

Newsletter, Volume 20, No. 2; Winter, 1999

Contents:

Clinical Trials Update

MIT Scientist Named Co-Chair of Research Board

NF Research Receives \$11.5 Million Boost Via U.S. Army

Gamma Knife Offers Another Option in NF2 Treatment

Research Calls

Annual Harvest Dinners are Held Around the Country

Chapter News: Waging The Fight Against NF at the Grassroots

Neurofibromatosis Symposium Held in Denver

NF Profile: Sgt. George "G.W." White Tenacious Teen Proves Doubters Wrong

Investing in NF: Founders' Fund Established

Investing in NF: Kudos to Our Volunteers!

Viewpoints on NF:

Older Adults: Perspectives

College-Age Students: Facing New Challenges

Your Turn -- Perspectives, Questions and Comments from Patients and Families

Pen Pals

CLINICAL TRIALS UPDATE

by Frank Lieberman, MD

NFFF Clinical Trials Coordinator; and Department of Neurology & Division of Neoplastic Diseases, Mt. Sinai School of Medicine, NY

This is an exciting time for researchers involved in the search for effective therapies for the tumors associated with NF1 and NF2. Discoveries in both neurofibromatosis and cancer research have enabled researchers to identify a number of chemical compounds that hold great promise in treating tumors in NF.

As the behavior and effect of the NF1 and NF2 genes has become better understood, scientists have begun to identify molecular abnormalities in the growth regulation of NF-related tumors, which can serve as targets for drug therapies. During 1999, it is anticipated that clinical trials will be organized for patients with plexiform neurofibromas associated with NF1 and meningiomas associated with NF2.

Clinical Trials in Context of Current NF Environment

First there is a caveat. As exciting as the possibility of clinical trials in NF is, it is important to understand the limitations of our knowledge as we move toward treatment trials. Drugs are tested first against cells derived from the target tumor. Drugs which kill or arrest the growth of the tumor cells in tissue culture are then tested in animal models of tumor growth. Although researchers have identified the growth pathway which the NF1 gene product helps regulate, neurofibroma cells are difficult to grow in the lab, so this first stage of testing has progressed slowly. One of the major advances in NF research has been the development of genetically modified mice which express the NF1 or NF2 mutations. These animals have provided a great deal of insight into the effects of the gene mutations, but they develop tumors very slowly. This makes drug screening very difficult. Researchers are working hard to refine the animal models so that testing of potential treatments can be performed more expeditiously.

We know from experience in evaluating cancer drugs, that only a fraction of the drugs which show promise in experimental studies using cell culture and animal models are ultimately effective in patients. One of the most important aspects of clinical trial design is insuring that even negative trials yield insight into how to select the next drug for study. The initial stages of clinical trial development are often only partially successful. And, it is important to realize that even successful studies will most likely yield small improvements upon which we will build over time.

The goals of designing clinical trials in NF are:

- Apply understanding of basic science of NF
- Make incremental improvements in therapy
- Minimize therapeutic side effects
- Learn from clinical trial results to identify other promising agents

The new cancer drugs that have been developed work differently than classic chemotherapy drugs, and may be especially helpful in NF to address the primary goal of preventing tumor growth. At this time, several different agents are being considered for treatment of plexiform neurofibromas in NF1 and meningiomas in NF2.

NF1 Clinical Trials

NF1 research has enabled scientists to learn how the NF gene mutation affects the function of cells. This knowledge makes it possible to identify drugs, such as the following, to correct the abnormal cell function caused by NF1 gene mutations.

Farnesyl Transferase Inhibitors (FTI) - Since NF1 is a disorder characterized by cell growth gone out of control, FTI drugs work by blocking the overabundant signals the cells receive telling them to divide and grow. Cancer patients have already begun to receive FTI in Phase I clinical trials for colon cancer to test the drug's safety. A Phase I trial of FTI in children with plexiform neurofibromas recently opened at the National Cancer Institute. Visual function will need to be monitored in clinical trials involving FTIs because they may cause dysfunction of cells in the retina of the eye.

Antiangiogenesis Drugs - These compounds interfere with the formation of abnormal blood vessels which tumors stimulate as they grow. This prevents tumor growth and may cause the tumors to shrink or disappear. Thalidomide is one example of an existing antiangiogenesis agent; and several new antiangiogenesis drugs are in development. Phase I clinical trials using thalidomide to treat meningiomas have begun and other antiangiogenesis agents are approaching clinical trials. Meningiomas are an attractive target for these agents, since new blood vessel formation is a prominent characteristic of these tumors.

Differentiation Induction Agents - This class of drugs inhibits cell division and causes tumor cells to behave like mature, non-dividing cells. Because several different classes of differentiation inducing drugs have been tested in patients with various types of cancers, we already know a substantial amount about the safety and administration of these agents.

Retinoids and aromatic fatty acids, are potential candidates for clinical trials in plexiform neurofibromas associated with NF1.

Retinoids, such as 13-cis retinoic acid (Accutane), are available as oral drugs, which may make them easier to administer.

Phenylbutyrate (PBA) is currently being tested as an intravenous infusion and would require administration using a portable pump for continuous delivery, because of the drugs' short half life in the blood. An oral preparation of PBA is also being tested in a

clinical trial treating malignant brain tumors; this may be an alternative to the intravenous version. The differentiation inducers, as a class, probably will require continued administration to sustain the growth inhibitory effects. There is preliminary evidence that certain types of synthetic retinoids may induce tumor cells to undergo cell death (apoptosis), a form of suicide in which the target cells produce enzymes which degrade the cellular DNA. These drugs may eventually become the agents of choice, since continuous administration may not be required.

