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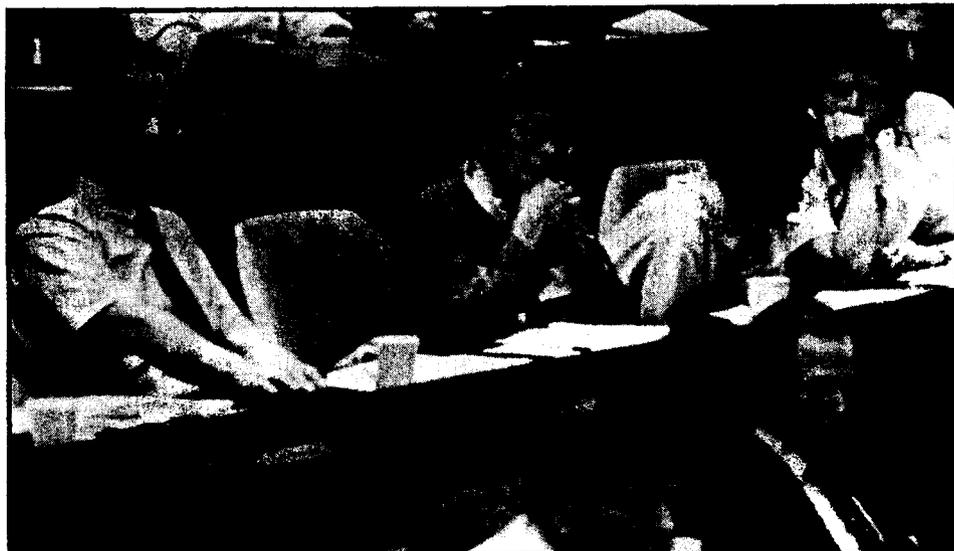
Providing information on Charcot-Marie-Tooth disease (or Peroneal Muscular Atrophy),
the most common inherited neurological disease

Historic Conference Focuses on CMT Research

Teri Daino, community leader and active in CMT support groups, attended the Arden House CMT Conference this summer. Teri was interested in helping her family and other CMT patients better understand "what was happening in the world of CMT research that may someday bring us a cure."

The conference attracted internationally prominent medical researchers and the topics were highly technical in nature. The task of summarizing approximately 24 hours of lectures and discussions was difficult and we thank Teri for her determined work on this report. Teri, for her part, enjoyed interviewing these dedicated scientists and learning the various ways they are working to solve the mysteries of CMT.

It was a glorious four days this summer when leading medical researchers from all over the world joined together for one very important reason. They came to exchange research information on Charcot-Marie-Tooth disorders.



Gene mapping specialists present at the Second International Conference on Charcot-Marie-Tooth Disorders included six shown above: (upper row, left to right) Thomas D. Bird, M.D. (Seattle VA Hosp.), Lowell I. Williams, M.D. (Columbus OH Children's Hosp.) and Anita Harding M.D. (Hammersmith Hosp., London); (lower row, left to right) Kenneth H. Fischbeck, M.D. (Univ. of Pennsylvania) and Roger V. Lebo, Ph.D. (Univ. of California, San Francisco). Also shown (far right) is Dr. Robert A. Ouvrier, a clinical neurologist from Sydney, Australia.

Photo by Lawrence A. Williams

years, a period that witnessed the majority of biochemical research done on CMT to date, the time was right for a second conference.

On June 28, 1987 the Second International Conference on Charcot-Marie-Tooth Disorders became the latest milestone in the history of this disease. The syndrome was first identified in 1886, in France, when the leading neurologist Jean Martin Charcot along with fellow physician Pierre Marie first described the symptoms of peroneal muscular atrophy. The same year an English physician, Howard Tooth, presented a similar report. It was some 90 years later that another milestone occurred. In 1976 Dr. Georges Serratrice organized the first international meeting on CMT, which was held in Marseilles, France. Very little research had been undertaken by this date so the meeting in France focused on the clinical aspects of CMT. After 10

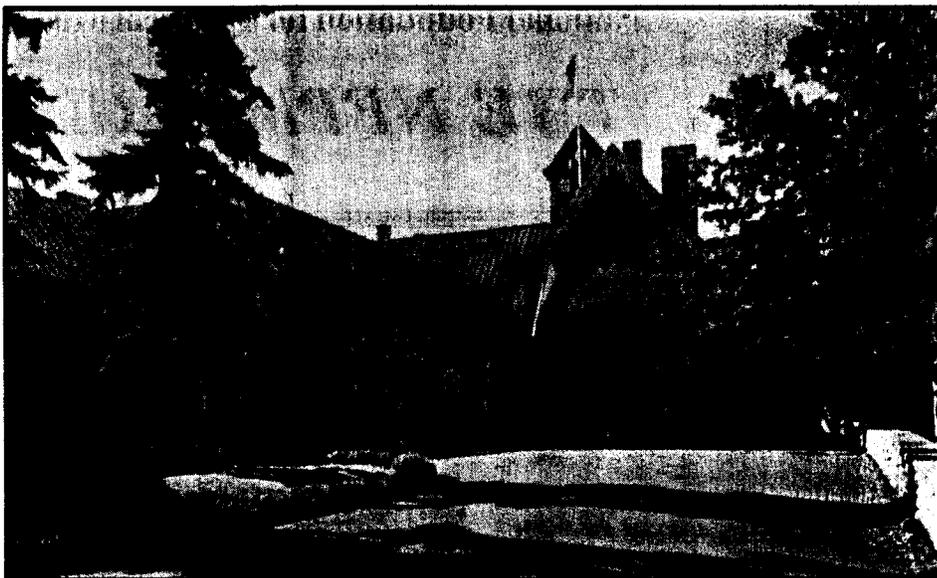
The setting for the Second International Conference on Charcot-Marie-Tooth Disorders was Arden House, a mountain retreat in Harriman, NY. Arden House was once the home of Ambassador W. Averell Harriman and was donated to Columbia University by the Harriman family to serve as a political and scientific conference center. Over fifty medical research scientists who specialize in treating CMT patients and studying CMT related issues presented papers at this meeting. The conference was technical in nature due to the format of physicians and biochemists talking to one

Inside:

National Organization for Rare Disorders Annual Conference	Page 10
World Health Organization Neuropathy Conference	Back Panel
Upcoming meeting focuses on psychosocial aspects of CMT	Page 4
Peroneal Muscular Atrophy, the basic facts	Back Panel
NFPMA Mailbox	Page 9
Not Your Neighborhood Shoe Store	Page 10
VCR Tape Rentals	Page 11
Dedicated Contributions	Page 11
Get in Touch	Page 11

another. This was an influential meeting with discussions that should affect the course of research on this syndrome for years to come. It also brought before the worldwide medical community the affirmation that CMT is an important disease. A feature article on this conference appears in the fall issue of **World Neurology**, the newsletter of the World Federation of Neurology. CMT is the most common inherited neurological disease, affecting approximately 125,000 Americans.

