee that every need will be met, but there are dedicated people working to meet almost every need.

1. The National Patient Air Transport Hotline (NPATH) number is 1-800-296-1217. This unique hotline makes referrals to appropriate charitable, charitably-assisted, and special-patient-discount commercial services based on an evaluation of the patient's medical condition, type of transport required, and departure/destination locations. Patient referrals are made to more than 45 different sources of medical air transport help.

2. The "special lift" medical air transport program operates in conjunction with the NPATH HOTLINE. Sponsors of large-scale disease research or experimental treatment pro-

grams can take advantage of this program, which will manage and coordinate the medical air transportation aspect of the special project—arranging to move large numbers of patients to and from special research or treatment facilities, nationwide.

Currently, a "Child-Lift 1" program is serving a special double-blind drug testing program for Congenital Lactic Acidosis. A "Child-Lift 2" program is transporting patients with Sturge-Weber Syndrome. Both programs are serving the Clinical Research Center of the University of Florida and are operated by Mercy Medical Airlift, a non-profit organization specializing in developing, assisting, and coordinating charitable medical air transportation.

To discuss possible future "special lift" programs, call Mercy Medical Airlift at 1-800-296-1191.

## Support Group Welcomes Regeneron Rep

By Dan Iacovella

**A**t the December meeting of the CMT Support Group of Westchester, Rockland and Fairfield, members enjoyed an informative presentation by Dr. Jessie Cedarbaum of Regeneron Pharmaceuticals, Inc. Regeneron is a publicly-traded biomedical research company devoted to developing drug treatments for a variety of peripheral neuropathies and neurodegenerative diseases. Dr. Cedarbaum's presentation focused on neurotrophic growth factors and the development of two promising advances: Brain-Derived Neurotrophic Factor (BDNF) to treat amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) and Neurotrophin-3 (NT-3) for diabetic peripheral neuropathy. Although neither is directly related to CMT, the treatment of ALS using BDNF may be helpful in the treatment of CMT Type II.

While he cautioned that the development of successful drug therapies is a lengthy process, Dr. Cedarbaum was hopeful that BDNF may be available to be prescribed to those suffering from ALS and similar diseases within the next 1½ to 2 years. He mentioned that of the drugs approved

by the Food and Drug Administration (FDA) last year, it took an average of 12½ years from the initial research for the drug to its approval. This lengthy time frame is the result of the extensive amount of time needed for initial lab testing on animals, three phases of trials on human patients, and then FDA review. In the case of drugs for fatal diseases, such as ALS, the FDA "fast-tracks" the process.

Dr. Cedarbaum was invited to speak as a result of the work of the members of the support group. At a prior support group meeting, Dr. David Dickoff of New York suggested that Regeneron be contacted. One member of the support group who was familiar with Regeneron established the contact and coordinated the presentation. Many in the support group found the information to be very helpful and hope to establish similar contacts in the near future. It is this kind of initiative by support groups that will ultimately help spread the word about CMT and result in more research targeted toward its prevention and cure.

## Letters to the Editor:

### Dear CMTA Report,

Thank you for your informative reports!

I would like to share a solution to a problem I have not seen discussed in the two plus years I have been a member: bed covers! The weight of bed covers (after several hours of use) make drop foot worse. The wire frames marketed would seem ideal; however, the feet stay cold.

J.C. Penney's "Special Needs Catalogue" has a leg wedge designed for use under the knees. The long side measures 9<sup>3</sup>/<sub>4</sub> inches and is perfect. The height keeps the weight of the covers off the toes and the covers still drape around the feet. Any size foot could benefit. The polyurethane foam wedge is heavy enough to hold feet up while on your back, or side. In addition, you can push against and straighten your toes...good exercise before sleeping. The cost is approximately \$25.00, which includes shipping/handling and tax.

It works for me and I hope it will help someone else.

—M.S., Georgia

### Dear CMTA Report,

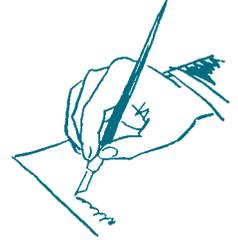
I am 25 years old and have lived with CMT most of my life, although I was not diagnosed with CMT until the age of 12. Until my parents moved to Massachusetts, we moved around a

lot, which meant that I saw several different family doctors. All of them, except for the last one, told my parents that I was just going through a clumsy phase and I would grow out of it. One doctor even suggested that I take up ballet to increase my coordination. My mom and I joined a class where I felt so out of place that I begged my mother to pull us out. We did pull out and I remained "clumsy" and even got worse as the years went by.