NF2 Clinical Trials

NF2 research also continues to make remarkable progress, but scientists are still unraveling information about the effect of the NF2 gene product, Merlin (or schwannomin), on tumor susceptibility. Without a clear picture of this role, trying to identify drugs which are likely to be effective in clinical trials in NF2 is more difficult. If we assume that meningiomas in NF2 are similar to sporadic meningiomas, we can apply the knowledge of meningioma biology to select drugs for clinical trials in NF2. Molecular Targets - Platelet Derived Growth Factor (PDGF) is one of the regulatory molecules that stimulates meningioma cells to grow inappropriately. Drugs are in development that block the growth signal resulting from PDGF stimulation. A compound known as SU-101 is an example of this type of drug. SU-101 is currently being tested in patients with malignant primary brain tumors, so its safety profile and administration are known. SU-101 is only available as an intravenous drug. Because the active form of the drug has a long half life in the blood, the drug can be given once every 2 weeks. Since only approximately 50% of meningiomas express the PDGF receptor on the tumor cell surface, a clinical trial of SU-101 for meningiomas might only select patients whose tumor tissue was shown by testing to express the receptor. We do not know whether the percentage of meningiomas with PDGF receptor expression is higher or lower in patients with NF2 than in sporadic meningiomas.

Hydroxyurea - This is a chemotherapy drug which has been used for many years to treat a type of chronic leukemia in adults. Hydroxyurea causes meningioma cells to undergo apoptosis in cell culture experiments. Hydroxyurea is available as an oral drug, and is easy to administer. Because hydroxyurea can suppress the bone marrow's production of white blood cells and platelets, weekly blood counts are required. Although the drug induces cell death for tumor cells in cell culture, in US trials of hydroxyurea for meningiomas, the most common result is growth arrest. It may be necessary to continue to take the drug to maintain the effect.

Hormonal Agents - Meningiomas frequently express receptors on their cell surface and divide in response to hormonal stimulation from estrogen and progesterone. A number of estrogen antagonists have been developed and tested in breast cancer patients and are candidates for testing against meningiomas. Tamoxifen has been shown to have an effect in non-NF meningiomas. Another estrogen antagonist which may have a more favorable side effect profile, raloxifene, has been tested in a large breast cancer prevention trial, and is a candidate for testing in meningiomas. The estrogen antagonists may cause hot flashes and sweats in premenopausal women. They may also increase the risk of developing blood clots in the leg veins, which may require anticoagulant drug treatment.

Other Approaches To Explore

In the initial studies, drugs will be evaluated one by one. It is also a possibility that a single drug therapy may not be as effective as the approach known as combination

therapy. There is experimental evidence that treatment with a chemotherapy drug followed by a differentiation inducer may be more effective than treatment with a differentiation inducer alone, for example. In fact, the strategy of designing regimens which combine drugs with different mechanisms of action and different side effects has been a successful approach to treating several different types of cancers.

What Are Clinical Trials?

Clinical trials provide a structure to test the safety and efficacy of a treatment. Before the Food and Drug Administration can consider a drug for approval, it must go through at least three phases of clinical trials.

Phase I -- A small number of patients participate to study a drug's safety, including the safe dosage range. These studies also determine how a drug acts in the body and the duration of its action.

Phase II -- Patients are treated with the dose of drug established in Phase I studies to determine the drug's effectiveness.

Phase III - The test drug is compared to established treatments. Phase III trials usually involve randomized assignment of patients to either experimental drug or an established treatment. If there is no established treatment, the drug is compared to a placebo.

Foundation Hires Clinical Trials Coordinator

The NNFF has hired Frank S. Lieberman, M.D., as clinical trials coordinator. Dr. Lieberman will manage the Foundation's upcoming clinical trials program for NF1 and NF2-related tumor treatments.

"With Dr. Lieberman on board, NF research has taken a giant step forward," Bellermand said. "Our commitment to finding effective treatments has been strengthened by establishing this new position. And, Dr. Lieberman's extensive experience in coordinating clinical trials in neuro-oncology makes him the ideal professional for this project."

Dr. Lieberman, a board certified neurologist, has been a co-primary investigator or co-investigator for clinical trials of SU-101, phenylbutyrate infusion, adenoviral gene therapy, and high dose chemotherapy and peripheral blood stem cell transplantation. He is currently a faculty member in the Department of Neurology and the Ruttenberg Cancer Center at Mount Sinai Medical School in New York City. Prior to joining Mt. Sinai, he was a member of the Department of Neurology at Memorial Sloan-Kettering Cancer Center. In addition, Dr. Lieberman is an assistant attending at Mount Sinai Hospital, and is a consultant in neurology for the Terrance Cardinal Cook Medical Center in Chicago.

Dr. Lieberman is a cum laude graduate of Franklin & Marshall College and was graduated from the University of Chicago, Pritzker School of Medicine. He completed postdoctoral training at the University of Chicago Hospitals as an intern in medicine and a resident in neurology. He was a research fellow in neuroimmunology at the University of Chicago.

MIT Scientist Named Co-Chair of Research Board

The National Neurofibromatosis Foundation has announced the appointment of Dr. Tyler Jacks as co-chairman of the NNFF Research Advisory Board (RAB). The RAB serves as the Foundation's peer review panel. The other co-chair is Dr. James Gusella, Harvard Medical School/MGH.

Dr. Jacks has already served a major leadership role in our research programs as a member of the RAB since 1994 and as co-chair of the "NNFF International Consortium on the Molecular Biology of NF1 and NF2".

Dr. Jacks' research has contributed significantly to advances in understanding the basic mechanisms underlying neurofibromatosis. His laboratory has developed functional mouse models for both NF1 and NF2. He has also been recognized as a major contributor to the understanding of the functions of several tumor suppressor genes, notably p53.

Dr. Jacks is currently an Associate Investigator at the Howard Hughes Medical Institute and an Associate Professor of Biology at Massachusetts Institute of Technology. He received his Ph.D. from University of California, San Francisco and a B.A. in Biology from Harvard University.

