

THE CMTA REPORT

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Providing information on Charcot-Marie-Tooth disease (a.k.a. Peroneal Muscular Atrophy or Hereditary Motor Sensory Neuropathy), the most common inherited neuropathy. Contents © 1994, CMTA. All rights reserved.

Exercise and Sports for Children with Neuromuscular Disease

The following article is reprinted from the September 1994 newsletter of the Research and Training Center on Neuromuscular Diseases at the University of California, Davis. The center is in the second half of a ten year neuromuscular research project which is funded by a grant from the NIDRR.

Neuromuscular diseases (NMD) involve the anterior horn, peripheral nerve, or muscle. They are uncommon causes of physical impairment and disability in children. Because of this, many physicians and physical educators have a poor understanding of either the beneficial or detrimental effects of exercise in these children. Excessive caution in the past has too often led to an isolated, sedentary lifestyle. This caution has little scientific support. However, those who deal with

children with NMD need to be aware of functional limitations so that expectations remain appropriate.

Exercise Pathophysiology in NMD

The ultimate cause of physical impairment in NMD is loss of normally functioning muscle fibers. Thirty to fifty percent of muscle tissue is lost before clinical weakness is appreciated, although exercise performance may be compromised at a lower percentage of loss. In the later stages of Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA), pulmonary or cardiac involvement become additional factors which may influence exercise performance.

A major concern with exercise in individuals with NMD is overwork weak-

ness. Overwork weakness was first suggested in DMD by muscle histologic examination, demonstrating that most degeneration occurs in muscles typically used during sustained physical activity. Muscle enzymes, used as a marker of muscle breakdown, were reduced by bed rest in dystrophic patients and elevated to a greater degree than normal controls after a vigorous strengthening program.

Exercise: Traditionally, high resistance exercise has been discouraged in NMD due to fears of overworking the weakened muscle. However, a survey of the research literature indicates studies with results ranging from no untoward effects to beneficial effects, with slowly progressive NMDs obtaining better results

(continued on p. 2)



Lorraine Middleton, Washington D.C. Support Group Leader; Dr. John Sladky, Neurologist, University of Pennsylvania; and Dr. Philip Chance, Pediatric Neurologist, University of Pennsylvania (CHOP), at the Philadelphia CMTA conference

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than DMDs. (*Editor's note: CMT is a slowly progressive NMD.*) Stronger muscles appear to strengthen more than very weak ones. Thus, starting an exercise regimen early in the disease when muscle fiber degeneration and weakness are minimal is generally recommended.

Measurement of exercise capacity is feasible in children and adolescents with NMD if they are able to climb stairs with the aid of a railing. In the absence of significant cardiac involvement, oxygen delivery to the muscles should be intact in NMD, with the exception of DMD. The limitation appears to be in oxygen uptake at the muscle cell level, which is proportional to the loss of active muscle tissue. Likewise, cardiac output seems to increase proportionally to increased oxygen consumption during exercise in muscular dystrophies, as in normal individuals. Little work has been done on the response of diseased muscle to endurance exercise. One study showed that adaptations to endurance exercise in NMD may not differ from that of normal individuals.

Respiratory Exercise: Several studies have indicated that respiratory muscle training in NMD either improves or maintains pulmonary function. While respiratory exercise training may have an impact on respiratory endurance, there is no evidence that the progressive course of restrictive lung disease in DMD can be delayed with an exercise program. Similar to skeletal muscle training, we would predict less improvement in patients with more advanced NMD. A cautious approach seems warranted in the later stages of respiratory weakness, since vigorous training may add to the work of breathing in individuals with limited respiratory reserve.

Contractures: Muscle imbalance leading to contracture may be an important factor in limiting performance. This is primarily a concern in children with DMD, although children with early onset SMA may also have significant contractures. Muscle shortened by contracture develops less maximal tension and fatigues more rapidly due to effects on the normal length-tension relationship of

skeletal muscle. Contractures may also contribute to the increased metabolic costs of task performance due to activation of muscle groups not usually needed.

General Exercise Precautions and Recommendations: Based on available data, we recommend submaximal strengthening exercises for post-puberty and adult patients with slowly progressive NMD. Because children normally increase strength more through the myogenic (protein synthesis and hypertrophy) component of strength rather than through the neurogenic (improved recruitment of motor units), the response of growing diseased muscle to resistance training is unknown. We feel that children should not focus on formal weight-lifting programs.

Although the incidence and risk of overuse weakness are still unclear, children with NMD should avoid exhaustive exercise, and rest periods are encouraged. As a rule, if the child feels fatigued or weak on the day following an exercise bout, the workload was probably excessive. Occasionally, the most deconditioned children require a supervised exercise program to obtain a fitness level that would allow participation in sports and games. In this situation, we follow the general goal of 20-30 minutes of aerobic exercise 3 days per week, monitoring for excessive fatigue or increased weakness. If the child can participate in exercise for 10-15 minutes without stopping, we would prefer exercise for enjoyment and socialization rather than in a strictly supervised program. Choices of recreational activity should provide a positive experience, be sufficiently challenging, and offer some opportunity for success.

Potential Benefits of Exercise in Children with NMD: Although direct benefits of exercise have not scientifically been proven, the empirical benefits of improved socialization, self-esteem, and independence cannot be minimized in NMDs. Lack of these often lead to isolation and loneliness. Regardless of any deconditioning, these components should respond to exercise. Adherence to a stretching program for contractures may maintain joint range of motion and should be made part of an enjoyable daily routine. Exercise during the childhood and adolescent years has been shown to lead to a more active lifestyle as an adult.

Exercise and Sports Programs for Children with NMD: Families and physical educators need to learn about

the effects of the disease. Often there are fears and caution due to lack of knowledge and the overriding concern of making impaired muscles even weaker. Discussion of fears with the physician, who can provide guidelines and support is most beneficial. The specific choice of activities may involve discussions among the individual, family, physical therapist, occupational therapist or adaptive physical education teacher. The natural history of the disease needs to be considered, so that an unexpected sense of loss does not occur with cessation of ability to exercise. Consideration should be given to the adaptability of sports to accommodate for increasing impairment.

Exercise Recommendations Based Upon Functional Level: Known Presence of NMD but No Overt Sequelae with Routine Activities: These children are less likely to require encouragement to participate in sports, but may have difficulty experiencing success and performing at a peer level, particularly in activities with high static or dynamic strength and endurance demands. Although there are no obvious limitations, exercise capacity may be limited, necessitating frequent rest breaks. Overwork weakness is a potential concern in a non-supervised setting, even at this mild level of involvement. For this reason, competitive sports such as football, distance running, sprinting or wrestling are not encouraged. Rather, these children are more likely to experience success with peers in such sports as golf, swimming or softball. A goal with this group is to help the child with slowly progressive NMD choose a "lifetime sport," meaning one that could be performed into adulthood to maintain fitness. Examples would be swimming or cycling.

Ambulatory Without Aids with Mild Muscular Fatigue, Mild Contractures or Reduced Endurance: There is often a component of non-myopathic disuse atrophy in this group because they have prematurely curtailed activity due to fear, familial pressures, or simply the inability to keep up with peers. With encouragement, children may continue physical education which helps maintain social interaction. Competitive sports are generally not possible but recreational ones definitely are appropriate, although they should avoid exercise to exhaustion and have frequent rest breaks. Professional supervision is not always necessary if the child can be trusted not to "overdue" it.

(continued on next page)

Write us: Letters - CMTA



601 Upland Ave.
Upland, PA 19015
Ph. 610/499-7486

Exercise - concluded

Swimming and water games are ideal sports to provide resistance, endurance and flexibility training in an enjoyable manner. Golf, hiking, cycling or table tennis are examples of other activities which may be popular among children with NMD. Children with reduced endurance may enjoy tandem cycling, canoeing or rowing with a parent, sibling or friend. These activities have reasonable neuromuscular skill demands, static and dynamic demands, and upper and lower body motion. We have found poor adherence to formal stretching programs in this population unless parents are insistent. This may become a control issue and increase stress at home. If the stretching program can be made part of warmup for a game or sport, cooperation may improve.

Ambulatory But Markedly Limited Due to Weakness, Advancing Contractures, Braces or Poor Endurance: These children often use braces for ambulation, are not functional runners, and demonstrate marked inefficiency with gait due to postural adaptations to compensate for weakness and contractures. Because of the significant weakness, there may be minimal strengthening response seen with conditioning activities. Water sports are ideal to provide freedom of movement and maintain fitness due to the elimination of gravity disadvantage. Support with flotation devices may be necessary. Pool ball games, relay races, tag and slalom walking in shallow water may be utilized.