The last doctor finally realized that there was something wrong with me because he had CMT in his family! I was the first in my family to be diagnosed with CMT. My grandmother had the disease but was diagnosed at a very young age with polio. At the time, polio explained the problems she had with her muscles and so a diagnosis was not taken any further. After my diagnosis, my father was diagnosed and now in my immediate family my father, myself, and one other sibling are living with CMT.

I am a single mother of a wonderful little 4-year-old boy. The things he does around the house are amazing!! I would love to hear from other mothers with CMT who are handling small children.

Please write to J.Sprague in care of the CMTA office.



### WRITE TO US!

Pat Dreibelbis, Editor

The CMTA Report

CMTA

601 Upland Ave.

Upland, PA 19015

*The CMTA reserves the right to edit letters for space.*

## Immunity and You: Perfect Together

Consider this: People who deny their illness, contrary to physical and psychological tests, have low levels of disease-fighting white blood cells; people who admit negative thoughts and feelings have an active immune system and they are less likely to have asthma, rheumatoid arthritis, diabetes, or aggressive cancer; people who write about traumatic events from their past and present get healthier and remain healthier; studies confirm that keeping a journal temporarily boosts the response of key immune system cells called T-lymphocytes; volunteer workers have fewer illnesses, live longer, and have better than normal health in several categories. A positive attitude is good for you and can make you healthier, as shown by the University of Pittsburgh Medical Center Department of Immunopathology. Vitamin supplements can boost immunity..

After a year of taking an over-the-counter vitamin, patients scored better on skin tests used to measure the immune system's reaction to strep, tuberculin, diphtheria and tetanus.



Source: The "Outlook", newsletter for the Myositis Association of America, Inc., June 1996.



Members of the CMTA's Medical Advisory Board answer questions from readers.

## Ask the Doctor

### Dear Doctor,

*Vitamin B-12 deficiency damages the myelin sheath surrounding the nerves, so that electrical impulses can't travel along them. Taking B-12 tablets can reverse the demyelination. Would B-12 tablets be effective in treating the demyelinating effects of CMT?*

### The Doctor replies:

Taking B-12 would offer no help to CMT patients because the demyelination in CMT is not due to a deficiency of B-12 in the body, but to a problem in the myelin formation mechanism. B-12 has been tried in the past and has been shown to be ineffective in treating CMT.

### Dear Doctor,

*The numbness, tingling, and crawling sensations in the feet and legs associated with CMT are typically worse at night. Taking 50 mg of diphenhydramine (Benadryl) at bedtime only seems to be helpful. Is there any problem taking it over the long term with regard to CMT or anything else?*

### The Doctor replies:

There should be no problem with the long term usage of diphenhydramine. One or two 25 mg Benadryl at night will be helpful in treating the symptoms associated with CMT, although it does nothing to make the CMT itself any better.

### Dear Doctor,

*Will nandrolone decanoate and testosterone cypionate help me rebuild the muscles which wasted away as a result of wearing AFOs? Does anyone have any experience with anabolic hormone therapy?*

### The Doctor replies:

Anabolic steroids can cause a temporary increase in muscle strength, but would probably not result in any permanent improvement. The

steroids should not pose any problems, but the dosage of testosterone should be carefully monitored so that virilizing (excessive hair and male characteristics) can be avoided. All steroids should be used under the guidance of an endocrinologist.

### Dear Doctor:

*Pain is something we have to live with...or do we? I had physical therapy for my hand after an operation several years ago. The hospital put my hand in melted parafin. I have been trying this same technique at home by melting the parafin in a double boiler and pouring it slowly over the painful area. The parafin is hot, but the temperature is tolerable. I have found the relief lasts for quite a while. Do you think a fresh supply of blood is being forced to the heated area, resulting in better circulation?*

### A physical therapist replies:

Parafin therapy is used primarily in the treatment of arthritis. It feels great while being used and reduces the pain temporarily. There is no permanent healing. There are home parafin baths available and they are the only safe parafin treatments, since parafin can easily explode if heated incorrectly. Parafin is useful in treating pain since it fully coats the hand rather than reaching only limited areas of the hand surface as a heating pad might do. However, the use of parafin in CMT patients is dangerous because sensory loss means that the patient might not feel how very hot the parafin is and they might be burned by it. If your hands get cold easily, you could potentially burn yourself because of compromised sensory reception. Further, there is no evidence to suggest that the parafin (the heat) improves circulation. What often happens is that the patient's hands feel better for a while and they move them more freely and more often and that movement is what actually improves the circulation.