In announcing the appointment Peter Bellermann, NNFF President said: "Dr. Jacks is a world class cancer biologist, whose pioneering work in NF1 and NF2 has brought the advent of treatments for the two disorders closer for all of us. To have Dr. Jacks lead our research effort with Dr. Gusella assures that the Foundation will continue to invest in cutting edge research."

NF Research Receives \$11.5 Million Boost Via U.S. Army

The United States Congress passed an \$11.5 million appropriation for neurofibromatosis research via the US Army Medical and Materials Command. This new appropriation represents a 17% increase for US Army NF research.

Thanks for this new appropriation go to all the legislators in the Senate and House of Representatives who voted for it, but especially Congressman Jack Murtha (D-PA), Congressman Bill Young (R-FL), Senator Ted Stevens (R-AK) and Senator Daniel Inouye (D-HI).

The US Army's NF research program began as a result of an initiative by the National Neurofibromatosis Foundation; and its members continue to be instrumental in gaining legislative support for it. During the past year, 12,385 Foundation members were involved in the legislative process.

"The US Army's NF research program is now the largest research effort in NF1 and NF2 in the world," Peter Bellermann, NNFF President said. "As such, it plays a critical role in all current advances towards effective treatments for the two disorders."

Bellermann notes that The US Army has a proud, albeit not very well known, history as catalyst for medical research. "The Army's research tradition reaches back to the early days of the Republic. It is characterized by rigorous peer review, innovative approaches to medical research and superb management of its grants and awards," Bellermann said. "All of which translate into rapid advances in NF research.

Therefore, we are as grateful to the men and women in the Army who manage the NF research program as we are to the legislators who fund it and the Foundation members who champion it."

Gamma Knife Offers Another Option in NF2 Treatment

By Georg Norén, M.D., Ph.D.

(Editor's Note: Dr. Georg Norén is the Director of the New England Gamma Knife Center, Department of Neurosurgery at Rhode Island Hospital. He is also an Associate Professor of Neurosurgery, Department of Clinical Neurosciences, Brown University School of Medicine in Providence, RI.)

The management of acoustic neuromas (vestibular schwannomas), the characteristic tumors of NF2 that grow on the hearing/balance nerves, is more challenging than for unilateral (sporadic) acoustic tumors. The good news is that now there are several different treatments available for those with acoustic neuromas.

This makes it easier to customize treatment to an individual patient's needs. On the other hand, the decision on a specific treatment becomes more complex with this array of choices.

This overview will cover the use of Gamma Knife radiosurgery for NF2 acoustic neuromas, and discuss the issue of single dose versus fractionated radiation treatment.

What Is Gamma Knife Stereotactic Radiosurgery?

The Gamma Knife was developed as a non-invasive tool to treat patients whose brain tumors and blood vessel malformations were previously considered too risky, or even impossible, to operate on. The Gamma Knife is not really a knife at all. In fact, it uses 201 pinpoint beams of radiation focused on the area of the brain where the tumor is located. The Gamma Knife also uses an imaging system that takes preoperative information from MRIs and CT scans to create a three-dimension map of the tumor site that enables the neurosurgeon to accurately deliver radiation to even deep-seated tumors.

This type of treatment has distinct advantages over conventional brain surgery:

- **Increased Access To Treatment** - Surgeons can treat patients who were previously poor candidates for surgery due to tumor location, age, health factors, or anesthesia risks.
- **Elimination of Major Post-Surgical Complications** -- Since the patient undergoes a non-surgical procedure, the risks of infection, hemorrhage, and other post-surgical problems are eliminated.
- **Preservation of Healthy Tissue** -- Because the Gamma Knife delivers a precise and targeted treatment, the risk is low that it would harm healthy brain tissue that surrounds the tumor.
- **Reduced Hospital Stay and Recovery** - The whole Gamma Knife procedure takes from a few hours to the better part of a day to perform. Except in children, it is performed under local anesthesia. Patients can return home just 24 hours after the radiosurgery and usually are back to work within a few days.

Worldwide, more than 9000 Gamma Knife treatments have been performed, one quarter of which have been in the U.S. Since 1974, my personal experience with the procedure is based on more than 700 treatments of acoustic neuroma patients, 130 of whom have NF2. In patients with NF2, post-surgical benefits include long-term control of tumor growth which occurs in 85% of patients, and unchanged or almost unchanged hearing in 60% of patients. After treatment, a small number of patients (less than 2%), however, experienced temporary facial weakness or numbness.

Single Dose vs. Fractionated Radiotherapy?

Radiosurgery is a concept based on delivering the full amount of radiation as a single dose. The radiation dose in radiosurgery typically is higher to the center of the tumor than along the periphery. Therefore, radiosurgery may not be ideal for situations where sensitive structures are located within a tumor. Frequently with NF2 (but not unilateral) acoustic tumors the hearing nerve fibers cut through the tumor. They may not tolerate this higher dose of radiation at the center of the tumor if delivered in one session.

Hearing preservation following Gamma Knife radiosurgery initially was uncertain with hearing loss occurring after most NF2 acoustic tumor treatments. More recently the results have improved as noted above. For single dose Linac radiosurgery there is almost no documentation available regarding hearing following treatment of NF2 acoustic neuromas. This may indicate that the results have been disappointing. Delivering the radiation in smaller fractionated doses may offer more protection to the hearing nerve fibers. The fractionated approach may, on the other hand, be less desirable as it is less targeted in its delivery and may cover a larger amount of healthy brain tissue.

Current Gamma Knife Strategies

NF2 acoustic neuromas usually respond very well to Gamma Knife radiosurgery. Most acoustic neuromas with a maximum depth of 3 cm are suitable for this technique. If hearing is useful, in particular if there is no hearing in the other ear, fractionated radiotherapy might be considered as an alternative to Gamma Knife treatment. In cases of small (intracanalicular) acoustic neuromas, early Gamma Knife radiosurgery should be considered, when hearing is still normal. Some preliminary results indicate good tumor control and better preservation of hearing under such circumstances. Residual or recurrent NF2 acoustic neuromas in general are very suitable for Gamma Knife surgery.