The meeting was important in several ways. It was an opportunity for medical scientists to meet fellow colleagues and discuss their work. It was also important for the rest of the medical community. After reading the articles and book that will be published on the proceedings, they will be more informed in treating their CMT patients. As CMT becomes better



Arden House, located 40 miles northwest of New York City, provided an inspiring location for three days of discussions on research aspects of Charcot-Marie-Tooth disease.

known, more research funding will become available and answers will be found. This article in the **NFPMA**

Report was written to help inform patients about the material presented at the conference.

Interesting Highlights For Patients

Dr. Anita Harding made the observation that CMT is not a disease but a syndrome. In other words, there is not just one cause for CMT but an unknown number of genetic defects causing a collection of similar clinical problems. She also noted, "The harder you look, the more types of HMSN appear." Hereditary motor and sensory neuropathy (HSMN) is the more accurate term for CMT, and is a term proposed by Dr. Peter James Dyck.

Dr. Robert Lovelace notices this diversity among his patients and he believes that clinically different types of CMT can occur within the same family. One could see how easily misdiagnosis can occur with some patients showing only some of the typical CMT indications, while others may have unexpected additional signs such as impaired speech or eye problems.

Dr. Austin Sumner is in need of nerve biopsy volunteers in the Philadelphia area. Similarly, Dr. Lyn Griffiths in Australia noted that blood samples

from large families are needed for DNA extractions. Also, Dr. Norman Latov would find it helpful to have a source of cells from patients with CMT for molecular analysis. He is at Columbia University in New York City. Dr. Guy Rouleau in Boston, and Drs. Victor and Rebecca Ionasescu in Iowa had the same general request for patient volunteers. Dr. Marvin Rozear in North Carolina and Dr. Kenneth Fischbeck in Philadelphia would like X-linked patient volunteers (those families where men are more affected than women and where there has been no father-to-son transmission of the disease). Patients may want to contact these researchers to volunteer their time and provide needed samples. Mailing addresses for these researchers are available from the NFPMA.

Dr. Pierre Bouche notes that in Paris patients are now willing to start a CMT association.

Dr. Richard Mayer would like to see more studies of motor nerve units in

patients since additional examinations will help make accurate conclusions. Dr. Mayer also optimistically states, "Newer drugs and therapy may be forthcoming especially for those patients with the demyelinating form (HMSN type I)." Summarizing the overall approach to work on CMT, Dr. Joseph Poduslo from the Mayo Clinic had this comment for CMT patients, "Through basic research combining the disciplines of molecular biology, cell biology, and biochemistry, an understanding of the mechanisms of CMT disease will be obtained, which in turn will provide therapeutic benefits."

Several researchers noted that more cooperation and information exchange among investigators of CMT would benefit all involved, avoid duplication, and probably speed up progress. As an example, the molecular geneticists present at the conference agreed that a central location such as the NFPMA, was needed for the reporting of negative results. Such findings might then be discussed with an experienced, non-partisan molecular geneticist and

then distributed to other researchers.

Dr. Lowell Williams has found evidence of altered immune system metabolism in half of the CMT patients she has studied. Hence, in addition to genetic and clinical diversity, the CMT patient population may also feature immunologic diversity.

Dr. Walter Bradley of Vermont, who has just finished one drug study on CMT, noted that he may be seeking to start a trial of a new drug in the future if preliminary studies are encouraging. Dr. Bradley recently tried the drug Cronassial (Fidia Pharmaceutical Corporation) on a group of CMT patients. Cronassial has been shown to be of some benefit to patients having diabetic polyneuropathy, but the drug did not help Dr. Bradley's CMT patients.

Dr. Peter James Dyck of the Mayo Clinic gave the keynote address. He started with an overview of his work with CMT, which spans three decades. He then offered physicians his view on how to treat CMT patients, stressing three points. First, the physician should tell the truth to the patient, including children. Second, emphasize the outlook, which is generally better than the worst case scenarios presented in textbooks. He asked physicians to provide hope since the

life expectancy of the CMT patient is normal. Thirdly, Dr. Dyck asked physicians to encourage their patients to turn outward to minimize the patient's preoccupation with themselves and their disease. Noting the unrecognized importance of the syndrome, Dr. Dyck stated, "Epidemiologic (disease frequency) surveys probably have underestimated the prevalence of inherited neuropathy because many cases remain incorrectly diagnosed or un-

diagnosed. It remains the leading cause of undiagnosed neuropathy referred to this investigator and may be the third most frequent cause of neuropathy in the USA after mechanical injury, compression and entrapment, and diabetes. Differences in natural history, mode of inheritance, class of neurons (axons) affected, neuropathologic abnormality and linkage to blood antigens distinguish kindreds with HMSN."

Emphasizing the international scope of this problem, Dr. J. S. Chopra of Chandigarh, India and Dr. Rachel George of Bombay, India presented lectures on their CMT clinical studies. Dr. Ding-Guo Shen of Beijing, China submitted a similar paper on his CMT clinical studies in China.