In school adaptive physical education is necessary, with stress on individual sports alongside peers to maintain socialization and goal oriented skills. In the proximally-affected syndromes, overhead activities such as throwing and basketball may be quite difficult, and sports with the arms maintained below the shoulders are more appropriate. Unless contractures are severe, three-wheeled cycling may be an enjoyable way for these children to remain active. §

Call for Articles

The CMTA Report welcomes your ideas and article suggestions. For example, you may submit a human interest story telling of your experience of living with CMT. Also, medical professionals can forward articles of a clinical or medical nature that would be of general interest to our readership.

Items of Interest

Item 1: The President's Committee on Employment of People with Disabilities has established a hotline called the Job Accommodation Network. If you have any concerns relating to adapting your job to disabilities or to repetitive-strain injuries or any type of disability and you need help finding aids or finding other adaptive approaches, call the hotline at (800)526-7234. You may be able to get very specific answers to solve your problem. Or you could get a referral to an appropriate governmental department, support group or service agency.

Item 2: Lubidet, USA, has recently introduced a device which provides gentle, effective, personal hygiene with a warm water wash and warm air dry. The device attaches to your existent toilet and can be installed without a plumber. It taps into the fresh water under the toilet and can be hooked up for right or left-handed use. No dexterity is required as it has a lever with an attachable extra four-inch wand that can be operated by elbow, finger, forearm or palm. Lubidet won first place in the 1993 National Product Design Competition and can be reached at 1-800-582-4338. Ask for Mary Kay for free information and additional details.

Item 3: A new book is available from Demos Publications entitled, "A Guide to Legal Rights for People with Disabilities" by Marc Stolman. The book is well-written and easily understood. Some chapter titles are: Disability Rights are Civil Rights, Who is Legally Considered Disabled, What About Job Discrimination, Insurance Problems, and What Government Benefits are Available. The book costs \$ 19.95 and can be ordered from Demos Publications, 386 Park Avenue South, NY, NY 10016 or by calling 800-532-8663.

Item 4: The CMTA has medical alert cards available once again. These cards are sent to contributing members with their thank-yous. The cards have been updated to include the newest additions to the medical alert list. If you need one and are not making a contribution, please request the card and include a stamped self-addressed envelope. The card is small enough to fit in a wallet and contains both the toxic drug list and the name, address, and phone number of the CMTA office. Carrying one at all times is advised.

Item 5: The following are numbers that you should make note of. They can connect you with services that you or your family might need one day.

- Disability Rights Education and Defense Fund
(resource for civil rights and ADA)
202-328-5185
- Social Security Administration
800-772-1213
- American Academy of Physical Medicine and Rehabilitation
(a list of physiatrists in your state)
312-922-9366
- ABLEDATA
(data base of assistive technology and rehab. equipment)
800-227-0216
- Yes I Can
(resource for equipment)
800-366-4226
- Prescription Footwear Association
(for board certified pedorthist in your area)
800-673-8447
- Ford Mobility Motoring Program
800-952-2248
- Physically Challenged Resource Center at Chrysler Motors
800-255-9877

Item 6: The National Easter Seal Society offers swimming lessons to people with disabilities. For more information, call or write: The Easter Seal Society, 70 East Lake Street, Chicago, IL 60601, (800)221-7827.

Item 7: The National Parent Network on Disabilities advocates for the rights of children with disabilities and their families. Membership provides parents, educators, and professionals with a newsletter, legislative updates, annual meetings and training events to support parents in their efforts to improve the lives of their children. Write: 1600 Prince St. Suite 115, Alexandria, VA 22314 or call: (703)684-6763.

Item 8: The Advocacy Center for Persons with Disabilities in Tallahassee, Florida offers a very comprehensive little packet of information on the Americans with Disabilities Act in both English and Spanish (Decreto para Americanos con Incapacidades). Single copies can be requested by calling: (800)342-0823.

§

Charcot-Marie-Tooth Disease: A Multi-Gene Disorder

by David L. Paul, Ph.D.

(This article is reprinted with permission of the author, Dr David Paul who is an Associate Professor of Neurobiology at Harvard Medical School. It appeared in On the Brain, a publication of the Harvard Mahoney Neuroscience Institute. The author writes, "I have been studying the mechanism of intercellular communication through gap junctions. I cloned many of the genes involved in the establishment of gap junctional communication but, until the CMTX locus was mapped by Kurt Fischbeck (physician and researcher at the University of Pennsylvania) and others, I never even suspected that problems with gap junction communication could result in CMT.")

Multi-gene diseases are a great research challenge: Many cruel and costly disorders are multi-genetic, including diabetes and perhaps manic-depressive illness. One such disease, Charcot-Marie-Tooth disease (CMT), is a heritable disorder of the peripheral nervous system (PNS), affecting one in every 2500 people. But, unlike the other disorders, CMT has begun yielding its secrets, offering hope to researchers of all multi-gene diseases.

...CMT has begun yielding its secrets, offering hope to researchers of all multi-gene diseases

Individuals affected by CMT (also known as Hereditary Motor and Sensory Neuropathy) display a slowly progressive muscular weakness in the extremities and mild loss of sensation. Clinical symptoms vary considerably in onset and severity: Beside muscle weakness and atrophy, patients may develop deformities of the hands or feet and gait disturbances are often evident, beginning with a tendency to "toe walk" in early childhood; severely affected individuals may later become wheelchair-bound, and activities as simple as buttoning a shirt can be painful and difficult. Currently, CMT is incurable, although surgery or physical therapy can sometimes ease symptoms.

In the most common subtype, CMT1, peripheral nerves propagate electrical impulses much more slowly than normal, although impulse strength is unaffected. High conduction velocity is made

possible by an insulating material called myelin which sheathes the axons of nerve cells, but in CMT1, myelin formation and maintenance are impaired, and, over time, it degenerates.

In the central nervous system, this pathology is called multiple sclerosis. But in the PNS, it is often the result of CMT1 and involves not nerve cells but special supporting cells known as "Schwann cell." In the PNS, the Schwann cell sends out a sheet-like extension that closely wraps the axon, forming myelin.

The molecular basis for CMT1 myelin degeneration was unknown until recently, when genetic linkage analysis was used to map the chromosomal location of genes involved. Surprisingly, at least four genes were involved, and the DNA from three of these genes had already been isolated and sequenced (cloned) in other studies.

If a cloned gene is near a presumed disease gene, it is possible that the genes are related. CMT linkage analysis indicated similar map positions to genes encoding three proteins: peripheral membrane protein 22 (PMP-22), myelin protein zero (P0) and connexin32 (Cx32). And in CMT patients, mutations in these genes were discovered involving several CMT variations.

PMP-22 and P0 are found in the Schwann cell membrane and are major components of myelin. Currently, the function of PMP-22 is not understood, but too much or too little normal PMP-22 harms myelination as much as PMP-22 with altered structure: The most common form of CMT1 occurs when one or both of the original copies of the PMP-22 gene are duplicated. Conversely, deletion of one original copy causes "Hereditary Neuropathy with Liability to Pressure Palsies," a condition like CMT1 except that it is episodic and usually lasts only a few weeks. Defects in myelination also occur when PMP-22 "point mutations" change the identity of amino acid residues in the protein. This can cause CMT1 or the related Dejerine-Sottas Syndrome.

In contrast, a function for P0 is suggested by its structural similarity to well-known "adhesion" molecules that hold cell surfaces together. Precise adhesion is critical for the wrapping and stable association of Schwann cell membranes during myelin formation. Significantly, the point mutations in P0 associated with

CMT1 affect the part of the protein most likely required for adhesion.

Cx32, unlike PMP-22 or P0, is mostly found in cells outside the nervous system. It was initially discovered in liver cell "gap junctions," channels for small molecules to cross between adjacent cells. But since Schwann cells aren't near enough to each other to form gap junctions, what is Cx32 doing in the Schwann cell? Cx32 could form intracellular channels connecting one wrap to the next, such channels would dramatically shorten the distance of intracellular pathways, which could be important for Schwann cell metabolism or for communication between axon and Schwann cell. One puzzling aspect of Cx32 mutation is that disease only strikes the PNS, though many cells outside the PNS express Cx32. It is possible that, elsewhere, other connexin genes can substitute for the mutated Cx32, while Schwann cells, for unknown reasons, cannot and therefore fail to function normally.