RESEARCH CALLS

Math Skills Development Project - Children With NF1

This project is designed to help us understand the development of arithmetic skills in young children, 5-9 years of age.

Participation will involve approximately four hours of psychological and academic achievement testing. Parents will receive a report of their child's test performance following the evaluation. The testing will occur at the Kennedy Krieger Institute in Baltimore, MD. Funding is available to help families with the travel costs and there is no charge for any of this testing.

For criteria for participation and more information, about this project, please contact Dr. Michele Mazzocco, Principal Investigator, Tel: 410-502-9313 or Laura Crowhurst, Research Coordinator, Tel: 410-502-9316; Fax: 410-502-9316; email:

crowhurst@kennedykrieger.org

Neurofibromas Needed

Dr. Nancy Ratner at the University of Cincinnati requires neurofibromas from NF1 patients for an ongoing study of tumor growth factors, growth factor receptors, and signaling pathways in neurofibroma cells. The study requires sterile tumor tissue covered by and shipped in tissue culture medium, on wet ice. Plexiform or cutaneous neurofibromas can be used. Some patient information (age, sex, criteria used to make the diagnosis of NF1) is required. Please have your physician contact Dr. Ratner at least 24 hours prior to removal of tumors. Dr. Ratner will pay shipping costs. For more information: Tel: 513-558-6079; Fax: 513-558-4454; email: nancy.ratner@uc.edu

Plexiform Neurofibromas/Peripheral Nerve Sheath Tumors

Drs. David Gutmann and Michael DeBaun are requesting information regarding families with NF1 and plexiform neurofibromas/malignant peripheral nerve sheath tumors (MPNSTs). They are specifically looking for families in which at least 2 generations of individuals with NF1 have either plexiform neurofibromas or MPNSTs for studies to determine what genetic factors might contribute or predispose to the development of these tumors. Please contact Dr. Gutmann at Washington University (tel: 314-362-7149) or gutmann@neuro.wustl.edu

Study of Environmental Risk Factors in NF2

The purpose of this study is to collect information about selected NF2 patients and relatives in order to investigate potential environmental factors in the development of NF2. Data will be collected through a structured questionnaire including medical records and occupational histories. Patients interested in participating should send their personal information (NF2 patient's name, mailing address, telephone, date of birth, date of NF2 onset, date of NF2 diagnosis, family history of NF2) to: House Ear Institute, attn: Jennifer Nelson, 2100 West Third St., Los Angeles, CA 90057

Genetic Analysis of ADD/ADHD

The prevalence of diagnosed Attention Deficit Disorder (ADD) and Attention Deficit Hyperactivity Disorder (ADHD) cases have risen dramatically in recent years, affecting a large percentage of children, adolescents and adults. The disorders are typically characterized by problems with sustained attention, hyperactivity and impulsivity. Although generally accepted as being caused, at least in part, by genetic factors, the precise inheritance patterns remains unknown. In a pilot study we have previously shown that children with NF1 are at significantly increased risk of developing abnormalities in attention variable. We now want to further test this hypothesis by examining children with the diagnosis of NF1 and compare their performance in an attention test with the performance of unaffected siblings. Criteria for individuals and families needed to participate in the research project:

- Families must reside in Southern California
- Families must have one child diagnosed with NF1 and a second which does not have NF1 (as conformed by a doctor's examination). Children should be between 6 and 16 years of age.
- Participants will be asked to take a brief computer test (20 minutes in length and arranged at a site close to their home).

Responses and questions should be directed to: Michael E. Goldsmith, Cedars-Sinai Medical Center, Div. of Neurology, 8631 West Third St., Suite 1145E, Los Angeles, CA 90048-0750; Tel: 310-855-2407; Fax: 310-659-2267; email: goldsmith@cshs.org

Researcher Seeks Blood Samples From NF2 Patients

Dr. Jan Dumanski, of the Karolinska Institute in Sweden is conducting a project focusing on the issue of clinical and possible genetic heterogeneity behind the development of NF2 and the identification of the factor(s) which are influencing the severe course of the disorder.

He would like to obtain blood samples from at least 100 unrelated patients with the severe or moderate (but not clearly mild) case of NF2. A mild NF2 is defined by the presence of vestibular schwannomas only, (without additional tumors), onset later than 35 years and slow progression of tumors. These could be sporadic or familial NF2 patients. In cases of NF2 families, it would be enough to obtain only one sample from a representative affected family member.

Researchers need blood samples (20-30 ml of peripheral blood) which would be used for extraction of DNA/RNA or at least 200 micrograms sample with high molecular weight DNA (not degraded) would be sufficient from each patient. Samples should be sent via FedEx and the laboratory will cover the cost of shipment.

Interested patients, scientists and clinicians should contact Dr. Dumanski prior to any shipment of samples as follows: fax: +46-8-527-73909; e-mail:

Jan.Dumanski@cmm.ki.se or <http://www.ki.se/cmm/dumanski.htm>

ANNUAL HARVEST FESTIVITIES ARE HELD AROUND THE COUNTRY

For the tenth successive year, Foundation members and their friends have celebrated the accomplishments in the fight against NF at Harvest Dinners around the country. These annual gatherings range from festive, glittering events to simple suppers in family homes. Whatever the form, each celebrates and gives thanks for the continued progress in NF research.

The New York /New Jersey Chapter, for example, celebrated the NNFF 20th Anniversary in the striking setting of the Tavern on the Green restaurant in New York City's Central Park. Honored were the NNFF Founders, Lynne Ann Courtemanche, RN, Dr. Allan Rubenstein and Joel Hirschtritt, Esq. Accepting her award, Ms. Courtemanche said, "The NNFF was a dream born out of frustration. Today the dream is a reality and the frustration has been replaced by the knowledge that treatments are near." That dream is being fulfilled because of the good works of generous donors like the Feinberg and Kany Families, who were also honored as recipients of the Foundation's 1998 Courtemanche Award.