Session 1 - Clinical Studies and Pathological Alterations

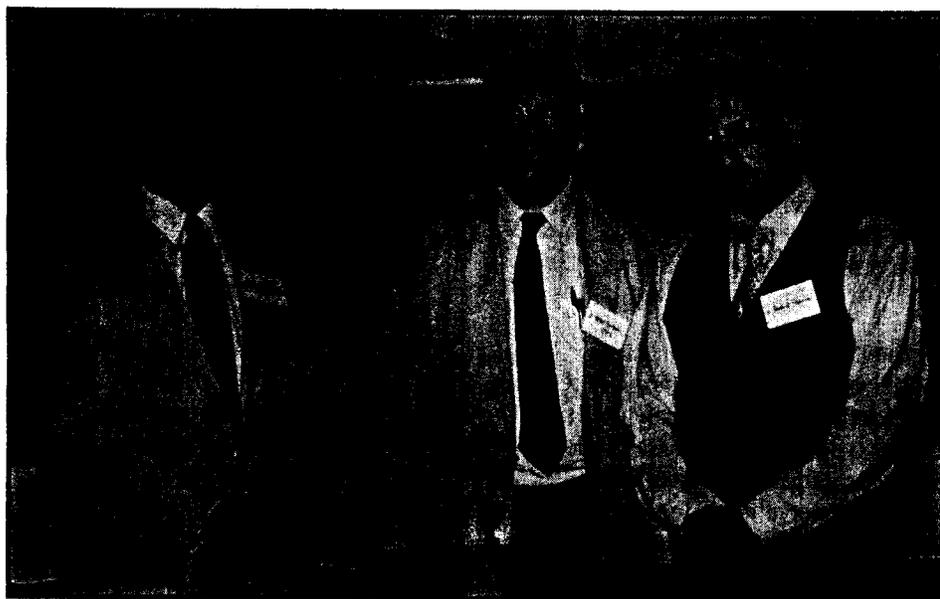
The speakers during this session were neurologists involved in clinical practice. They see CMT patients and are also involved in research at medical schools and neurologic institutes.

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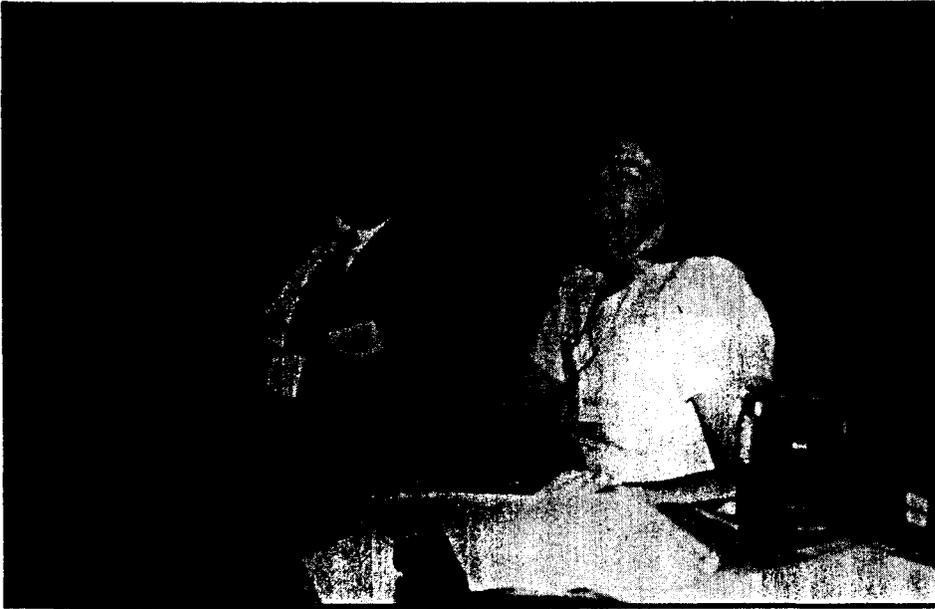
Internationally recognized clinical neurologists were well represented at the Second International Conference on Charcot-Marie-Tooth Disorders, including: (upper row, left to right) Jack H. Petajan, M.D., Ph.D. (USA), J. S. Chopra, M.D. (India) and Richard L. Masland, M.D. (USA); shown below, Anica Jusic, M.D. (Yugoslavia).

Photo by Laurence A. Williams



Peter James Dyck, M.D. of the Mayo Clinic (center) presented the keynote lecture at the Second International Conference on Charcot-Marie-Tooth Disorders. Shown with him are the conference organizers, Robert E. Lovelace, M.D. (left) and Howard K. Shapiro, Ph.D. (right).

Photo by Laurence A. Williams



Caught in mid-interview, Mrs. Teri Daino is seen here discussing clinical studies on CMT with Dr. Constantin Vasilsecu of Bucharest, Romania.

Dr. Harding of London, U.K. is working on classifying the different types of HMSN in her clinical studies. More recently she has been doing genetic linkage studies looking for evidence that some CMT families have a genetic defect, a DNA coding error, somewhere on chromosome number one.

For the last 12 years Dr. Robert Ouvier of Camperdown, Australia has been classifying the peripheral neuropathies in children to aid in their prognosis and genetic counseling. He also is investigating Schwann cells in young patients.

Dr. Lovelace of New York City is involved in extensive clinical studies and noted the heterogeneity of his CMT patients. It is very common to see not only different degrees of symptoms in different families but, most interestingly, much variability of clinical aspects among members of the same family. Dr. Lovelace's studies have focused on this puzzling issue of symptom variability.

Dr. Georges Serratrice of Marseilles, France has been studying the relationships between CMT and spinal degenerations. To date, these relationships are not clearly established. Dr.

Serratrice, like Dr. Lovelace, has devoted much of his time to the question of clinical variability.

Dr. Jose Berciano of Santander, Spain studied patients with CMT from 1974-1984 in the geographic area of Cantabria in order to establish figures for the prevalence of CMT. He found the ratio of CMT patients to the general population of Cantabria was 28.2 cases per 100,000. He also assessed the relative frequency of the several types of CMT disorders.

Dr. Hitoshi Yasuda, of Shiga, Japan is trying to shed light on the reasons or mechanisms of nerve fiber loss in CMT. He has focused on examination of structures within peripheral nerve axons and how these structures are affected in different types of CMT.

For the past four years, Dr. Hans Goebel of Mainz, West Germany has been identifying and classifying the familial type of CMT II associated with giant or enlarged axons, as well as correlating nerve and muscle biopsy findings. He has found that enlarged CMT axons result from a structural abnormality within these cells. This abnormality is the excess accumulation of internal supporting protein elements known as neurofilaments.

Session 2 - Clinical Neurophysiology and Clinical Heterogeneity

Here again the speakers were clinical neurologists who are also involved in research. The majority of their research concerned tests on nerve conduction velocities (the speed at which messages are transmitted along nerve fibers).