A specific diagnostic test for one form of CMT1 is now widely available; others will likely follow soon to allow many families to seek genetic testing and counseling. In the future, more detailed information about the function of genes involved in CMT will permit the design of rational therapeutic strategies. §

HONORARIA	
IN HONOR OF:	BY:
Maxine Hardy	Bruce & Judith Park
George Hardy	"
Lucille Park	"
Bliss Park	"
Michael Park	"
Lorraine Middleton	M/M Marvin Tiewsky
Lorraine Middleton	Anne Mehringer
Lorraine Middleton	Ronald & May Springwater
Lorraine Middleton	Mona Wineburg
Lorraine Middleton	M/M C.T. Cross
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Rebecca Sand	Sybil & Irwin Whitman
Samuel Doss & Ola Conner	Ann Criscuolo
Clint Rall	Inge Boskovich
The 50th Anniversary of Leonard & Marcie Streff	

**Charcot-Marie-Tooth Association
STATEMENT OF FUNCTIONAL EXPENSES**

for the year ended June 30, 1994 with comparative totals for 1993

	<u>Program Services</u>	<u>Management And General</u>	<u>Fund Raising</u>	1994 <u>Total Expenses</u>	1993 <u>Total Expenses</u>
Salaries and benefits	\$23,040	\$ -	\$ -	\$23,040	\$21,102
Publications and supplies	27,854	222	3,110	31,186	25,967
Occupancy and office expense	11,752	185	38	11,975	9,568
Conference expense	10,878	-	-	10,878	5,969
Professional fees	1,760	1,750	200	3,710	4,298
Depreciation	<u>1,285</u>	<u>-</u>	<u>-</u>	<u>1,285</u>	<u>1,101</u>
TOTAL EXPENSES - 1994	<u>\$ 76,569</u>	<u>\$ 2,157</u>	<u>\$ 3,348</u>	<u>\$ 82,074</u>	<u>\$ 68,005</u>

See auditor's report and notes to financial statements

Notes to financial statements - June 30, 1994 and 1993

NOTE 1 - SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Nature of Organization

The Charcot-Marie-Tooth Association (the Association) was incorporated under the laws of the Commonwealth of Pennsylvania as a nonprofit corporation in October 1983 and is registered with the Commonwealth of Pennsylvania as a charitable organization. The Association was established to sponsor, encourage and undertake scientific investigations of the causes and cures of Charcot-Marie-Tooth Disease. The Association receives the majority of its support from private donations.

Contributions and Recognition of Donor Restrictions

The Association reports gifts of cash and other assets as restricted support if they are received with donor stipulations that limit the use of the donated assets. When a donor restriction expires, that is, when a stipulated time restriction ends or purpose restriction is accomplished, temporarily restricted net assets are reclassified to unrestricted net assets and reported in the statement of activities as net assets released from restrictions.

Donated Services and Property and Equipment

Volunteers have donated their time in the organization's program and administrative services and its fund raising campaigns. The value of this contributed time is not reflected in these statements since it is not susceptible to objective measurement or valuation. The Association occasionally receives donations of property and equipment. The value of these assets are not considered material and are therefore not reflected in the Association's funds.

Financial Statement Presentation

In 1994, the Association elected to adopt retroactive to 1993, Statement of Financial Accounting Standards (SFAS) No. 117, Financial Statements of Not-for-Profit Organizations. Under SFAS No. 117, the Association is required to report information regarding its financial position and activities according to three classes of net assets: unrestricted net assets, temporarily restricted net assets, and permanently restricted net assets. In addition, the Association is required to present a statement of cash flows. As permitted by this new statement, the Association

has discontinued its use of fund accounting and has, accordingly, reclassified its financial statements to present the three classes of net assets required. This reclassification had no effect on the change in net assets for 1994 and 1993.

Property and Equipment and Depreciation

Property and equipment are reported at cost. Depreciation is provided on a straight-line basis over the estimated useful lives of the assets.

NOTE 2 - TAX STATUS

The Association is exempt from income tax under Section 501(c)(3) of the Internal Revenue Code and accordingly the financial statements do not reflect a provision for income taxes.

NOTE 3 - CONCENTRATION OF CREDIT RISK

The Association maintains cash account balances at one financial institution. The total of these balances are insured by the Federal Deposit Insurance Corporation up to \$100,000. During the year, the Association may have cash balances in its financial institution in excess of this limit. At June 30, 1994, balances were in excess of insurable amounts by approximately \$9,000.

NOTE 4 - FUND FOR RESEARCH GRANTS AND EDUCATION

Funds have been designated and restricted for research grants and education as follows:

Designated by board from contributions received prior to July 1, 1993, included with unrestricted net assets.	\$14,179
Restricted by donors as a result of an annual appeal conducted in fiscal year 1994	<u>21,493</u>
	<u>\$35,672</u>

**Calling All
Graphic Artists!**

The CMTA is calling for entries in a contest to create a new, spiffy, eye-catching logo for the organization.



The logo will be incorporated as part of the CMTA stationery and The CMTA Report. A \$50 prize will be given to the designer whose logo is selected.

So, if you are an artist looking to add an "award-winning design" to your portfolio, please submit your entry by March 15, 1995, to:

CMTA Logo Contest
601 Upland Avenue
Upland, PA 19015

The winner will be announced in the Spring edition of The CMTA Report.

Rex Morgan, Jr.
Public Relations Chairman

Weight Training Sets the Stage

by Ben Feen

(This article is reprinted with permission of Muscle and Fitness magazine, September, 1994.)

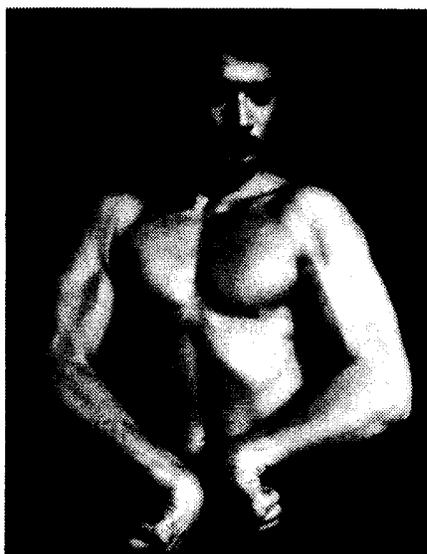
I always had an unusual walk - even when I was a child. My storklike gait must have been comical to the other youngsters, as kids usually teased me pretty badly about it. As a result, I felt inferior throughout most of my youth. My mother took me to a podiatrist who diagnosed my problem as "tight tendons." He prescribed a series of stretches that, he said, would cure it, but the stretches didn't help.

Things went from bad to worse. One day I couldn't put gloves on because my fingers wouldn't straighten; my mother then realized something was seriously wrong. After a number of tests, exams, scans, and a biopsy, I was finally diagnosed with Charcot-Marie-Tooth disease. CMT attacks the myelin (fatty portion of the nerves) in the lower arms and legs, which serve as insulation for the electrical signals from the brain. For an unknown reason, when a person is afflicted with CMT, this layer of fat dissolves.

Over the next few years my hands atrophied, but it was my legs that were hit the hardest. My ability to walk normally deteriorated and, in turn, I got more and more down on myself. I had surgery to correct some tendon problems and ended up in a wheelchair for six weeks. As luck would have it, two years later I was in a car accident and I ended up on crutches for six months. My feet were completely unusable. I could still walk, but from the knees down I couldn't move a muscle.

Call for CMT-X Participants

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



Ben Feen

After the accident, I was put into an adaptive physical education program my sophomore year in high school. The school had recently hired Ron Russ, a former trainer for the Chicago Blitz and Chicago Bears football teams. Ron put me on a light stretching and low impact resistance-training regime, but I never really got into it and the following year I was put back in a regular gym class.

About that time, I discovered my love for theater. I enjoyed working backstage, building sets for our school plays, but I never thought I could pursue a career unless I took some serious steps to do something to increase my strength and overcome my disability.

My senior year, I approached Ron with a deal: I wanted him to be my private trainer. He was agreeable and we worked out a way to do it around my class schedule. And so, we began in earnest. Every morning for 45 minutes I'd lift, beginning with two 25-pound dumbbells (then the heaviest weights in the training room) for presses. I'd also do concentration curls, triceps extensions and dumbbell rows.

When I was able to do three sets on the dumbbell press with 35 pounds, Ron bought a weight set and benches for the training room and I started doing barbell bench presses with 70 pounds. Ron kept acquiring equipment and I added leg extensions and hip abductions/adductions.



At the beginning of my senior year, my 5'7" frame carried 130 pounds. With Ron's encouragement and guidance, I lifted religiously. Gradually my confidence grew and I became crew head for our theater program as manager of set construction.