Guests at this year's Washington Chapter annual event were treated for the first time to a Casino Night in addition to their annual diner dance and auction. J&H Marsh McLennan and Nintendo of America were sponsors of the evening which raised record funds for NF research.

Kudos to Steve Sandler and Elka Belfer who managed another well-attended Harvest Feast and Silent Auction for the Connecticut Chapter in West Hartford. Suzy Crisci, President of the Idaho Chapter, and friends, also organized another successful

Harvest Dinner and Silent Auction. The event now in its ninth year was the best attended to date.

The 10th Annual Night of Chance was held in Los Angeles in November at the Sheraton Universal Hotel. This festive dinner and dance included a casino night where guests "gambled" with NF play money and celebrities from television and motion pictures joined in as croupiers.

The Utah Chapter celebrated with its very first Harvest Dinner in September. Former Senator Jake Garn was the keynote speaker and President Laurie Roderick reported that a good time was had by all at this inaugural fete. Another first-time event was organized by the newly formed South Carolina Chapter. Their non-traditional Harvest Luncheon was held at the All-Star Café in Myrtle Beach with many members and their children in attendance.

CHAPTER NEWS:

Waging The Fight Against NF

There are many ways to raise funds for NF research programs and promote awareness of neurofibromatosis within your community. Recently several state Chapters and individual members of the Foundation organized activities and fund raising campaigns that are excellent examples of ways to support the fight against NF.

Enlist Support From National And Local Businesses:

Stock Brokers Contribute

On Miracle Day, the first Tuesday of every December, CIBC World Markets' financial consultants, sales and trading staff around the globe donate their fees and commissions, while the firm donates the retained portion of those commissions to children's charities. This year NNFF was among 130 recipient organization in the U.S. Children with NF and their families were invited to participate in the kick-off skating party for Miracle Day in New York City. Our participation was made possible by NNFF Board Director and Head of US Equities for CIBC Oppenheimer, Thomas Gallagher, who co-chaired the event this year. He is pictured here with some of the Miracle Day Skating Party participants.

NF Declared "Charity of Choice" of Supermarket Chain

Safeway customers were able to make contributions to NNFF in Washington, Idaho, Alaska and Montana by way of canisters and the Safeway coupon book, thanks to the NNFF Washington State Chapter.

Shop For A Good Cause

Shoppers at The Bloomingdale's Shopping Benefit in Los Angeles enjoyed great savings, live entertainment, fashion events and, at the same time, supported their favorite charity. The event was held at the Century City branch of the famous department store. The NNFF California Chapter was one of the local non-profit organizations which benefited from the day's festivities.

Fly For NF

The Colorado Chapter is a recipient of the Frontier Airlines Cares Fares Program. Anyone purchasing Frontier tickets can designate the Chapter as a recipient of 10% of the ticket cost.

Contribute Through Work:

United Way Campaign

Debbie and Jay Hanney of Pompano Beach, FL, who both work for Costco Wholesale,

arranged for two of the national chain store's branches to designate a portion of their United Way contributions to the NNFF.

Educate the Educators:

Panel Discussion in Denver

Rod Slaght of Denver and Sarah Ferrara of Pueblo, CO participated in a panel discussion about genetics before an audience of 260 high school biology students and teachers. The two Colorado chapter members were part of a panel of individuals affected with various genetics disorders who were brought together to enlighten the audience about each represented disorder. The panel discussion was part of the 48th Annual Meeting of the American Society of Human Genetics held in Denver in October.

Supporters In Motion:

1998 Chicago Marathon

Northern New England Chapter President, Jeff Brown participated in the 1998 Chicago Marathon at the behest of Anita Carter, President of the Illinois Chapter. Anita encouraged 31 walkers and runners to take part in the race and raise funds on behalf of NNFF. She hopes to broaden participation in 1999 to include other NNFF Chapters.

Walk In The Woods

100 walkers turned out to support the Connecticut Chapter and hike through the Steep Rock Nature Preserve in Washington Depot, CT on a beautiful fall day.

"Take Steps for NF"

"Fredbird", the St. Louis Baseball Cardinals mascot hosted the 11th Annual Missouri Chapter Walk/Run. 450 participants turned out for either the 10K, 3K, and 1/2 mile Fun Run.

Bowl With A Twist 92 KSJO Radio sponsored a "Frozen Turkey Bowl" for NNFF in San Jose, CA.

NEUROFIBROMATOSIS SYMPOSIUM HELD IN DENVER

(Ed. Note: The following synopsis is based on reports provided by Arvid Heiberg, MD, PhD, National Hospital, Oslo, Norway; and Bruce Korf, MD, PhD, Harvard Medical School and Boston Children's Hospital.)

About 150 geneticists and clinicians attended The Neurofibromatosis Symposium in late October in Denver, Colorado. This annual symposium, sponsored by the National Neurofibromatosis Foundation, was held in conjunction with the 48th Annual Meeting of the American Society of Human Genetics. The following are highlights from the symposium.

Information collected through the Database over past years, has enabled researchers and clinicians to identify several patterns in NF manifestations and has expanded their ability to diagnose and manage NF related problems. Three separate reports concentrated on the NNFF International Database, which is managed by the Department of Medical Genetics at the University of British Columbia, under the direction of Dr. Jan Friedman.

The first of these was presented by Patricia Birch, M.Sc.. Her report updated the audience on the new, improved version of the NNFF Database, which promises to make the Database more accessible to clinicians. Among the improvements, the Database will now give clinicians the opportunity to enter data via world wide web from a questionnaire divided in 7 areas of specialty, such as, ophthalmology, dermatology, genetics, etc.