Dr. Bouche of Paris, France has studied 231 patients with CMT and is looking for a correlation between the degree of muscle involvement he observed clinically and decreases in their motor nerve conduction velocities. In most cases he has found no significant correlation. He has been on this course of research for the past four years. Dr. Bouche has also done some genetic linkage studies on his families.

Dr. Austin Sumner of Philadelphia is involved in trials of new pharmacologic agents that may be of value in CMT and clinically related disorders. Dr. Sumner, a clinical researcher for the past 20 years, has been involved in

You Are Invited

Clinical and psychological aspects of CMT will be discussed Saturday, January 30th, 1988, at a Columbia University symposium. The conference is **PSYCHOSOCIAL WELL BEING IN MUSCULAR DYSTROPHY AND ALLIED DISEASES: III. PERSPECTIVES FOR THE FUTURE**. This meeting is being organized by the Foundation of Thanatology. Medical professionals, social service professionals, patients and their families are welcome to attend. The meeting will be held at the Columbia Presbyterian Medical Center. For more information, contact Martin Lazarus at (914) 779-4877 or write to the Foundation of Thanatology, 630 West 168th St., New York, NY 10032.

nerve conduction velocity studies as well.

The research goals of Dr. Richard Mayer, pursued during twenty years of related research, are to better understand how peripheral nerve diseases alter the function of muscles and therefore help improve motor nerve-muscle function.

For the past twenty years, Dr. Ludwig Gutmann of Morgantown, WV has studied nerve conduction velocities in CMT patients as the disease progresses from birth to adulthood.

Dr. Paolo Pinelli of Milan, Italy has been involved for 15 years in electrodiagnostic work trying to find how different types of peripheral nerves are affected in CMT and the degree to which the central nervous system may also be involved.

Dr. Constantin Vasilescu of Bucharest, Romania has been studying CMT patients for the past 20 years doing clinical diagnostic work and some limited testing of commercially available drugs.

Dr. F. Leblhuber of Linz, Austria has been doing electro-diagnostic studies of CMT families and also genetic linkage studies for the past six years.

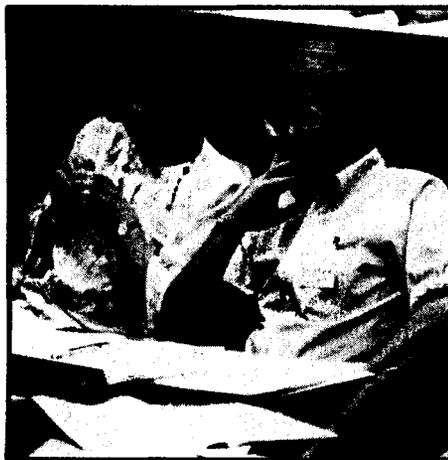
Dr. Edo Bottacchi of Aosta, Italy lectured on his clinical and electrodiagnostic studies of patients with hereditary spastic paraplegia (HSP). His patients, like CMT patients, show lower leg weakness. However, HSP patients also show increased tendon reflexes. These reflexes, not found in CMT, are associated with uncontrollable muscle movement (spasticity).

Session 3 - Axonal and Schwann Cell Metabolism

The researchers grouped into this session have focused their attention on studying the neuron, more commonly known as the nerve cell. The axon is a long, thin extension from the body of

a nerve cell which at its far end connects with a group of muscle cells or with another nerve cell. For motor nerves which connect to lower leg muscles, such as the peroneal muscles, the nerve cell bodies are located within the spinal column and their axons extend down the legs. These axons may be three feet in length, although microscopic in width. The larger peripheral nerve axons are surrounded by a kind of insulation known as the myelin sheath. Demyelination, or the breakdown of the sheath, is one of the reasons why CMT impulses travel at a slower speed than normal nerve impulses. Schwann cells, helper cells which lay close by nerve axons, produce myelin. Groups of smaller peripheral nerve axons are surrounded by Schwann cells which simply encompass them without forming the multi-layer insulation known as myelin.

For about seven years Dr. John Griffin of Baltimore has been constructing experimental models that reproduce important pathologic features of



Prominent authorities on neuromuscular diseases in attendance at Arden House included the husband and wife team of Dr. W. King Engel and Valerie Askanas from the Neuromuscular Center of the USC School of Medicine (Los Angeles).

peripheral neuropathies. He is trying to reconstruct the sequence of cell changes that lead to pathologic changes.

Dr. David Pleasure of Philadelphia for the last five years has been trying to better understand Schwann cell-neuronal interactions and the development of CMT-related disorders. Dr.

Pleasure's research team has focused specifically on work to characterize the role of one axon "signal" molecule, cyclic AMP, in stimulating Schwann cells to perform their support role for neurons.

For about eight years Dr. Poduslo of Rochester, MN has been following research to understand the mechanisms by which Schwann cells control the expression of their myelin-specific gene products and whether these forms of regulation are altered in CMT and related disorders.

Dr. Kristjan Jessen of London, U.K. has been studying how Schwann cells in normal nerves depend on information "signals" from axons for the maintenance of normal structure and function.

Dr. Monique Dubois-Dalcq of Bethesda, MD has been interested in the proteins of myelin-forming cell surfaces, both in the central and peripheral nervous systems. These proteins are key markers of the health of the Schwann cells and similar cells which support neurons in the central nervous system.

Andrew Dean, a Ph.D. graduate student in St. Louis, also has been studying Schwann cells. He is most interested in the proteins excreted by the Schwann cell that form a matrix beyond the cell. Within this matrix Schwann cells will move and differentiate to surround nerve axons.

For the past fifteen years Dr. Akio Ohnishi of Kitakyushu, Japan has been studying how the nerve fiber degenerates and regenerates. He described two patients who appear to have an unusual type of CMT. Nerve biopsy samples from them showed abnormal structure of the myelin membrane produced by Schwann cells. This abnormality showed sections of unfolding of myelin away from axons, instead of around axons.

Since 1979 Dr. Latov of New York City has been investigating the causes and treatment of diseases that affect the peripheral nervous system. Most of his

Continued, Page 6

work deals with those diseases which are caused by the immune system. Dr. Latov summarized what is known about how degenerative changes in peripheral nerves can induce immune reactions which then cause additional nerve damage.