## Newsletter Publication Schedule

Those interested in submitting articles or letters to *The CMTA Report* should be aware of our deadlines. Space permitting, newsletters will contain letters to the editor and patient profiles.

**Spring Issue:** April 23rd

Theme: "Salute to Volunteers."

We welcome your recommendations on candidates to be profiled.

**Summer Issue:** July 23rd

Theme: "New Developments in CMT."

**Fall Issue:** October 22nd

Theme: "Annual Review."

We encourage patients, doctors, and researchers to consider submitting articles for inclusion in the newsletter. *The CMTA Report* benefits from individual contributions and various perspectives.

# 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

Theresa Gaskell 602/979-0299

## California

\* Janice Hagadorn 805/985-7332 after 5  
(Oxnard/Thousand Oaks)

\* Denise Miller 805/251-4537  
(Canyon County/Saugus)

\* Freda K. Brown 707/573-0181  
(Santa Rosa)

Gary Oleze 619/944-0550 after 6

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

Lisa Parks 916/751-2019

916/673-5099

Richard Zall 714/492-9877

(Orange County)

## Colorado

\* Dr. Gregory Stilwell 719/594-9920  
(Denver area)

Roberta Cummings 719/846-5611

## Connecticut

Mary Rehm 203/744-2786

\* Kay Flynn 914/793-4710  
(Fairfield)

## District of Columbia

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

## Florida

William Brady 904/443-6271

Mary Beeler 407/295-6215 9 am-8 pm

Harold Wilson 407/465-3656

Pat Ports 407/965-3691

M-W-F 4-9 pm

Joe Ellenbogen 305/921-4660

Edward Carhart 305/567-1066

9:30-5:30

Beatrice Bannister 407/737-3267

Robyn Cohen 407/622-5829

M-F 8-9:30 pm anytime weekends

Erika Stilwell 305/232-9066

\* Walter Sawyer 561/336-7855  
email: charlie@tcol.net

## Georgia

Nancy Lee McCutchen 770/925-1020

## Kansas

\* Ardith Fetterhoff 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 9 am-7 pm  
(Boston)

Jim Lawrence 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

Rosemary Mills 320/567-2156

Grace Wangaard 612/496-0255

## Missouri

\* Ardith Fetterhoff 816/763-2176  
voice mail 816/756-2020

Allan Degenhardt 816/942-1817

Carol Haislip 314/644-1664

Lisa Minzer, RN 314/978-0557

## New Hampshire

Mary Knightly 603/598-5451

## New Jersey

Janet Saleh 908/281-6289

Linda Muhlig 609/327-4392

Gary Orson 609/584-9025

M-F 6-10 pm & 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 pm  
(New York City)

Abby Wakefield 212/879-9517

\* 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 pm

## North Carolina

Emily Louer 704/849-2367

Diane Rodden 910/584-3655

\* Susan Salzberg 919/967-3118 5-9 pm  
(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

## Oregon

Marianne DeStafano-  
Hill 503/585-3341

## 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 pm

## Texas

Karen Edelson, DPM 214/542-0048

214/542-0122

M-T-Th 8:30-5

## Virginia

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

## West Virginia

\* Joan Plant 304/636-7152 after 6 pm  
(Central)

Barbara Compton 304/636-5456 24 hrs.

\* Denotes support group leader

## 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.

## 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, Macrochantin)  
Nitrous oxide (chronic  
repeated inhalation)  
Penicillin (large IV  
doses only)  
Perhexiline (Pexid)  
Taxol  
Vincristine

Lithium, Misomidazole  
and Zoloft can be used  
*with caution.*

Before taking any med-  
ication, 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).
- ...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  
1-800-606-CMTA**

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