Another Database study entitled "Use of NIH Criteria for diagnosis of NF1 in Children" was presented by Kim DeBella. The data represented 1893 individuals under the age of 21 with NF1 who were studied to determine the age at which features included in the NIH Diagnostic Criteria appear. Almost all the subjects studied met two or more diagnostic criteria by 8 years of age. 75% of those studied have 2 criteria by the age of 1. All subjects met two diagnostic criteria by 20 years. 99% of the patients developed café-au-laits before the age of 1 year. Axillary freckling reaches a maximum frequency of 90% in patients by 7 years of age and Lisch nodules affect a maximum of 73% of patients by age 10. Neurofibromas are present in 48% of 10 year olds and 84% of 20-year -old patients. The usual order of appearance of the NIH criteria in children with NF1 is café-au-lait spots, axillary freckling, Lisch nodules and neurofibromas.

The third presentation based on information culled from the Database was given by Jacek Szudek. His study examined the population distribution of height and head circumference of the 2374 people with NF1 in the Database. The findings suggest that the heads of NF1 patients grow at a greater than normal rate until the end of puberty and may continue growing for a longer period of time than those of the unaffected individuals. Heights in NF1 patients increase at a rate slower than normal from birth beyond puberty.

Dr. Bruce Korf (Harvard Medical School/Children's Hospital Boston) discussed the multi-center, U.S. Army-funded natural history study of plexiform neurofibromas. Very little is known about the "normal behavior" of these tumors, and it is therefore extremely difficult to predict their growth rates at different points in life. Measuring the size of plexiform neurofibromas presents another set of extraordinary challenges. The study led by Dr. Korf is designed to address both issues.

Dr. Frank Lieberman, a neuro-oncologist from Mt. Sinai Medical Center in New York, gave an excellent overview of the potential for clinical trials and treatments based on newer cellular and molecular understandings of NF. (See related article on page 1.)

A presentation by Dr. Elizabeth Schorry (University of Cincinnati) found that hypertension (HTN) is more common in patients with NF1 due to renal artery stenosis, pheochromocytomas (adrenal gland tumors), as well as narrowing of the aorta. Dr. Schorry noted that HTN is an infrequent, though potentially serious complication of NF, and therefore, yearly monitoring of blood pressure is advocated throughout the lifetime of NF patients.

Other presentations included: Dr. David Rodenhiser (University of Western Ontario) who reported on "Site specific methylation in the NF1 promotor interferes with binding of CREB and Sp1 transcription factors". Dr. Paola Riva (University of Milan, Italy) presented "FISH and analysis by means of a 17q11.2-site-specific YAC contig of 9 NF1 patients with large deletions" which described mapping a large deletion in the NF1 gene that is associated with severe cases of NF characterized by severe impairment of mental development and distinct facial structures. Dr. Margaret Wallace (University of Florida) discussed "Cryptic out-of-frame NF1 exon splicing in neurofibromas". Dr. Michael Baser presented "The natural history of NF2" and Dr. Leah Burke (Allegheny University of Health Sciences) explained an "Unusual presentation of NF2" which may have implications for others with early onset of NF2.

INVESTING IN NF: FOUNDERS' FUND ESTABLISHED

In celebration of the National Neurofibromatosis Foundation's 20th Anniversary, the Foundation's first generation of leaders and supporters have initiated a fund to honor

its Founders, Lynne Ann Courtemanche Shapiro; Allan E. Rubenstein, M.D.; and Joel Hirschtritt, Esq.

The purpose of the Fund is to support and nourish new National Neurofibromatosis Foundation programs which help children and young adults affected by Neurofibromatosis to better understand NF, and to foster their ability to live their lives as fully and richly as possible, in spite of NF. The Fund will initially help support the Foundation 's Kids' Council and the NNFF International Summer Camp programs. Joan Engel, former NNFF Chair, is the originator of the Founders' Fund. "The Founders' Fund is intended to help do what Lynne, Allan and Joel could only dream about 20 years ago," Engel said. "We hope to honor their entrepreneurship and volunteerism by challenging ourselves to an ongoing, dedicated effort to raise equal program support from the NNFF and philanthropic communities at large. We therefore, turn to our friends first. If you wish to contribute to this fund directly and/or you have personal connections to other charitable sources for support of such vital programs, please let us know by calling The NNFF Founders' Fund: 800-323-7938. Thank you so much."

Kudos To Our Volunteers!

The National Neurofibromatosis Foundation is fortunate to attract exceptional volunteers. These people bring creativity, talent, energy, and tremendous dedication to their efforts on behalf of NNFF. The Foundation recognizes the most outstanding of these volunteers through a series of awards for excellence. The following were honored during 1998:

Feinberg Family, NJ/NY	Courtemanche Award
William Tarbart, FL	Courtemanche Award
Elka Belfer, CT	Public Service Award
Nancy Brown, MA	Public Service Award
Marcia Miller, IL	Public Service Award
Donna Oettinger, NJ	Public Service Award
Sara Baker, NY	National Volunteer of the Year
Tyler Jenner, NY	Chapter Volunteer of the Year

****[Contents](#)

NF Profile: Sgt. George "G.W." White

Tenacious Teen Proves Doubters Wrong

Semper Fidelis. This motto of the United States Marine Corps means "Always Faithful". And no one knows better about keeping the faith than George White, a 15

1/2 -year-old with NF1, who has defied the odds to participate in the Young Marines of the Marine Corps League.

The Connecticut resident, known to all as G.W., dreams of following in his father's footsteps with a career in the military. G.W. was told by doctors that NF-related muscle weakness would prevent him from participating in the physically rigorous training that is part of the official youth program of the Marines.

Proving the doctors wrong was all the motivation G.W. needed. At age 14 he enrolled and now holds the rank of Sergeant. The road to this success has been especially tough. Many of the required physical tests take G.W. longer to master than his non-affected peers, and the written tests pose a challenge for him due to the learning disabilities common to people with NF.