By the end of my senior year I had gained 15 pounds (and an inch in height). I bench pressed 190 and did leg extensions with 200 pounds for reps. I was also accepted into the Theatrical Technology Department at the University of Illinois at Urbana-Champaign.

I'm now in my second semester and am doing what I love - theater and weight training. I'm regaining some of the strength in my legs and hands, but I'm also pushing my limits on everything else. I recently became assistant to the technical director of the theater department for the summer season. Now I recommend weight training to all of my friends, and several of them have at least given it a shot.

My point is this: If you give up in the face of adversity, you're missing a perfect opportunity to make yourself a better person. Life is like lifting weights; if you're not putting in some serious effort, you're not getting anywhere. Laziness never built a body or a soul. §

¿ Habla usted Español?

The CMTA announces the publication of a Spanish edition of our CMT Informational brochure (gray brochure). For a copy check the block on the order form on page 15. For multiple copies contact the CMTA office.

Do you know of anyone famous who is a CMT patient? Do you know anyone famous who would advocate for CMT? The CMTA is looking for a well-known person to be a spokesperson for CMT. If you know of such a person, contact the CMTA; we will do the rest.



Research Update

A recent study from The Mayo Clinic involving severely affected type 2 CMT patients has been published in the May issue of *The Annals of Neurology*, (May;35(5):608-15). The title of the article is, "Hereditary Motor and Sensory Neuropathy with Diaphragm and Vocal Cord Paresis", and the authors are P.J. Dyck, W.J. Litchy, S. Minnerrath, T.D. Bird, P.F. Chance, D.J. Schaid, and A.E. Aronson. The abstract of the article is as follows: "We describe two kindreds with an autosomal dominant inherited disorder characterized by a variable degree of muscle weakness of limbs, vocal cords, and intercostal muscles and by asymptomatic sensory loss, beginning in infancy or childhood in severely affected persons. Life expectancy in severely affected patients is shortened because of respiratory failure. Because nerve conduction velocities are normal and it is an inherited axonal neuropathy, we classify the disorder as a variety of hereditary motor and sensory neuropathy type II (HMSN II) (HMSN IIc). The present report provides further evidence for heterogeneity among the hereditary motor and sensory neuropathy type II disorders. In one large pedigree with the type IIc disorder, no linkage to DNA markers known to map near the HMSN IA locus on chromosome 17p or the HMSN IB locus on chromosome 1q was demonstrated." (Editor's note: CMT type II represents about 1/3 of all CMT diagnoses, and severely affected type II patients represent an even smaller percentage of CMT patients.)

Another recent article of interest entitled, "Abnormal Responses to Cold Stress in Charcot-Marie-Tooth I Syndrome", appeared in *The Archives of Physical Medicine and Rehabilitation*, vol. 75, July 1994, pp 787-791. The authors of this article are Lowell L. Williams, Robert F. Vieth, and Francis S. Wright. The study was undertaken because CMT patient surveys have indicated that intolerance to cold is a frequent problem with CMT patients particularly older patients. The findings of the investigators as summarized in the abstract are as follows: "In Charcot Marie Tooth syndrome (CMT, Hereditary Motor Sensory Neuropathy), patient complaints of cold intolerance are common but their peripheral responses to cold have not been documented. Using digital plethysmography, a simple test of vascular reactivity with 1 minute cold stress, 20 unrelated adult CMT patients showed a significantly increased average heart rate and decreased average arterial

The Gift of Hope: A Tissue Donor Program

The "Gift of Hope" tissue donor program is administered by the National Neurological Research Specimen Bank at the VA Wadsworth Medical Center in Los Angeles, California. The following questions and answers provide information about the Gift of Hope program.

Is an autopsy required for donation to the specimen bank?

No. A simple tissue removal procedure, limited to the brain and related neurological tissue, is all that is required. The bank will make arrangements for this to be done. Disposition of the body is handled in the usual manner by the family. If an autopsy is already planned, neurological tissues for donation to a bank may be taken at that time.

Is there any cost connected with the donation? Who pays if there are costs?

The bank will pay for any incidental expenses which may occur as a result of tissue donation. Most donations do not involve any extra costs at all; personnel who assist in the donation process usually donate their services to aid this important research program. If, however, there are special expenses which arise, the Bank has resources to pay for them. Funeral arrangements and expenses remain the responsibility of the donor and family.

Will the tissue donation interfere with any family plans for funeral or burial procedures?

oxygen saturation following cold when compared to fifty age-matched normal controls. There did not appear to be a unique or characteristic CMT vascular reaction to cold stress in CMT patients because their abnormal peripheral vascular responses were variable. Variability in CMT neuropathic responses to cold is consistent with the known irregular segmental demyelination of CMT peripheral nerves as well as abnormal sweating patterns. Though understanding the precise patterns of CMT patient peripheral nerve disturbances remains difficult, awareness of CMT patient's abnormal responses to cold may facilitate CMT patient care and rehabilitation." For a reprint of this article send a business sized stamped self-addressed envelope to the CMTA requesting the "Cold Response Reprint." §

No. Donations to the Bank will not delay or complicate your funeral, cremation, or burial plans. Moreover, the procedure leaves no visible marks or changes should viewing at the funeral be contemplated.

Can brain and neurological tissue be donated to the Bank and the rest of my body to a medical school?

In general, this cannot be done. Most medical school anatomical gift programs are intended to provide gross anatomy educational training for medical students and do not allow partial donations. Donations to the Bank's "Gift of Hope" donor program directly supports research directed toward the prevention, treatment and cure of your or your family member's neurological disease.

Who should sign the Authorization Form?

The donor may sign to authorize donation, or the closest relative or authorized representative. The closest relative is (1) donor's spouse, (2) an adult son or daughter, (3) either parent, (4) an adult sister or brother, (5) a guardian or (6) any person authorized to make arrangements for the deceased. Only the one person highest on the list needs to sign. The "next-of-kin" gives consent for tissue donation again at the time of the prospective donor's death.

May the mortuary embalm the body?

Yes, but tissue must be donated before embalming, if embalming is planned.

How quickly should the Bank be notified of death?

The Bank should be notified immediately upon death, if possible. A minimum number of hours between death and tissue donation insures maximal research value.

Can anyone sign up as a donor?

Yes. We have recently developed a "Donor Program for Normal Controls" in response to the increased scientific demand for normal, non-affected, tissues for comparison with diseased tissues.

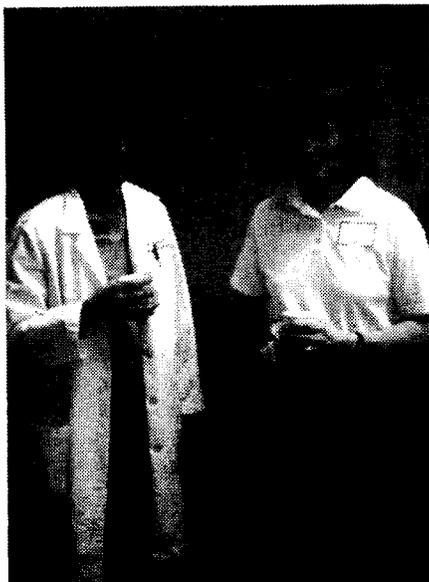
If you are interested in becoming a tissue donor, please contact the office of the CMTA for more detailed information. A packet will be mailed to you for your consideration. §

1994 IN REVIEW

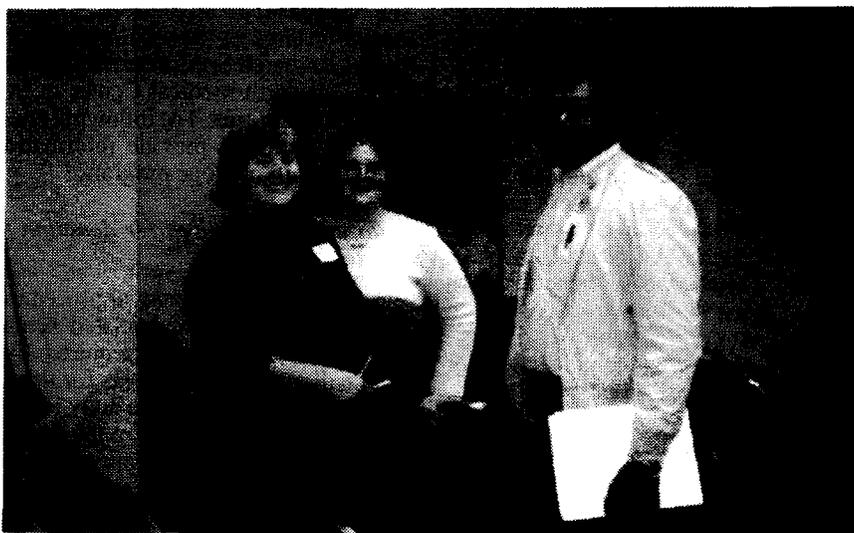
The past year has been another year of growth for the Charcot-Marie-Tooth Association (CMTA). At this time (Fall, 1994), we have 6,800 people in our data base and they represent patients diagnosed with CMT, their families, medical professionals, and friends.