Dr. Sidney Kahn of Philadelphia has concentrated on acquired (not genetic) disorders of the peripheral nervous system which are associated with antibodies. He recently studied blood samples from 16 CMT patients from two families to see if their blood has anti-nerve antibodies. No evidence of a CMT related immune problem was found in these families. Dr. Kahn noted that it is conceivable that other CMT patients may have immune related problems.

Session 4 - Chromosome Linkage Studies on Peroneal Muscular Atrophies and Genetic Heterogeneity

This group of researchers is concentrating on finding out more about the genes which cause CMT. The genetic basis of each inherited disease lies in a coding error in a particular gene. Many genes are connected end-to-end to form each of the chromosomes present in human body cells. Each gene provides the code for a specific protein and proteins, in turn, regulate cellular and body metabolism. Each body cell in a female has 22 pairs of autosomal (genderless) chromosomes and a pair of X chromosomes. Each body cell in a male has 22 pairs of autosomal chromosomes, one X chromosome and one Y chromosome.

The most successful CMT gene mapping work done so far is on the X-linked variety. For X-linked kindreds, male patients usually have far greater evidence of the disease. Female carriers having the CMT trait on one of their two X chromosomes may show only mild CMT symptoms or none at all. Yet such female carriers can pass

the disorder on to either male or female children. What makes X-linked CMT families distinct is the absence of father to son transmission. When a father passes his one X chromosome to a child, the child is female, and would necessarily be a CMT carrier if the father has X-linked CMT. When such a father passes his normal Y chromosome on to a child he has a normal son.

Dr. Kenneth Fischbeck (Philadelphia) has been doing gene mapping studies on X-linked CMT families for about five years, assisted by Drs. Allen Roses and Marvin Rozeat of Durham, NC and others. The frequency of X-linked CMT has never been firmly established, but Dr. Fischbeck suggested that between 10% and 33% of all CMT cases may be of the X-linked variety.

The X chromosome has been well studied in recent years, and the sites of several other X-linked genetic diseases have been located (most notably that of Duchenne muscular dystrophy). More than 200 DNA probes, or markers, for particular sites on the

gene site is near the middle of the X chromosome. Studies are now under way to determine its location more precisely.

Unfortunately, medical scientists looking at families with autosomal dominant CMT, where the problem is not on the X chromosome, have faced a more complex challenge. Progress here has been more difficult to come by. Yet a number of determined efforts are now being made to understand the different genetic origins of the autosomal dominant varieties of CMT. As discussed at the Arden House conference, these efforts may be summarized as follows.

Lyn Griffiths (Sydney, Australia) is a Ph.D. candidate currently trying to localize the gene or genes causing CMT type I, the clinical type showing autosomal dominant inheritance and swollen "hypertrophic" peripheral nerves. For the past three and one-half years she has been using known chromosome number one markers to test for genetic linkage, as well as developing new probes from a



One shot for the record. During a morning break in the lecture agenda medical specialists and NFPMA program associates adjourned to the back of Arden House for a group photo.

X chromosome are now known. Dr. Fischbeck has shown that the region of the X chromosome identified by the DNA marker DXY-S1 lies near the CMT gene site. This observation has also been seen in two other laboratories. These studies indicate that the CMT

chromosome one DNA fragment library. Her studies are based on analysis of DNA from 420 blood samples from 21 CMT I families. Her work to date suggests that perhaps one quarter of the families studied show preliminary evidence of a genetic

defect on chromosome one. For the other families no positive data is available yet to determine where other CMT genes may be located.

Dr. Philip Chance (Nashville, TN), a colleague of Dr. Thomas Bird, is now continuing Dr. Bird's earlier CMT studies. Dr. Chance's work, like Lyn Griffiths' studies, show that CMT I can result from at least two genetic defects, one of which is on chromosome one. His studies suggest that the CMT gene on chromosome one is located near the middle of the chromosome.

Dr. Victor Ionasescu (Iowa City) has studied 18 CMT I families using chromosome one DNA markers. Here again, preliminary results show that about one quarter of the families may have a genetic defect on chromosome one.

A CMT I family first shown by Dr. P. Michael Conneally (Indianapolis, IN) to have a genetic defect clearly linked to the Duffy blood group marker site on chromosome one is now being studied further by Dr. Roger Lebo of San Francisco. Dr. Lebo is also studying several other CMT I families and one family having CMT II (autosomal dominant inheritance, no nerve swelling). As is the case with other investigators, Dr. Lebo's findings are still preliminary. However, his laboratory program includes two promising aspects, a method for sorting chromosomes before they are subjected to additional analysis and a chromosome one DNA fragment library.

Further evidence of genetic heterogeneity in CMT I was presented by Drs. Harding, Bouche and Lowell Williams (Columbus, OH). Dr. Guy Rouleau (Boston) described an initial study on a large family having a hereditary sensory and motor neuropathy. This is a neurological disorder quite similar to CMT, but showing more damage to peripheral sensory nerves. Dr. Rouleau's work so far indicates that this family does not have a genetic defect on chromosome one, nor on chromosome 22.

As more chromosome analysis work is done on CMT families the question of other CMT gene sites is becoming more of an issue. Clearly, only a minority of CMT I families have a genetic defect located on chromosome one. A possible lead, still most preliminary, for resolving this issue may have been provided by Dr. James Lupski (Houston). As reported at Arden House, he has found a CMT family which also carries a second genetic disorder, von Willebrand disease. The von Willebrand protein is one of the elements involved in blood clotting. A deficiency of this protein is a separate clinical disorder, distinct from CMT. But in Dr. Lupski's unusual family each CMT patient also has von Willebrand disease. This suggests that each of these patients may be missing a piece of DNA that spans two neighboring genes. Earlier studies by Dr. Lebo and coworkers have shown that the von Willebrand factor gene is located on chromosome number 12. Drs. Lebo and Lupski are now checking to see if there is direct evidence of a CMT gene site on chromosome 12.

There was agreement among all of the geneticists present at the Arden House meeting that families such as the one described by Dr. Lupski, where CMT is consistently associated with a second distinct genetic disorder, present the best opportunities for making dramatic progress in defining CMT genes. Where two or more genetic problems "co-segregate" in a family they result from the absence of a relatively large piece of DNA. This makes molecular genetics research much easier and faster. Finding such an unusual family considerably hastened the identification of the gene for Duchenne muscular dystrophy. In these situations, of course, important progress on the other disease(s) is made at the same time. Members of those rare CMT families where another genetic defect passes through the family with CMT are urged to contact the NFPMA. Simple arrangements can then be made for taking the small blood samples needed for genetic studies.