The Young Marines training mirrors that of the Marine Corps, with the exception that they do not handle firearms or train for combat. Instead the program focuses on perfection of drilling exercises, physical fitness, discipline, self-esteem building, and the importance of community services. While the program was designed to prevent drug abuse among the nation's youth, G.W.'s grandmother encouraged him to join because she hoped it would increase the shy young man's self-confidence.

Anyone who meets G.W. today can see the involvement has paid off. He is brimming with self-assurance and sheer determination. Those who met him when he attended last summer's NNFF International Summer Camp for teens were immediately impressed and drawn to his quiet strength and leadership qualities.

G.W. was diagnosed at the age of two months. The manifestations of NF he has experienced are café-au-lait spots, scoliosis, large head size, as well as general muscle weakness and LD. Otherwise, he rates his health as excellent.

G.W. has stunned both his superiors in the Young Marines and his peers by shattering the troop record for sit-ups. He completed a whopping 123 in just two minutes.

Because of his muscle problems, the leaders allowed G.W. to perform modified, yet challenging, crunch-style sit-ups for the test. His mother, Sandy White-Ouellette, a long-time NNFF Connecticut Chapter volunteer, noted strong opposition to these reasonable accommodations came not from the troop leaders, but from G.W.'s peers. He retains the tenacious spirit in the face of such resistance that he cultivated in grade school. When G.W. was in grade school, his classmates teased him about his large head. He recalls that he "would just tell them that I needed a bigger head because I have a bigger brain".

G.W. is aware that all branches of the United States military bar those with NF from serving their country and could forestall his dream of becoming an Air Force pilot and an astronaut. He is hopeful that that policy will change in time for him to enlist. If not, he is hoping to parlay his interest in the environment into a career as a forest ranger.

With G.W.'s faith in himself, it's easy to believe he will make his dreams come true.

VIEWPOINTS ON NF:

(Editor's Note: The following is the first in an occasional series about issues of importance to older adults with NF. Columnist Porter Colley is retired and lives in Massachusetts. In addition to various volunteer activities, she is an annual lecturer about NF at Harvard Medical School and the Massachusetts Institute of Technology.)

Perspectives on NF and Older Adults

By Porter Colley

From the time we are born to the time we exit this life, we are categorized in many ways, age being the most common. Certainly, people with NF could be seen as a category unto itself. But, for those of us with NF (I have NF1), our needs and concerns at different stages of our lives -- infant, toddler, teen, etc. -- are unique. As a senior citizen, I recognize that my issues with NF today are very different from those I faced in my 30s or 40s. The NNFF understands this as well, and the folks there have asked me to provide my perspective on topics of interest to older adults with NF.

As an older adult, I realize that how we age is different for each of us. I like to imagine that at a certain point different parts start to wear out -- just like an old car. If you are in good health and have money to take care of yourself, you probably have it made.

Sure, there are things common to aging that go with the territory. But, when you live with NF there are additional problems. For some of us, the golden years are not all they're cracked up to be. For example:

- Some of us can no longer drive. We cannot get to support groups and other NF meetings.
- Many have hands that are not as strong due to arthritis. When you have tumors that continue to grow in size and number the internal and external tumors of hands, including fingers make it impossible to do simple things, i.e., grasp, pick up, hold etc. ...and they can exceedingly painful.
- Tumors that continue to grow in size and number cause hygienic problems. There are so many, so close together, you cannot get your body clean - even with help. Brushes are too painful - the tumors hurt anyhow.
- Isolation. When you are unable to reach out and touch and be touched by someone - especially for those living alone. Sometimes touch is very painful. Mine are - it hurts to be hugged! In fact, the golden years are more like the saying "Life is just a play with a badly written third act." It seems that members of the geriatric crowd are the characters in that act and it should be rewritten to meet our interests and needs.

Therefore, I invite my fellow players in this production of life to let the NNFF know the issues you want addressed. My role will be to provide a peer's perspective about these concerns. Please send your ideas for future column topics to me c/o NNFF; 95 Pine Street, 16th Floor, New York, NY 10005.

VIEWPOINTS ON NF:

College-Age Students With NF Face New Challenges By Katie Reber

My name is Katie Reber and I am 21 years old. I have neurofibromatosis Type 1. Diagnosed at age one, I am the first person in my family to have NF. Currently, I am a junior at a small, academically rigorous, liberal arts college in northern New England. I am a biology major with a minor in anthropology. My activities include the student theater organization, the biology club, the handbell choir, and acting as an admissions tour guide. I also have several jobs at school -- I work as a research assistant for a biology professor, as a tutor in the biology department, and as a greenhouse technician.

Upon entering college, I faced many issues of adjustment. Some of these issues were directly related to NF. These issues centered around how I told people about this element of my life. Do I tell my new friends? My roommates? People I date? If so, when?

Also, college was the first time that I was dealing with my NF alone. It was unsettling to find a new neurofibroma and not have my parents right there to tell. While, they were only a phone call or e-mail away, their caring responses still seemed distant. I have found ways to deal with these issues, but new issues are now presenting themselves. I am starting to seriously plan my future and wondering what effect NF will have on my decisions.

Do I need to choose a graduate school where I can be close to my doctor? Should I choose an occupation that really calls to me or one that has good health insurance? What effect will NF have on my adult life?

I realized that there must be other college students with NF who are facing these issues. I can talk to my parents, but they do not quite understand college life. And, my friends at school can try their hardest to understand my issues with NF, but they just can't quite relate. So, I got the idea to start a network of mutual support for people my age. That's when I contacted the NNFF to help me get my idea off the ground.

We are considering several ways to proceed: starting a bulletin board section just for us, creating an online listserv for mailings, or a more formal council to pursue additional ideas. At this point, we invite all college students with NF interested in mutual support to write to me to express their interest in building this community. Please contact me via mail c/o NNFF; 95 Pine Street, 16th Floor, New York, NY 10005, or via e-mail at ksr77@hotmail.com

YOUR TURN

(Ed Note: This feature of Neurofibromatosis News was developed to encourage patients and their families to their share concerns, questions and perspectives with others. When appropriate, medical specialists answer questions raised by readers. The answers can only cover generally applicable situations, and cannot take the place of consultations and specific medical care. If you would like to share your views or raise any questions, please submit them in writing to Fran Morris, Editor, NNFF, 95 Pine St; 16th Fl; NY, NY 10005 or via fax: 212-747-0004 or email: nnff@aol.com)

Social Security Benefits

Eligibility for disability benefits due to NF depends upon the limitations you have as a result of both physical and mental impairments. Additional information can be obtained from Social Security Administration (SSA) by calling 1-800-772-1213. Most people apply for benefits on their own, but often an application is denied and they may need assistance in pursuing an appeal. If you need legal representation to assist you in obtaining Social Security disability or SSI benefits, contact your local legal services program and your local bar association referral offices. You can also get a referral from the National Organization of Social Security Claimants Representatives by calling: 1-800-431-2804.

Wedding Bells for Pen Pals

Dear NNFF: I would like to thank you for putting my name in the Pen Pal area of your newsletter. Otherwise I would not have met Michele. We are planning to get married in 2001. Neither of us thought there was someone out there for us. Thank you for bringing two lonely hearts together. - J. S. Littlefield

New Format Welcomed

The new format is great! Those who are visually impaired can now read with ease. The clarity of the print as well as the bond of the paper, makes it very legible. It is a big step forward for the entire NF population. Congratulations! - R. Needel, Quincy, MA

(The following message was received via the NF Bulletin Board on AOL)

Life Is A Bakery

I am 15 and have spent many sleepless nights worrying about my NF. My mother recently gave me some very good advice: "Look at life as a bakery, she said. "We are the cookies. God is the cook, he makes the cookies. God makes all kinds of different cookies, from sugar cookies to chocolate cookies. You're a chocolate chip cookie!" This was a bizarre way of putting it. After she left, I stared at the walls and then I started to laugh...I gotta lighten up...I should be lucky that these birthmarks (café-au-laits) are my greatest threat so far. There are so many people suffering from even greater things. So my message is ... don't waste time worrying day and night, it's stressful. Be aware of your problems and do whatever it takes to help make it better, but please don't worry. - Saria

Donating Tumor Tissue

I am having surgery to remove a plexiform and was wondering if there was any way for me to donate it for NF research. - D.S., Ft. Lauderdale, FL

Yes, but you have to plan well in advance. You will need to provide us with a summary of your condition and/or type of tumor, so that we can determine which scientist to recommend and then we can put your doctor in touch with scientist. Also, cooperation of the your surgeon is needed at time of surgery, since tumors need to be harvested in the operating room and placed in the correct medium for shipping to scientists. (Please refer to the Research Call section of this newsletter for NNFF affiliated scientists currently looking for tumor tissue.)

Pen Pals

- Would love to talk with anyone who has NF. I'm 21. - Megan Alexander, 1082 S. Dahlia H-408, Denver, CO 80222 or Themeegs20@aol.com
- I'm interested in chatting about NF1 or 2. I have NF, my daughter who has NF2 needs support. Please write me at LBPsalms.aol - Laverne
- Write me so I can become a good friend, I am 33 and have NF1. - Suzanne Benitez, 8237 S. Madison, Indianapolis, IN 46227
- Adult looking for pen pals. - Barbara Baines, 2016 Mobile Dr., Rockymount, NC 27804
- I think this is a great way to get to know others with NF, find some support and maybe even some bits of helpful information. I'm 30 years old with NF2. Would like to hear from others with NF2 or NF1. - Teresa Bartholomew, 262 South 100 East, Spanish Fork, UT 84660 or Striplitho@msn.com
- Mother of an 11 year old with NF who has had to deal with facial reconstruction would like to hear from others. - email: Dbarr41088
- My name is Twyla, I'm 14 and have NF1. I don't know anyone else with NF, so please write to me. - tsnodgrass@hotmail.com
- I'm 19, a dedicated sci-fi fan and will answer all who write. - April Misty Ford, 324 Willow St., Woonsocket, RI 02895 or wyoum@aol.com
- I don't know many people with NF and would like to hear from others. I'm 28. - Jason Swift, 1290 Lake Road, Rochester, NY 14580 or email: Jswift39

- My daughter and I have NF. I would like some penpals to talk with about what its like to NF. - Judy Brewer, Box 340 LaPlace, LA 70069
- Adult woman with NF from across the Atlantic would like to write. - Jenny Cicharski; 43 West Drive Gardens; Soham, Ely Cambs CB7 5E7 England
- My name is Mike Albright. I am an adult with NF2 and live in South Florida. I'm looking for others who can identify with early deafness, physical handicaps, etc. email: albright@gatenet
- I am looking to speak with a parent of a child or someone with both NF1 and Agenesis of the Corpus Collosum (ACC). My 3 year old son has both NF1 and complete ACC and I have not been able to receive any information on manifestations/experiences/treatments when both disorders are present within one individual. Please contact me at: lesli.woodall@choicepointinc.com - Lesli Woodall
- 51 year old man looking to correspond with others. - William Miller; 625 Chamberlain Circle; Marietta, GA 30008
- Would like to hear from anyone in the New Orleans, LA area. I'm a 52 year old widow with NF. Please write. - Gisela Cagnolati, GISELAFROMLA@webtv.net
- I am an adopted female with NF. At the time of my birth (4/12/62) in Hempstead, NY my name was Rebecca Jean Silver. I'm seeking my birth parents and sister who may also have NF. If you have any information, please contact me at 973-492-9080 or at CINDYMUDD@aol.com - Cindy Mudd
- I would like to correspond with young adults 19-28 years. - Tara Moore; 4139 Parkdale; Dennison, TX 75020
- 24 year old would like to hear from other with NF1 and children with NF1. - Lashanda Warren; 1416 Marshall Ave. Apt. B; Norfolk, VA 23504