The CMTA Board of Directors currently has seventeen members. They are: Karol B. Hitt, President; Robert Daino, Vice-president; Diane Freaney, Treasurer; Michael Molinari, Corresponding Secretary; Donald J. Perrella, Recording Secretary; Robert E. Lovelace, M.D., Chairman of the Medical Advisory Board; Rex S. Morgan, Jr.; George Crohn, Jr.; Ann Lee Beyer; Diana Eline; Gary Griffith; Gerald S. Hartman; J. Rodman Steele, Jr; Ed Butchko; Jack Walfish; Steven Khosrova; and Susan Elmer.

Our regional patient/family conference program took us in June to Rochester, NY where our hosts were neurologists Ann Moss and Charles Thornton, and the host institution was the University of Rochester Medical Center, Strong Memorial Hospital. In September neurologist Phillip Chance was our host at Children's Hospital of Philadelphia at the University of Pennsylvania Medical Center. In November our conference host was neurologist Carlos Garcia, and that meeting was at University Hospital of New Orleans, part of Louisiana State University Medical Center. Hundreds of CMT patients, their families and friends met for full day programs about CMT



Dr. Ann Moss, neurologist and host of Rochester NY conference and participant



New Orleans Conference Participants

genetics, neurology, research, and therapies. We are deeply indebted to our host physicians and institutions for giving so freely of their knowledge, time, talents, and facilities. We thank them and laud them for their contributions.

At the Philly conference Dr. Chance was awarded the CMTA's "Outstanding Research Award" for his CMT research contributions. Dr. Chance has further earned the respect of his fellow researchers for the discovery of the genetic cause of hereditary neuropathy with liability to pressure palsy (HNPP).

Work has progressed on the physician's handbook, and we anticipate it will be published in early 1995. The book is being written by CMT physicians and therapists for primary care physicians (family practitioners, pediatricians, and internists), who have CMT patients in their practices. The book is comprised of ten chapters and a list of resources.

In 1994 the CMTA's informational brochure, the "grey brochure", was published in Spanish. This is the first Spanish publication we have done and we have plans to follow this with Spanish editions of CMT FACTS I & CMT FACTS II. The CMTA REPORT continues to be sent quarterly to all who request it. This publication consists of information about CMT research, current medical opinions and therapies, as well as, reader generated articles, letters from readers, and announcements. Frequently, the newsletter contains a call for participants from a researcher who needs patients for a

CMT research project, and we are delighted to be able to provide this service.

Two new programs have been added to the scope of the organization. The first is the "Gift of Hope" program, and it is a means for CMT patients to contribute tissue to CMT research. The "Gift of Hope" is administered by the National Neurological Specimen Bank.

The second program is our chapter development project. A chapter is in the formative stage in Northern New Jersey under the direction of CMTA vice-president Bob Daino. Chapters differ from support groups in that they are legal entities and have guidelines and responsibilities that support groups do not have. There will be more information about chapter formation in the next issue of the CMTA REPORT.

Our list of friends to thank for contributions of time and talent during the past year include Dale Stell, Steve Khosrova, Laura McCann, Herman Baron, Patti Wall, Kathy Parry, and Elia and Lynn Dionne. Needless to say, we thank our support group leaders, telephone contact persons, and members of the board of directors for their immeasurable contributions. As always, it has been my pleasure to speak and meet with many of you individually. It is my contact with you and my work on your behalf which makes being president of the CMTA a pleasure.

Respectfully submitted,

Karol B. Hitt
President

CMTA Medical Advisory Board Meets

Ask the Doctor



Dr. James Lupski & Dr. Carlos Garcia

The CMTA Medical Advisory Board met during the October neurology meetings in San Francisco. Dr. Robert Lovelace chaired the meeting, and Dr. Roger Lebo was in charge of presentations. Dr. Lebo began with an overview of current CMT research. (See Summer, 1994 CMTA REPORT, "Research Update")

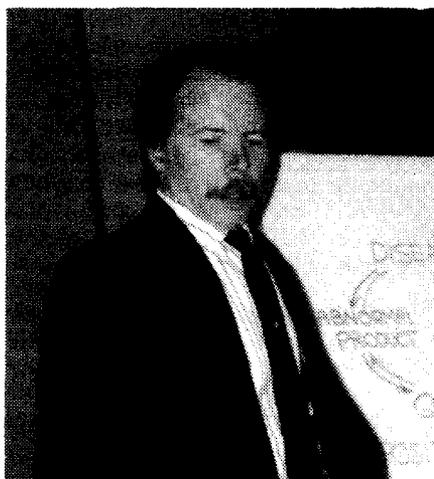
Michelle Mendoza, a physical therapist at the University of California at San Francisco, spoke on the benefits of exercise for the CMT patient. Ms. Mendoza offered the following reasons for a CMT patient to be in an exercise program: increase muscle strength for mildly affected and unaffected muscles; maintain and increase bone density; facilitate joint lubrication and cartilage nutrition; minimize abnormal stresses put on joints; maximize function; combat depression; mood elevator; improve sleep; and finally, but very important, the patient takes an active role in his/her health. Ms. Mendoza stressed the definite benefit of stretching exercises for the CMT patient, and emphasized that each patient must be evaluated and an exercise program devised specifically for that patient.

Dr. John Hsu, Chairman of Orthopedics, Rancho Los Amigos Children's Hospital, Los Angeles, spoke on orthopedic concerns in CMT children. Dr. Hsu said that 15% of the CMT children he sees have kyphoscoliosis (an abnormal backward curvature of the spine combined with a curvature of the spine to one side). Dr. Hsu advocates the recognition and treatment of disabling conditions in children with the problem areas being the feet, hands, and spine.

The program continued with a presentation by Monica Wohlfred, a genetic counselor at the University of California

San Francisco. She defined genetic counseling using this definition from the American Society of Human Genetics: "Genetic counseling is a communication process which deals with the human problems associated with the occurrence or the risk of occurrence of a genetic disorder in a family. This process involves an attempt by one or more appropriately trained persons to help the individual or family to:

- Comprehend the medical facts, including the diagnosis, probable course of the disorder, and the available management.
- Appreciate the way heredity contributes to the disorder, and the risk of recurrence in specified relatives.
- Understand the alternatives for dealing with the risk of recurrence.
- Choose the course of action which seems to them appropriate in view of their risk, their family goals, and their decision.
- Make the best possible adjustment to the disorder in affected family members and/or to the risk of recurrence of that disorder." §



Dr. Roger Lebo

Dear Doctor:

I am interested in finding out more information about the harmful side effects of pyridoxine (B6) and nitrous oxide. Is it harmful for my daughter who has CMT to use nitrous oxide when having dental work done? Many of the dentists in my area use it routinely on their young patients. My daughter gets quite nervous and it seems that it would make life easier for her to have the gas for the dental work.

In regards to pyridoxine, I would like to know where I could find the research reports on its negative effects. I have been told that it is possible that a natural form of B6 may have a different effect than a synthetic form of the same thing. I'm interested in knowing which form of the vitamin was used in the studies. Also, I'm quite interested in finding out more about the negative effects of pyridoxine as I believe that my taking prenatal vitamins during my two pregnancies may have caused muscle weakening and fatigue. I have recently discovered that most prenatal vitamins contain pyridoxine. I noticed a weakening of my muscles, especially in the fingers, thumb and lower extremities, during both of my pregnancies. I also remember that I slowly regained most of my strength after delivering my girls and also stopping the use of my prenatal vitamins. Any information you could share would be appreciated.

The doctor replies:

Patients with CMT should have some concerns about the harmful side effects of pyridoxine vitamin (B6) and nitrous oxide. Although the lack of vitamin B6 has been associated with polyneuropathy, both experimental studies in animals as well as studies in man, have reported that excessive doses of pyridoxine produce a sensory neuropathy. Dr. H. Schaumburg and his associates have reported that pyridoxine in doses of 500 mg or more a day can result in a predominantly sensory neuropathy that is due to the degeneration of the sensory neurons. It has been recommended that pyridoxine therapy consists of no more than 50-100 mg per day. Mega-vitamin therapy should not include B6 therapy. The studies indicated that only sensory nerves were involved, and therefore it is not likely that pyridoxine itself would

(cont'd on page 12)



The Physical and Psychological Effects of CMT



The following is taken from a survey conducted by Bianca Phelan for her degree. The information for the survey came from the membership of the Australian CMT organization. We present it for your information and because of the interest it holds for our readership. It is reprinted with permission from the Autumn 1994 issue of CMT Australia.

Physical Effects of CMT

People seem to notice periods of degeneration and periods where their condition remains stable. The feet and lower leg are more often affected and more severely affected, with 64% of symptoms, than the hands and arms with 26% affected. People encountered a range of physical problems which are listed below. The percentage indicates the number of people who nominated that problem as their major problem or inconvenience.

- Walking/running - especially upstairs, on slopes or on uneven ground 24%
- Fumbly fingers, with handling money, doing button, lack of strength to open jars/bottles, difficulty holding a pen 14%
- Balance 12%
- Participating in sports 11%
- Falling and tripping 10%
- Finding comfortable, presentable shoes 10%
- General pain and disrupted sleep due to cramps 5%
- Severely reduced mobility 5%
- Fatigue 3%
- Difficulty standing or sitting for prolonged periods due to pain, cramps and numbness 2%
- Sore, callused and corned feet 2%
- Inefficient circulation causing hot and cold hands and feet 2%

Seventy one percent of respondents to the questionnaire have had some successful treatment for their condition. Of that number, 29% have had physio-

therapy, which was used to minimize the deterioration. Twenty percent have had podiatry treatment.

Orthotic devices are commonly used to prevent foot rolling or flopping, with the aim of correcting the gait. Twenty-two percent have had corrective surgery - more often to the feet than to the hands. However, there was a mixed response as to the effectiveness of the surgery.

Psychological Effects of CMT

CMT definitely has psychological implications. As CMT progresses, people find they can no longer do what they once could. Frustration and a feeling of helplessness is a common result.

However, each person has a unique response to it, some coping better than others. Eighty-four percent of respondents believed their "differences" were noticeable to others. Sixty-one percent of respondents said they felt CMT had affected their self-esteem, with some stating that self-esteem had become their greatest problem.

Factors mentioned as contributing to loss of self-esteem ranged from strangers' reactions/comments, to the effect on employment. Thirty-one percent of respondents said that CMT had affected their employment, involving a revision of career direction, employment area and early retirement.

A few people mentioned that they were occasionally accused, falsely, of being drunk. Others were sometimes spoken to more loudly and clearly, as though an intellectual disability always accompanies a physical one. A number said that people often asked them if they had hurt their leg or foot.

Some people find that CMT inhibits their social activity. For example, many social activities revolve around physical activity, from being a member of a team for competitive sports, to playing a game of tennis, to dancing at nightclubs to walking on the beach. All of those activities can pose a problem for a person with CMT. This, in itself, can have a negative impact on self-concept.

The usual status quo on diagnosis of CMT is that three generations discover at the same time, what their similar problems are collectively called. In my experience, I observed a pattern of responses to CMT across the three generations:

The older people tended to deny having a problem or simply ignored it.

The middle generation experienced a mixture of relief at finally discovering that there was a reason for all their "faults" and guilt at having passed it on to their children.

The younger generation had a mixed reaction of anger, indifference, and depression.

In one sense, it is good to know about CMT and what possibly lies ahead, but this knowledge brings with it responsibilities, such as not neglecting treatment and choosing whether to bring children with a disability into the world.

Surprisingly, only 44% of the respondents felt that their decision to have children would be influenced by the fact that they have CMT.

Many respondents emphasized that the benefits of community education would be greater for young people with CMT as the perception of self is at its most fragile stage during adolescence, when CMT may first be making its presence known. Generally, it is more accepted for an elderly person to be disabled than it is for a young person.

In conclusion: People often talk about the importance of accepting a disorder such as CMT. I think this basically means being aware of your own capabilities and establishing a lifestyle and goals within your limits. This also includes having reasonable and realistic expectations of those around you. Therefore, you can be satisfied with what you do achieve. Since doing this survey, I have learned that it is not as important to focus on CMT as it is to be aware of and informed about it. §



Blood Test Available

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

Just the fax.

Is your office upgrading and replacing your current fax machine? We have a need for an auxiliary fax machine to be used off site. Of course, the donation would be a charitable contribution.

Letters to the Editor

Dear CMTA,

I hope this letter finds you all in good spirits. I am writing this letter in response to phone calls I have received from other people diagnosed with CMT. My name is Eda Adams and my name and phone number are in the newsletter as a contact person. I have decided to write a letter about myself and the people who have contacted me.

I am 30 years old and have been diagnosed for three years. I have a four year old son named Joseph and a husband named Cory. I, like many other people, am relieved to finally put a name to my illness which, for me, is closure on a very hard part of my life. I have afo's which are non-hinged because of ankle muscle atrophy. I have hand braces to help with bad days when I need the strength to hold things. I also have an electric wheel chair to help me get around at home. We have a farm-like home with many animals who need our attention.

I am in pain the majority of the time. The pain I feel is a stabbing, burning, cramping pain with a lot of numbness and tingling. Nothing seems to relieve it. I have tried many things to control pain including the T.E.N.S. machine with no success. I am currently trying low dose anti-depressants that the doctor hopes will hit the right neuro-transmitter in my brain and shut down the pain messages. I would be interested in any reader comments concerning pain control.

In a few days, I will be going to pool therapy to strengthen my muscles and help in range of motion. I am hoping this will do me some good. I ride the stationary bike and I do soup can exercises because that's about all I can handle, weight-wise.

I am putting my sights on starting a support group in my area of Folsom or El Dorado Hills, California. If anyone in that area is interested, please call me. I have, what I feel, are the best doctors in my area helping me. I am close to UC Davis which has a wonderful PM&R clinic. (physical medicine and rehabilitation)

I would like to share my feelings about one of the people who has called me. I received a call recently from a woman who touched my heart in a special way. She informed me that she had recently written a letter that was published in the newsletter. She has lost her hearing and uses a form of communication that was

foreign to me. That did not slow us down one bit. She made me laugh, which is a healing thing all in itself. When I went to the newsletter to look for her letter, I realized why I had bonded so quickly with her on the phone. I had read her letter when I was down and out and I needed something or someone positive to help me get over the blues. That was your newsletter and her letter to the editor. I remembered reading her letter and laughing.

Thank you CMTA and thanks to that wonderful woman who helped me cope and not feel so alone. Contact people are there to help and give support to callers. But, believe me, it helps to get phone calls like the one I got, so everyone benefits.

Eda Adams

Dear CMTA,

After receiving your newsletter for some time now, I feel prompted to write and express my feelings concerning CMT. I appreciate all the people who have taken the time to write and tell of their personal experiences with CMT. The articles have been honestly written and have come from the heart. I have read of many things I can identify with. I also find interesting the medical articles written on this subject. I hope more research can be done on this disability as well as finding ways to treat this disease.

Like many others, I didn't even know there was a name for what I had until my early twenties. I have never consulted a medical professional about my disability, but my mother and two of my four brothers have been diagnosed with CMT. (I am the youngest and the only daughter.) My feet are quite wide and have extremely high arches. My toes are curled around instead of straight. I have another problem, though, that I have not read about in the newsletters and that is a knee dislocation occurrence. Believe me, it is not pleasant and fortunately does not happen very often.

While growing up I assumed that my family was the only one in the world with this disability. Someday I hope to be able to attend a support group meeting so that I can talk with others about CMT. I live in North Dakota and have quite a tricky time of getting around on the ice and snow during the winter. I'm slow, but I eventually reach my destination. Finding comfortable shoes is almost impossible. I usually end up buying shoes which are too long because the shoes that fit the length of my foot will not fit the width.

Dress shoes with high heels are definitely out of the question. My ankles turn quite easily, so I pretty much have to stay on flat pavement when I walk.

Having CMT has definitely affected my life. I truly feel, though, that it has made me more aware of, and sensitive to, the needs of others. My oldest brother is the one who found out about your organization and newsletters. I'm so grateful for his passing along this information to me. I just wish your publication came out monthly instead of quarterly. It has helped me tremendously knowing that there are others who face many of the same challenges that I do. I know that I have much to be thankful for in my life. Thanks for the invitation to send letters concerning our experiences with CMT. It helps me to write about my feelings.

L.D. Grand Fork, ND

Dear CMTA,

I have had the problems described in the articles you sent me since about 1983 or 84. That's when it started. I was considered disabled by Social Security in 1985.

I live in north east Missouri and have been seen by quite a few doctors including several neurologists. The closest diagnosis was from the last one I saw. When he saw my feet and arches, he said my problem was probably hereditary. After doing an electrical stimulation of the nerves in my legs, he said I should check with family members for similar problems.

I hadn't done anything about it since then mainly because I didn't know what to do until I saw a small advertisement in a weekly shopper to send for free information.

I have spent the weekend with the info you sent me and now I need more. I want the physician referrals for my area. Your information has been a Godsend to me because I thought I was nuts. I'll write more later...after I read the handbooks!

For now I am thankfully,

R.N., MO

Attention Dejerine-Sottas Families

If you would like to communicate with other D-S families, please send a letter to the CMTA giving us permission to release your name to other D-S people. We are in the process of forming a supportive D-S network.



Patient Profile: Clayton James Malone



Clay Malone

Clay is the 1994 MDA Junior Goodwill Ambassador for the state of Oklahoma and appeared on the Labor Day telethon. He was born on December 21, 1988 and was diagnosed at age 2 with a rare form of Charcot-Marie-Tooth disease. He uses leg braces to help him walk and wears a body brace for the scoliosis which has reached a 35 curve.

Clay lives in Edmond, Oklahoma, with his parents, Jim and Maggie Malone. Jim is a flight engineer with the Air Force at Tinker AFB and Maggie is becoming a certified public accountant (CPA).

Clay starts kindergarten this fall and is excited about that new adventure. He loves trucks and trains and likes painting, singing, and playing games.

He has enjoyed the attention he receives as an MDA Ambassador and has previously served as the Western and Central Oklahoma MDA Jr. Goodwill Ambassador.

As his mother wrote, "Clay adapts well and loves life."

The CMTA congratulates Clay on the honor of being chosen an MDA Ambassador. §



Ask the Doctor - cont'd from p.10

produce weakness or motor involvement. Purified pyridoxine has been used in the studies. Any of the natural foods that contain pyridoxine would have the same chemical, but they have other ingredients as well. I would suggest that patients with CMT use only small doses of pyridoxine such as the recommended amounts of 2.5 or 5 mg a day. Additional therapy would be indicated only if they are using a drug that depletes them of pyridoxine.

Nitrous oxide has also been reported to produce a predominantly sensory polyneuropathy in moderate abuse and prolonged over-use may produce a myeloneuropathy, which involves the spinal cord as well as sensory nerves. Random or small use of nitrous oxide is not likely to cause any peripheral nerve dysfunction, but abusing nitrous oxide can certainly result in a neuropathy followed by a myelopathy, if used more extensively. Most dentists use only minimal amounts in the therapy of patients. I suggest that any patient with CMT have only limited and infrequent exposures to nitrous oxide.

For further information on pyridoxine, you can research the following: Schaumburg, H.H., et al, NEJ Med, 309, 1983. Annals Neurol, 12, 1982.

Dear Doctor:

My right leg is 1/2 inch shorter than the left leg. As a result of my gait, I have both low back pain and some right knee pain on the inside. My back pain sometimes keeps me from doing normal everyday things, especially when it comes to bending down. I had an MRI in January of 1994 which said, "Charcot-Marie-Tooth disease may appear as an enlarged nerve root on the MRI scan, however, this finding is not present. I have degenerative arthritis, C3-C5, and degenerating discs L1-L5. There is no evidence of spinal stenosis, however, lateral recess stenosis is suspected at right L4-L5 level."

I would like to know if an epidural can affect CMT. I have low back pain and nerve pinching. I find it hard to get out of bed in the morning. I can't sit or stand for long periods of time before I feel the low back pain. Is the use of epidurals a safe method to get relief from my pain?

The Doctor replies:

CMT may put an increased strain on the lumbosacral spine because of abnormal walking dynamics. However, in general,

The Summer Research Fund Appeal: An Update

By now, most of you should have received either a "bake sale" or "golf tournament" promotion geared to raising money for the research fund of the CMTA. To date, approximately \$5,300.00 has been raised by that appeal.

The CMTA would like to applaud the efforts of one of our members, Marilyn Dodge, who made our fundraiser her own personal effort to raise money for the research fund from her friends and co-workers. Marilyn reprinted the fundraiser on "shocking" pink, green and yellow paper to catch the attention of her friends. Her efforts netted the research fund more than \$600.00. The CMTA certainly appreciates all of Marilyn's work on behalf of the research fund. Her success demonstrates that even one person, located across the country in California, can work for the good of the whole organization.

If you would be interested in sending either the golf or bake poems to friends and family, they are always available from the office of the CMTA. We supply the poems as well as the stamped business envelopes and the remittance envelopes. Your task would be to find probable donors and sign the forms so that your friends or relatives know that you are making the request.

Please consider this means of raising money to fund CMT research. §

there is not an increased incidence of lumbar disk disease in patients with CMT disease. Epidural corticosteroid injections, sometimes combined with a small amount of local anesthetic, can be helpful in people with low-back pain and sciatica, resulting from degenerative disease of the lumbosacral spine. These injections are not curative, but can partially relieve symptoms for a period of time awaiting the natural recovery of the condition, which occurs in most people.

I know of no increased risk that someone with CMT might have while undergoing an epidural steroid injection. The peripheral nerves are somewhat more sensitive to damage from any neurotoxic agent in all types of CMT disease, but epidural corticosteroids are not specifically neurotoxic. §

Charcot-Marie-Tooth Disease: A Multi-Gene Disorder

by David L. Paul, Ph.D.

(This article is reprinted with permission of the author, Dr David Paul who is an Associate Professor of Neurobiology at Harvard Medical School. It appeared in On the Brain, a publication of the Harvard Mahoney Neuroscience Institute. The author writes, "I have been studying the mechanism of intercellular communication through gap junctions. I cloned many of the genes involved in the establishment of gap junctional communication but, until the CMTX locus was mapped by Kurt Fischbeck (physician and researcher at the University of Pennsylvania) and others, I never even suspected that problems with gap junction communication could result in CMT.")

Multi-gene diseases are a great research challenge: Many cruel and costly disorders are multi-genetic, including diabetes and perhaps manic-depressive illness. One such disease, Charcot-Marie-Tooth disease (CMT), is a heritable disorder of the peripheral nervous system (PNS), affecting one in every 2500 people. But, unlike the other disorders, CMT has begun yielding its secrets, offering hope to researchers of all multi-gene diseases.

...CMT has begun yielding its secrets, offering hope to researchers of all multi-gene diseases

Individuals affected by CMT (also known as Hereditary Motor and Sensory Neuropathy) display a slowly progressive muscular weakness in the extremities and mild loss of sensation. Clinical symptoms vary considerably in onset and severity: Beside muscle weakness and atrophy, patients may develop deformities of the hands or feet and gait disturbances are often evident, beginning with a tendency to "toe walk" in early childhood; severely affected individuals may later become wheelchair-bound, and activities as simple as buttoning a shirt can be painful and difficult. Currently, CMT is incurable, although surgery or physical therapy can sometimes ease symptoms.

In the most common subtype, CMT1, peripheral nerves propagate electrical impulses much more slowly than normal, although impulse strength is unaffected. High conduction velocity is made

possible by an insulating material called myelin which sheathes the axons of nerve cells, but in CMT1, myelin formation and maintenance are impaired, and, over time, it degenerates.

In the central nervous system, this pathology is called multiple sclerosis. But in the PNS, it is often the result of CMT1 and involves not nerve cells but special supporting cells known as "Schwann cell." In the PNS, the Schwann cell sends out a sheet-like extension that closely wraps the axon, forming myelin.

The molecular basis for CMT1 myelin degeneration was unknown until recently, when genetic linkage analysis was used to map the chromosomal location of genes involved. Surprisingly, at least four genes were involved, and the DNA from three of these genes had already been isolated and sequenced (cloned) in other studies.

If a cloned gene is near a presumed disease gene, it is possible that the genes are related. CMT linkage analysis indicated similar map positions to genes encoding three proteins: peripheral membrane protein 22 (PMP-22), myelin protein zero (P0) and connexin32 (Cx32). And in CMT patients, mutations in these genes were discovered involving several CMT variations.

PMP-22 and P0 are found in the Schwann cell membrane and are major components of myelin. Currently, the function of PMP-22 is not understood, but too much or too little normal PMP-22 harms myelination as much as PMP-22 with altered structure: The most common form of CMT1 occurs when one or both of the original copies of the PMP-22 gene are duplicated. Conversely, deletion of one original copy causes "Hereditary Neuropathy with Liability to Pressure Palsies," a condition like CMT1 except that it is episodic and usually lasts only a few weeks. Defects in myelination also occur when PMP-22 "point mutations" change the identity of amino acid residues in the protein. This can cause CMT1 or the related Dejerine-Sottas Syndrome.

In contrast, a function for P0 is suggested by its structural similarity to well-known "adhesion" molecules that hold cell surfaces together. Precise adhesion is critical for the wrapping and stable association of Schwann cell membranes during myelin formation. Significantly, the point mutations in P0 associated with

CMT1 affect the part of the protein most likely required for adhesion.

Cx32, unlike PMP-22 or P0, is mostly found in cells outside the nervous system. It was initially discovered in liver cell "gap junctions," channels for small molecules to cross between adjacent cells. But since Schwann cells aren't near enough to each other to form gap junctions, what is Cx32 doing in the Schwann cell? Cx32 could form intracellular channels connecting one wrap to the next; such channels would dramatically shorten the distance of intracellular pathways, which could be important for Schwann cell metabolism or for communication between axon and Schwann cell. One puzzling aspect of Cx32 mutation is that disease only strikes the PNS, though many cells outside the PNS express Cx32. It is possible that, elsewhere, other connexin genes can substitute for the mutated Cx32, while Schwann cells, for unknown reasons, cannot and therefore fail to function normally.

A specific diagnostic test for one form of CMT1 is now widely available; others will likely follow soon to allow many families to seek genetic testing and counseling. In the future, more detailed information about the function of genes involved in CMT will permit the design of rational therapeutic strategies. §

HONORARIA

IN HONOR OF:	BY:
Maxine Hardy	Bruce & Judith Park
George Hardy	"
Lucille Park	"
Bliss Park	"
Michael Park	"
Lorraine Middleton	M/M Marvin Tiewsky
Lorraine Middleton	Anne Mehninger
Lorraine Middleton	Ronald & May Springwater
Lorraine Middleton	Mona Wineburg
Lorraine Middleton	M/M C.T. Cross
Iris Golmitz	Karen Gabel
Carol & Stuart Feen	Vivian & Michael Feen
Charles & Thomas Lynch	Christopher Lynch
Paul J. Terrell	R.T. Strafford
Leah Vaknin	Leon Gelman
Megan Ann Knuth	Mrs. R.H. La Sogga
Megan Ann Knuth	Ellen Knuth
Megan Ann Knuth	Bill Thiry
Megan Ann Knuth	Augusta Lions Club
Megan Ann Knuth	Guy Blumenthal
Rebecca Sand	Sybil & Irwin Whitman
Samuel Doss & Ola Conner	Ann Criscuolo
Clint Rall	Inge Boskovich
The 50th Anniversary of Leonard & Marcie Streff	

CMTA Contacts

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

* denotes support group leader

Alabama / Greater Tennessee Valley

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

California

*Janice Hagadorn 805/985-7332 after 5
(Oxnard/Thousand Oaks)
*Sheila Levitch 805/254-5322
*Denise Miller 805/251-44537
(Canyon Country/Saugus)
*Gary Oleze 619/944-0550
10am-5:30 pm 619/436-2116
(San Diego)
*Freda K. Brown 707/573-0181
(Santa Rosa)
Eda Adams, will return calls
916/677-6460
Jeanne Amour 408/258-9122
Clair Bumgarner 209/874-4963
Felice Gail Viggers, 805/492-2840
Verna M. Sabo, 818/892-6706
Mary Micalizzi, after 6pm
619/441-2432
Bob Hedge, 9am-5pm 310/645-2761

Colorado:

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

District Of Columbia:

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

Florida:

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

Georgia:

Nancy Lee McCutchen 404/925-1020

Kansas:

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

Louisiana

Bobbie Marberry 504/872-0895

Maryland

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

Massachusetts

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

Michigan

Robert D. Allard 517/592-5351
*Suzanne Tarpinian 313/883-1123
(Detroit)
Laurie Vasquez 517/893-4125

Mississippi

*Julia Prevost 601/885-6482
*Henry & Brenda Herren 601/885-6503
(Jackson)

Minnesota

Grace Wangaard 612/496-0255

Missouri

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

New Hampshire

Mary Nightly 603/598-5451

New Jersey

*Janet Saleh 908/281-6289
(Sommerville)
*Teresa Daino 201/934-6241
(Englewood)
Linda Muhlig 609/327-4392
Gary Orson, Mon-Fri 6pm-10pm
& weekends 609/584-9025
Russell Weiss 908/536-6700

New Mexico

Jesse Hostetler 505/536-2890

New York

Joe Ehman 716-442-4123
Internet: KOLOB@Multicom.Org
Alan Latman 800/227-1343
*Diana Eline 201/861-0425 before 9pm
(New York City)
*Abby Wakefield 212/722-8052 (NY)
*Lauren Ugell 516/433-5116
(Long Island)

Amy Gander is interested in forming a CMT support group in the area encompassed by zip codes 12202 through 12309 in New York State. If you are interested in being a member of her group, please call Amy at 518/373-9907 and let her know of your interest.

*Bernice Roll 716/584-3585 (Rochester)

*Kay Flynn 914/793-4710
(Westchester County)
Amy Gander 518/373-9907
Angela Piersimoni, after 2pm
607/562-8823
Sharon McAvey, afternoon & evening
718/380-3792
William Carrington, 4pm-11pm
718/486-6953

North Carolina

*Susan Salzberg, 7am-3:30pm
919/286-0411 x 6586
5pm-9pm 919/967-3118
(Durham)

Ohio

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

Oklahoma

Leah Holden 405/255-4491

Oregon

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

Pennsylvania

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

Rhode Island:

Robert Matteucci 401/647-9154 PM

Texas

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

Virginia

*Mary Jane King 804/591-0516
(Tidewater)
*Thelma Terry 804/838-3279
(Tidewater)

West Virginia

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

Washington

Marlene Russell 206/484-3116

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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. §

MEMORIALS

IN MEMORY OF: BY:

Oren Moreland, Jr. James Harrison	Dallas and Mary Hel Minna Sand & Family
Doris Steckler Doris Steckler	Virginia Benzie James & Kathryn Wolf
Doris Steckler Doris Steckler	Glenice Hansen Toni Steckler Andemon
Doris Steckler Doris Steckler Charlie Dezers	Roberta Steckler Edward Steckler Peggy Jumper
William Coangelo William Coangelo William Coangelo	Joan & Jack Walden M/M John Ahrens The Sunshine Club Collingswood
William Coangelo Edward Scarsella Andrew Geary	M/M Mark Evans Flora Motta John Geary
Harry F. Schaller Nancy M. Schaller Winifred Murfitt Jack Goldman	Harry P. Schaller Harry P. Schaller Pauline Nelson David & Sari Goldman
Arthur Wegehof Andrew Geary, Sr. Ralph Binford Mrs. Irene Galiardo	Margaret Wegehof Mrs. Mary Geary Marilyn Dodge M/M Frank Gunnison
Julie Held Donald Broom Donald Broom	James Held Susan Fekete The Cardiologic Department Matt & Ruth Den Dulk
Andrew Geary	Edna Kluepner Fae Steinecker Russell & Anna Leach
Clarence Kluepner LaVon Steinecker LaVon Steinecker	Juanita Davis Louise & Keith Peterson
Ruth Davis May Griffin	Shirlee Bank Gordon Bradwick Karol B. Hitt Rick Fender
Lowell Bank Robert G. Bradwick Robert G. Bradwick William F. Fender	

CMTA Membership/Order Form

Name: _____

Address: _____

Phone Number: _____

Tell us about yourself:

- CMT Patient Medical Professional
 Interested Supporter CMT Family Member

Enclosed is:

- \$25 \$50
 \$100 other

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

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

Publications and Tapes available from the CMTA

(Check to order)

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

Please make checks payable to the CMTA

Return completed form and payment to the CMTA, 601 Upland Ave., Upland, PA 19015

Total amount enclosed: _____

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

MEDICAL ALERT



Certain Drugs Toxic to the Peripheral Nervous System

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

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

Lithium, Misomidazole and Zoloff
can be used with caution

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

Referrals Available

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

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

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

CMT...

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

THE CMTA REPORT

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

Charcot-Marie-Tooth Association

Crozer Mills Enterprise Center
601 Upland Avenue
Upland, PA 19015

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