Session 5 - Experimental Drug Trials and Metabolic Studies on CMT Syndromes

In recent years there have been four experimental drug studies involving CMT patients.

In his keynote address Dr. Peter James Dyck referred to successful use of prednisone, a corticosteroid drug, for experimental treatment of several CMT patients who also had clinical signs of an immune system problem. Prednisone is a drug that generally suppresses the immune system. While this contributes to our understanding of CMT-like disorders, long term use of prednisone can lead to serious side effects, including muscle atrophy, and Dr. Dyck does not recommend this drug as a general treatment of CMT.

Dr. Walter Bradley (Burlington, VT) has used a purified extract from cow brain to see if it would improve the symptoms of CMT. The drug, known as ganglioside, has been produced by Fidia Pharmaceutical Corporation. It has been shown to be of some benefit to patients with other types of neurological diseases, such as diabetic polyneuropathy. Dr. Bradley designed a comprehensive procedure for clinically monitoring CMT patients during his study. Fifteen CMT I (hypertrophic) and 15 CMT II (axonal) patients were tested. After one year Dr. Bradley found that no beneficial effects could be demonstrated. However, this does not rule out the possibility that a more prolonged treatment period may yield positive results.

Dr. Pinelli has tested thyroid releasing hormone on several CMT type I patients, but only transient beneficial effects were noted.

Dr. Williams gave 20 CMT type I patients a dietary supplement of essential fatty acids for one year. Only slight improvement was noticed at the beginning of the experiment, which was attributed to a placebo effect. Besides her recent drug study, Dr. Williams has

Continued, Page 8

studied the biochemistry of different types of fat in CMT patients and various biochemical details of their immune systems. She has recently noted that some CMT patients show alterations in both of these areas, which may be related to one another and may play a role in the clinical expression of CMT.

Metabolic studies are investigations of how the body internally processes the food we eat, the various chemical fates of food components. There may be reason to believe that the CMT body does not act the same as a normal body. Dr. Howard Shapiro (Philadelphia) is screening organic acids found in urine samples from two CMT families. From each sample he has measured 150 components, resulting in a broad overview of metabolism. One of these families, apparently X-linked CMT, does not show any information significantly different from that of normal donors. However, results from the second family, which has CMT type I, suggest that these patients may have a partial block in the ability to metabolize a class of by-products of sugars, known as furan-aldehydes. Dr. Shapiro is now following up on this interesting preliminary lead.

The final speakers at the Second International Conference on Charcot-Marie-Tooth Disorders were physicians that treat CMT patients in the fields of physical rehabilitation and orthopedic surgery.

Dr. Stanley Meyers (New York) offered to patients the advice that early rehabilitation measures are necessary to maintain strength and to prevent the development of foot bone deformities. Dr. Meyers feels each CMT patient must be evaluated and treated on an individual basis.

Dr. Robert Clark (Columbus, OH) has seen CMT patients in his orthopedic surgery practice for the past five years. He finds that there are fairly characteristic problems that develop in CMT and patients may benefit from both nonoperative and operative methods of treatment.

Dr. John Hsu (Los Angeles) discussed his experience with surgical procedures on 37 young CMT patients, between 7 and 19 years old. About half of the operations were "soft tissue procedures," such as tendon transfers. The rest were bone operations, such as the bone fusion triple arthrodesis procedure. As Drs. Meyers and Clark did before him, Dr. Hsu emphasized the importance of early, careful evaluation, and thoughtful choice of treatment for each patient.

Final Highlights

The Second International Conference on Charcot-Marie-Tooth Disorders was sponsored by the National Foundation for Peroneal Muscular Atrophy in association with the Neurological Institute of Columbia University. The convenor and program chairman was Robert E. Lovelace, M.D., F.R.C.P. and the co-convenor was Howard K. Shapiro, Ph.D.

This conference was supported in part by a grant to the NFPMA from the National Institute of Neurological and Communicative Disorders and Stroke (grant #NSPA 1-R13-NS24812-01). Corporate sponsors for the conference included Fidia Pharmaceutical Corporation and TECA Electronics Corporation. Private support for this meeting was provided by grants to the NFPMA from Frank T. Crohn, Sr. and the estate of Seymour Shapiro. Additional support was provided by NFPMA membership donations.

A book on the proceedings of the conference will be published by the firm of Alan R. Liss, Inc. (New York) under the editorship of Drs. Lovelace and Shapiro. This publication will be suitable for the medical community, and therefore might be too technical for the non-medical reader. If you would like more information on some aspect of the conference, please write to the NFPMA. Details about the availability of the conference proceedings publication will be in future editions of the **NFPMA Report**.

It is interesting to note that three of the medical scientists who lectured at this conference are themselves CMT patients: Drs. Williams, Lupski and Shapiro.

When researchers at the conference were asked what type of obstacles stood in their paths, few expressed that they had not encountered any. Many mentioned that not having enough time was a problem, and not enough patient involvement was frequently noted. Of course, several researchers noted the critical need for funds to support research on this medical problem. Some believe that very little funding has been allocated by the National Institutes of Health for CMT disorders. Indeed, as Dr. Shapiro notes, "The very idea of awarding research grants to study CMT has only been seriously discussed within the past few years." Perhaps you, the reader, can help by writing to some key people. Tell them your opinion, make your voice heard - help fight CMT by influencing research funding priorities, and by donating your own time and resources to the efforts. To make your voice heard write to:

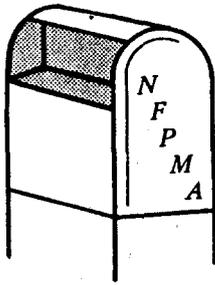
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Senator Lowell P. Weicker, Jr.,
Chairman
Subcommittee on Labor, Health &
Human Services, Education and
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Dirksen Building, Room 131
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NFPMA Mailbox



August 14, 1987
Dr. Howard Shapiro
NFPMA

Dear Dr. Shapiro:

Thank you so much for lending us your videotape ("CMT: Medical Mystery") for the NIH Centennial Celebration. You helped make our video festival a great success.

Sincerely,

Pat Duncan
Office of Scientific and Health Reports
National Institute of Neurological and
Communicative Disorders and Stroke

* * * * *

August 2, 1987

Dear Dr. Shapiro:

I want to thank you for your speedy response to my request for information concerning the NFPMA. The material that you sent was absolutely fascinating.

... Between age 28 and 35 I underwent several surgical procedures, including bilateral triple arthrodesis on the ankles and the Jones osteotomies on all the toes. Since my sister's feet were even worse than mine, I was finally able to convince her to undergo similar surgery last year. She is still wearing casts on both feet at this time. I have been full weight-bearing without pain for the last two years.

My sister has elected never to have children, since she is adverse to passing this disease to her children. I myself put this decision off for many years; however, on May 18, 1987, my wife gave birth to our beautiful little girl, Mollie... For the present, she is completely healthy and normal, which is the pattern of CMT in our family. Our prayer is that she will remain thus

to adulthood. However, if she does develop CMT, I feel much more able to do something for her...

I am sending a copy of your newsletter to both my sister and mother, both of whom now live in Southern California. I am also giving a copy to my orthopaedist... and plan to publicize your organization when possible. Needless to say, I am thrilled to know of your work. Once again, thank you.

Sincerely,

D. D.
Simpsonville, SC

* * * * *

September 5, 1987
Mrs. Karol B. Hitt, Program Associate
NFPMA

Dear Karol:

Sorry about the delay in returning the VCR tapes. Since I treat many people with CMT, I especially enjoyed the programs. I look forward to possibly contributing to your group and welcome any correspondence. Keep up the good work!

Sincerely,

Dr. Guy R. Pupp, D.P.M.
Dearborn, MI

* * * * *

September 26, 1987
Karol B. Hitt, Program Associate

Dear Ms. Hitt:

Please accept my heartfelt thanks for your help with the optic/CMT references. I have sent my neuroophthalmologist copies of the materials along with your suggestions for a Medlars (medical literature) search. It certainly feels wonderful to get a response to a question regarding CMT. Subterfuge, ignorance and contradictory indications seem to be the norm, I'm afraid. Thanks so much for your help...

Yours sincerely,

P. W.
Old Tappan, NJ

July 20, 1987

NFPMA Report:

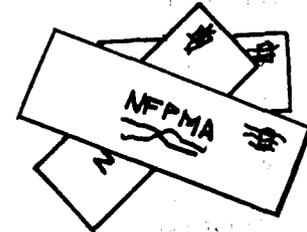
Thanks for sending me the paper, also the green folio (information kit) some time ago.

I have CMT but did not know this until I was over 75 years old. A bad fall put me in a hospital for 10 days. A neurologist was called in and said I have Charcot-Marie-Tooth disease, and that there was no help for it... but I have learned a lot from the **NFPMA Report**.

... Thanks again for papers and Report.

Yours sincerely,

Mrs. E. S.
Johnstown, NY



The NFPMA Report is published by the National Foundation for Cerebral Muscular Atrophy, a non-profit organization incorporated in the Commonwealth of Pennsylvania (established 1985) editors of the NFPMA Report are Mary Crowley Tracy and Lydia Brennan. Inquiries may be addressed to:

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National Foundation for Cerebral
Muscular Atrophy
University City Science Center
3624 Market Street
Philadelphia, PA 19104
(215) 664-6010

A Correction
As a follow up to the article in our spring issue on rehabilitation medicine the editors of the NFPMA Report want to clarify the requirements for Board Certification in Physical Medicine and Rehabilitation. Since 1982, to become certified in this specialty a physician is required to enter a three-year residency program after completing one year of internship in medicine or surgery.

NORD Conference Spring 1987

by Karol Hitt

NORD
P.O. Box 8923
New Fairfield, CT 06812



...out of the darkness
into the light...

The fifth annual conference of the National Organization for Rare Disorders (NORD) was conducted in May of this year in Washington, D.C. This NFPMA staff member, as well as representatives from 27 other national health foundations, attended the three day conference. Sixteen other member foundations were represented by proxy. For those unfamiliar with NORD, it is an advocacy organization which acts as a clearinghouse for information about rare diseases and their treatments. A disease is considered rare when less than 200,000 Americans are afflicted. NORD encourages and promotes research on rare disorders, and educates the public about the existence and treatment of rare chronic disorders. Additionally, they monitor and report on legislation in Congress relevant to orphan drugs and rare disorders.

The first day of the conference focused on the development of voluntary health agencies. On the second day the group convened at the National Institutes of Health (NIH), where presentations of NIH research and clinical programs were given. Included in the day was a tour of NIH's outstanding clinical facilities. The evening banquet honored Senator Orrin Hatch and Congressman Jamie Whitten for

their dedicated efforts on behalf of the more than 20 million Americans afflicted with rare diseases. These gentlemen have truly been advocates not only for their constituents, but for all disabled Americans.

The third conference day highlighted the Food and Drug Administration (FDA). One little-known resource available from the FDA is its excellent magazine, the *FDA Consumer*. Published ten times per year, subscriptions can be had by sending a check for \$9.50 to the Superintendent of Documents, Government Printing Office, Washington, DC 20402. This magazine contains a wealth of information about current consumer issues in a very readable format.

The concluding conference address "How to Increase Public Awareness of a Little Known Disorder," advocated the importance of the individual, as

well as the media, in spreading the word about a disease. If every CMT patient would educate just his/her own friends about CMT, this would be a start toward more public awareness and understanding of the disease. Likewise, if every patient would write to his/her state and national elected representatives requesting funds for CMT research, these politicians would become aware of the disease and hopefully respond to the need. The NFPMA urges you to write to your representatives as to promote public awareness of CMT.

This conference participant was left with the philosophy that to solve our own problem we must not only act individually, but also band together to help one another and become a strong advocacy group. You can take a step now by sending in your membership check and address form to the NFPMA. We need your support. All contributions are tax deductible.



Every CMT patient has his or her own foot story. For some patients buying shoes is only a minor problem, but for others it can be quite a dilemma. CMT patients would do well to visit a pedorthist, a person trained to provide prescription footwear and related devices to patients referred by the medical profession. For information about pedorthists in your area contact the **NFPMA Report**. Special thanks to Morton Hack, D.P.M., Certified Pedorthist, for his interest and financial support. For information concerning special shoes in the Michigan area contact:

Hack Shoes
26221 Southfield Road
Lathrup Village, Michigan 48076
Telephone: (313) 557-4230

NFPMA Dedicated Contribution Record for the Summer 1987

Contributor

Edythe J. Masel
Karol B. Hitt
Marie Mitchum
Dr. Allan Rothman's office staff
Ann & Ronald Beyer
Kathryn & Richard Pugh
Kathryn & Richard Pugh
Libbie Pitegoff
Libbie Pitegoff

Contributor

Faye L. Bradwick
Mary J. Beirne

In Memory Of

Jay Masel
Virginia B. Lee
Jerome Rothman
Jerome Rothman
Samuel T. Kantor
N. Blake King
Mrs. Julius Hyman
Irving Greenberg
Ethyl Grossman

In Honor Of

Sophia L. Bradwick
Maria Owens

Get In Touch

You can keep up-to-date on our activities and help spread the message of the NFPMA. If this issue was not mailed to you, we invite you to join our mailing list by filling out the form below. If you are already on our list, kindly send the name of anyone else interested in the **NFPMA Report**. You can also use this form for VCR tape rentals. Mail this form to:

NFPMA REPORT University City Science Center
3624 Market Street
Philadelphia, PA 19104

Name: _____

Address: _____

Telephone: (_____) _____

Tell us about yourself (optional):

- | | |
|---|---|
| <input type="checkbox"/> CMT patient | <input type="checkbox"/> Interested supporter |
| <input type="checkbox"/> Medical professional | <input type="checkbox"/> CMT family member |
| <input type="checkbox"/> Research scientist | Other _____ |

ATTENTION FEDERAL EMPLOYEES!

You can support the work of the NFPMA by checking our name on your Federal Combined Appeal Program.

NFPMA REMEMBRANCES

Your gift to the NFPMA can honor a living person or the memory of a friend or loved one. Acknowledgement cards sent *in honor of* or *in memory of* will be mailed by the NFPMA on your behalf. These donations are a wonderful way to keep someone's memory alive or to commemorate happy occasions like birthdays and anniversaries. They also make thoughtful thank you gifts. You can participate in the memorial and honorary gift program of the NFPMA by completing the form below and mailing it with your check to **NFPMA, University City Science Center, 3624 Market Street, Philadelphia, PA 19104**.

Name: _____

Address: _____

Phone Number: (_____) _____

Memorial Gift

In memory of: (name of deceased)

Send acknowledgement to:

Name: _____

Address: _____

Honorary Gift

In honor of: (person(s) you wish to honor)

Send acknowledgement to:

Name: _____

Address: _____

Occasion:

- | | |
|--------------------------------------|--|
| <input type="checkbox"/> Birthday | <input type="checkbox"/> Holiday _____ |
| <input type="checkbox"/> Wedding | <input type="checkbox"/> Thank-you |
| <input type="checkbox"/> Anniversary | <input type="checkbox"/> Other _____ |

Amount Enclosed: _____

Check if you would like the amount of your gift revealed.

VCR Tape Rental

The NFPMA will rent four lectures which were taped at patient conferences sponsored by the Foundation. The tapes are for play on a VHS VCR. Beta tapes are not available. The speakers are authorities in their fields and lecture topics include: Neurology, Physical Therapy, CMT Genetics, and Orthopedic Surgery. Single lecture tapes (1 hour, 15 min.) rent for \$10, and the double lecture tapes (2½ hrs.) rent for \$15. The rental fee includes prepaid return postage. To order a tape, fill out our *Keep in Touch* form and send it with a check or money order to the NFPMA, University City Science Center, 3624 Market Street, Philadelphia, PA 19104.

Please check the appropriate boxes:

- | | |
|---|---|
| <input type="checkbox"/> Mailing list request | |
| <input type="checkbox"/> Physical Therapy—\$10 | <input type="checkbox"/> CMT Neurology—\$10 |
| <input type="checkbox"/> Orthopedic Surgery—\$10 | <input type="checkbox"/> CMT Genetics—\$10 |
| <input type="checkbox"/> Physical Therapy/Orthopedic Surgery (on one tape)—\$15 | |
| <input type="checkbox"/> Neurology/Genetics (on one tape)—\$15 | |



**CMT Research
Presented at
W.H.O.
Conference**

NFPMA Director of Scientific Program, Howard Shapiro, Ph.D., recently attended the World Health Organization (W.H.O.) conference held in Geneva, Switzerland, August 31 - September 2, 1987. Responding to the conference's topic question, "Peripheral Neuropathies: What is Significantly New?", Dr. Shapiro gave an overview of current CMT research in various world-wide institutions. Dr. Shapiro will report on the events of the conference in our next issue.

Peroneal Muscular Atrophy (CMT) . . .

- . . . is the most common inherited neurological disease, affecting approximately 125,000 Americans.
- . . . is also known by its historical name, Charcot-Marie-Tooth disease, for the three doctors who first reported on it in 1886.
- . . . is slowly progressive, causing deterioration of peripheral nerves which control sensory information and muscle function of lower legs and forearm voluntary muscles.
- . . . causes degeneration of peroneal muscles (located on the front of the leg below the knee) and subsequent atrophy of additional lower leg and forearm muscle groups.
- . . . causes foot-drop walking gait, foot bone abnormalities: high arches and hammer toes; problems with hand function; occasional lower leg and forearm muscle cramping; loss of some normal reflexes; occasional partial sight and/or hearing loss problems; and in more severe cases may cause scoliosis (curvature of the spine).
- . . . does not affect normal life expectancy.
- . . . has no effective treatment, although physical therapy and moderate physical activity are beneficial.
- . . . is usually inherited in an autosomal dominant pattern, affecting half the children in a family with one PMA parent.
- . . . is present in the world-wide population, with no apparent link to any one ethnic group.

Special Note

Regular NFPMA-affiliated patient family support group meetings are now held in New York and New Jersey. For more information contact:

Ann Lee Beyer (NJ) 201-391-4624

Linda Goldfarb (NY) 212-481-3419

THE NFPMA REPORT

information on Charcot-Marie-Tooth disease from the

National Foundation for Peroneal Muscular Atrophy

University City Science Center
3624 Market Street
Philadelphia, PA 19104

TO: