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Landmark Article in JAMA by Dr. David Gutmann and CCAB:  
NNFF Clinical Care Board Revisits and Expands Diagnostic and Management Criteria for NF1 and NF2

In what is destined to become a landmark article in the history of neurofibromatosis research, the Foundation's Clinical Care Advisory Board (CCAB) under the leadership of Dr. David Gutmann (Washington University, St. Louis) revisited and substantially expanded the diagnostic and management criteria for NF1 and NF2.

Published in the July 2, 1997 issue of the Journal of the American Association (JAMA), Dr. Gutmann and the CCAB, in consultation with key scientists and clinical experts around the world, stated that "there has been significant progress toward a more complete understanding of the molecular bases for neurofibromatosis 1 and neurofibromatosis 2". Given this progress, the group set out to "determine the diagnostic criteria (for NF1 and NF2) recommendations for the care of patients and their families at diagnosis and during routine follow-up, and the role of DNA diagnostic testing in the evaluation of these disorders".

It was an ambitious undertaking which involved a review of all published reports from 1966 to 1996 and of studies presented at national and international meetings. All studies were "analyzed by consensus from multiple authors...The main results of the review were qualitative." These then were reviewed by clinical directors worldwide through the Internet Web site of the National Neurofibromatosis Foundation.

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### **Foundation's 1997 Research Awards Announced**

NNFF Medical Director Dr. Allan Rubenstein announced the Foundation's 1997 research awards. "These awards," said Dr. Rubenstein, "are the result of another extremely rigorous peer review process with applications from all parts of the United States and abroad. The general excellence of the applications was impressive; and I only wish we could have had additional resources to fund even more projects. As it

is, however, the projects selected by the peer review panel, the Research Advisory Board, and approved by the Foundation's Board of Directors, includes exciting new ideas which, if successfully pursued in the laboratory, will bring us closer to effective treatments for both NF1 and NF2. Our congratulations go to all the winners in this year's exciting competition." The awards were as follows :

The Mark B. Wallner Foundation Award  
Dr. Nina F. Schor  
University of Pittsburgh  
1-Year Grant  
Project Title: "NGF Receptors, Apoptosis and Neurofibromin"

Recent studies suggest that proteins like neurofibromin (the protein produced by the NF1 gene) play a role in blocking the ability of another protein called nerve growth factor to protect nervous system cells from death. Patients who make abnormal neurofibromin may therefore have unchecked nerve growth factor activity, and may have cells that continue to live and divide thus making tumors, when they should be dying off during development. Dr. Schors' studies will test this idea in nerve cells derived from neurofibromin-deficient mice. Studies leading to a better understanding of the interaction between neurofibromin and the nerve growth factor protein may ultimately pave the way for the design of drugs that can block the cell death-preventing effects of growth factor in patients with NF1.

The Steven and Lottie Walker Family Fund Award  
Dr. Jan Friedman  
The University of British Columbia, Canada  
1-Year Grant  
Project Title: "Updating and Modernizing the NNFF International Data Base"

Dr. Friedman and associates developed and maintained the NNFF International Data Base since 1990 with support from the National Neurofibromatosis Foundation, Inc. The Data Base represents a multicenter collaborative system for the collection of extensive demographic information, descriptions of signs and symptoms, basic measurements and certain psychological information on individuals and families with NF. Twenty-nine NF clinics throughout the world voluntarily enter data into the Data Base on a regular basis. Complete data on 2500 patients are currently available to qualified investigators for use in appropriate studies. The purpose of this grant is to update and modernize the technical aspects of the Data Base to make contributions by a larger number of participating centers less time consuming and less costly while at the same making the extraction of data by investigators more efficient and easier to perform. An updated and modernized version of the NNFF International Database will assure that this facility will remain a central resource for the growing number of scientists interested in neurofibromatosis.

The Texas NF Foundation Award  
Dr. Gladstone Airewele  
Baylor College of Medicine  
1-Year Young Investigator Award  
Project Title: "Optic Pathway Tumors and Second Primary Brain Tumors in NF1: A Nested Case-Control Study"

Dr. Airewele will study 642 patients with NF1 who were seen at the Baylor College of Medicine between 1978 and 1996. These patients will be traced, interviewed, and medical records reviewed. The main goal of the study is to look more closely at the group of patients with optic pathway tumors to see if there is an increased incidence of other tumors, especially brain tumors. This investigation has the potential benefit of gaining the ability to identify NF1 patients who are more likely to develop other tumors, and who would therefore gain from regular medical examination, especially of the eye and the brain. The results of the study will form the basis of a later study to determine the genetic differences associated with the development of Optic Pathway Tumors and second brain tumors.

The Barrie and Faith Sommerfield Family Fund Award  
Dr. Frances Lesley Hannan  
Cold Spring Harbor Laboratory  
1-Year Young Investigator Award  
Project Title: "Regulation of Adenylyl Cyclase By the NF1 Protein"

Studies at the Cold Spring Harbor Laboratory in the fruit fly *Drosophila* have shown that the NF1 protein neurofibromin not only regulates the well-known cancer protein Ras but that neurofibromin also regulates the activity of a pathway which is involved in synthesis of cyclic AMP (cAMP), a small molecule that is a very important intracellular messenger. The hormone PACAP (Pituitary Adenylyl Cyclase Activating Polypeptide) stimulates cAMP production in humans and other mammals. It also induces electrical activity in the muscle cells of fruit flies. This electrical response requires the simultaneous activation of both Ras and cAMP pathways. Dr. Hannan and colleagues have shown that the PACAP-induced response is completely abolished in NF1 mutant flies. Furthermore, this response does not result from elevated Ras activity, but is actually caused by a blockade of the cAMP pathway. The defect appears to reside in the misregulation of an enzyme called adenylyl cyclase, which synthesizes cAMP. The PACAP-induced response can be restored in NF1 mutants by supplying cAMP or by the drug forskolin, which bypasses external signals and directly stimulates the adenylyl cyclase enzyme to synthesize cAMP. Since the *Drosophila* NF1 protein is very similar to the human NF1 protein it is likely that a similar mechanism operates in humans, and that drugs like cAMP, forskolin or their derivatives could possibly be effective therapeutic agents for the treatment of neurofibromatosis. The aim of Dr. Hannan's study is to test whether there is a direct physical interaction between the NF1 protein and the enzyme adenylyl cyclase. She is also interested in determining the effect of normal and activated Ras proteins on adenylyl cyclase activity. In order to extend the results in *Drosophila* to vertebrates, adenylyl cyclase activity in a mouse NF1 mutant will also be examined.

The Peter and Margie Feinberg Family Fund Award  
Dr. Jonathan A. Epstein  
University of Pennsylvania  
1-Year Grant  
Project Title: "The Cardiac Abnormality of NF1 Deficient Mice"

The mouse model for NF1 offers an attractive *in vivo* model for studies of the function of the NF1 gene product neurofibromin. These mice die during embryogenesis because of a severe cardiac defect that includes a gross

overabundance of cells located in the region where heart valves normally form (something which does not happen in embryogenesis in humans with NF1). Abnormal development of the heart valves and the division of the primordial heart tube into separate chambers and great vessels accounts for most forms of congenital heart disease including some medical problems thought to be related to NF1 such as Noonan and Leopard syndromes. Distinct cell types contribute to this region of the heart, and it is not clear which cell type requires neurofibromin for proper function. Nor is it clear what cardiac signaling pathway is disrupted by neurofibromin deficiency. Dr. Epstein will conduct experiments that will elucidate the cell type of the abnormal cardiac cells in the NF1 mutant mice, and test candidate signaling pathways for abnormal function. Results are expected to shed light on the essential cellular function of neurofibromin in vivo as a regulator of cell growth and differentiation. The experiments are also expected to make clearer the potential role of neurofibromin in the development of human congenital heart defects.

The Keller Research Fund Award  
Dr. Brooke McCartney  
Duke University  
1-Year Young Investigator Award  
Project Title: "Genetic Analysis of Dmerlin Function"

Although Merlin, the NF2 protein, has been identified, we still do not have direct knowledge of its normal function, or the reason(s) that mutations in this gene result in NF2. Fully elucidating the functions of the NF2 gene will require a combination of experimental approaches including genetics, molecular biology and biochemistry. Although it is currently difficult or impossible to effectively combine these approaches to study humans, in certain organisms, most notable the mouse and the common fruit fly *Drosophila melanogaster*, such combined experimental approaches are possible and have been used to examine the functions of a rapidly growing number of genes. With this in mind, Dr. McCartney and colleagues have identified a Merlin homologue in *Drosophila* and have generated mutations that result in lethality or viable adults with visible defects. Dr. McCartney will examine the cellular function of Merlin by genetically identifying proteins which interact with it in the cell. In this way she hopes to begin to understand how Merlin functions, and ultimately how loss of Merlin function in human cells causes NF2.

The Joseph S. Byrka Family Fund Award  
Dr. Sonja Rasmussen  
University of Florida, Gainesville  
2-Year Young Investigator Award  
Project Title: "Genetic Studies of Tumorigenesis in Neurofibromatosis Type 1"

Dr. Rasmussen proposes to study the genetics of tumor formation using a large set of benign and malignant tumors from patients with NF1. Loss of the NF1 gene has been shown to be important in formation of some benign and malignant tumors. However, since the NF1 gene loss was seen even in cutaneous neurofibromas, additional genetic changes probably occur in plexiform neurofibromas and malignant NF1 tumors. Dr. Rasmussen plans to study the NF1 gene thoroughly for gene changes (mutations) using methods proven efficient in mutation identification. She will also study NF1 tumors for changes in the TP53 gene, the most frequently involved gene in human cancers, since preliminary studies have suggested that this

gene may be involved in NF1 tumor formation. Finally, Dr. Rasmussen will use a technique called comparative genomic hybridization (CGH), which allows for comparisons of genetic material from tumors with normal genetic material to identify genetic regions that have been lost or gained. With these studies the investigator hopes to achieve a better understanding of NF1 tumor formation which should make improved strategies for the prevention and treatment of NF possible.

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A Report:

Advances in Mouse Models for Neurofibromatosis by: Karen Cichowski. Ph.D.  
Massachusetts Institute of Technology

(Ed. Note: Dr. Cichowski, a 1996 NNFF Young Investigator Awardee, wrote the following. It reflects comments which Dr. Tyler Jacks and she made in a joint presentation to the NNFF Council of Fellows in New York City on May 27, 1997.)

The cloning of the genes responsible for NF1 and NF2 represents a critical step forward in our understanding and ultimate treatment of these disorders. Not only does this information allow for future possibility of gene therapy, it enables us to study the normal (and abnormal) function of these genes; a prerequisite for rational drug design. Their identification has also provided the necessary first step in generating potential mouse models of NF1 and NF2, which will allow a unique means of studying disease progression as well as the environmental and genetic factors involved. To this end, mice carrying mutations in either NF 1 and NF2 gene have been generated.

In the course of examining these animals over several years we have observed both similarities and differences between the symptoms exhibited by these animals and those seen in NF patients. In this discussion we will describe these mice, outline the different approaches that have been used to generate them, and illustrate how studying these animals has and will continue to improve our understanding of NF1 and NF2.

The Genes and their Disease

Although patients with NF1 and NF2 exhibit different symptoms, both are predisposed to developing various benign and malignant tumors. These disorders have therefore been classified as familial cancer syndromes. Analysis of mutations found in patients has further revealed that NF1 and NF2 belong to a family of genes known as tumor suppressors. These genes normally function to prevent the inappropriate growth of cells and in this way serve as cancer protection mechanisms. The fact that NF1 patients are predisposed, among other things, to neurofibromas, optic gliomas, myeloid leukemia and tumors of the adrenal gland, while NF2 patients develop schwannomas, meningiomas and ependimomas illustrates the pivotal role these genes play in the prevention of very specific types of cancer.

The explanation for why NF patients are prone to developing these tumors is based on the fact that normally humans carry two copies of every gene. In order for one of these tumors to arise in a person without NF1 or NF2, both copies must be mutated in a single cell. This requires two, independent, spontaneous events and therefore is a relatively rare occurrence. Patients with NF, however, are born with a mutation in

one copy of the NF1 or of the NF2 gene, therefore only one additional event is required for a tumor to develop.

#### The Generation of Mouse Models

In an attempt to create animal models for NF1 and NF2, mice carrying mutations in one copy of each of these genes were generated. Since these animals possessed genetic defects similar to those present in patients with NF, it was expected that symptoms similar to those observed in humans might develop. Interestingly, these mice did exhibit some features of NF1 and NF2, but not others. Mice with NF1 mutations were predisposed to several types of tumors, most notably myeloid leukemia and adrenal tumors, which do arise in some patients with NF1. Furthermore, as in humans, a mutation in the second copy of the NF1 gene was detected in tumor samples. This supports the theory that both copies of the gene must be defective in order for cancer to occur. Remarkably, these animals also exhibited learning and memory deficits reminiscent of those associated with some patients with NF1. Clearly, these animals will be extremely useful in studying these specific aspects of the disease. Unfortunately however, these mice did not exhibit some of the hallmark features of NF1. Most importantly, they did not develop neurofibromas. Mice carrying NF2 mutations have also been generated and like the NF1 mice, show a dramatic predisposition to several different types of cancer; however, they did not develop any tumors characteristic of the human disease.

While both types of animals appear to only partially fulfill the goal of developing animal models for NF1 and NF2 they will still be extremely useful in studying the function of these genes in the development of cancer, in addition to facilitating the identification of other genes/factors involved. For example, one possible explanation for why these animals do not develop some of the characteristic tumors observed in humans is that a mutation in another tumor suppressor gene is required. Fortunately, mice containing mutations in many of these other genes have already been generated, making it relatively straightforward to produce animals with mutations in multiple genes. Thus these mice provide a unique means of investigating the involvement of other genes in disease progression.

These animals will also be useful in the design and testing of potential therapies. Although many of the tumors that develop in these mice are not identical to those that arise in humans, they still represent a manifestation of a defect in the tumor suppressing function of these genes and therefore provide an important biological readout of the effectiveness of therapeutic agents.

An alternative explanation for why these mice do not develop many of the tumors associated with NF1 and NF2 is that spontaneous mutations do not occur as frequently in mice as they do in humans. Therefore, a second mutation in the critical cell type might not occur in the life-span of a mouse (1.5-2 years). As a means of circumventing the need for a second spontaneous event to occur, we attempted to generate mice with mutations in both copies of the NF1 or NF2 genes. Surprisingly, a role for both NF1 and NF2 development was revealed, as embryos did not survive past day 13.5 or day 7 of gestation, respectively. While these animals will not serve as disease models, investigating the role of these genes in the process of development should certainly provide insight into their function.

#### A Model for Neurofibroma Formation

As described previously, one of the potential explanations for why neurofibromas do not develop in mice with only one mutation in the NF1 gene is that a second

spontaneous mutation does not occur quickly enough in the relevant cell type. However, when every cell in a mouse embryo has a mutation in both copies of the NF1 gene, it cannot survive past the 13th day of development. We therefore generated mice referred to as "double knock-out chimeras". In this strategy both copies of the NF1 gene were mutated in mouse cells in culture. The cells were then injected into very early (normal) mouse embryos and the embryos were implanted into a surrogate female mouse. The presence of the normal cells in these animals (white) allowed them to survive past the critical stage of development while some mutant cells (black) were still present.

We have studied 18 surviving animals and have observed multiple neurofibromas in all but one of these mice. However, while these tumors are quite similar to those observed in patients with NF1, there still are some differences that remain. We are therefore continuing our efforts to improve this system. Regardless, these animals should be extremely useful for investigating the mechanism of neurofibroma formation and testing various therapies.

Three experimental approaches used to generate animals with mutations in the NF1 and NF2 genes have been described. In addition to serving as models for specific aspects of the human disorders, the mice generated by each of these approaches will enable us to investigate these genes in the context of a whole animal. These studies should ultimately provide some important insight into their function, facilitating the development of future therapies.

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#### Research Calls:

##### NF2 and Unilateral Vestibular Schwannomas

The Neuroscience Center at the Massachusetts General Hospital is conducting a research study investigating the correlation between NF2 and unilateral vestibular schwannomas in children and young adults. Because unilateral vestibular schwannoma is primarily a tumor in older adults, occurrence in the young is always troubling, especially since in some cases of NF2 there have been many years difference between the appearance of the first and second tumor. The goal of our study is to determine the probability of NF2 developing in patients presenting with a unilateral vestibular schwannoma from age 0 to 25. This information will be clinically significant since the management of sporadic vestibular schwannomas and NF2 is very different. In order to determine the presence of NF2, the study will involve molecular genetic analysis of tumor and blood specimens from individuals who were diagnosed with a unilateral vestibular schwannoma before age 25. If a patient has already had surgery we can often use the archived tissue kept by the hospital. For further information contact: Mia MacCollin, MD or Alex Clark at MGH East, Bldg. 149, 13th St., Charlestown, MA 02129; tel: 617-724-9584 or email: [apclark@acs.bu.edu](mailto:apclark@acs.bu.edu)

##### NF1 and Pseudarthrosis

Researchers at the University of Utah are conducting a project on people with NF1 who have leg bone problems. Dr. John Carey, Dr. David Viskochil and David Stevenson will study the psychosocial aspects of treatment and the natural history of this complication of NF1. They are looking for anyone who has NF1 and

pseudarthrosis or bowing of the tibia. The project should promote understanding about pseudarthrosis care with hopes of improving the lives of those with this condition. The researchers have developed a short questionnaire for the family to fill out. If you are interested in participating, please contact David Stevenson at: Univ. of Utah, Sch. of Medicine, Dept. Peds. & Med. Genetics, 413 MREB, Salt Lake City, UT 84112; Fax: 801-585-7252; Tel: 801-581-8943.

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#### Filming new PSA with Packer's Mark Chmura

The tight end who scored for the Green Bay Packers in this year's Superbowl XXXI, came to New York and filmed new Public Service Announcements (PSA's) for the Foundation. The 30- and 60-second messages feature Chmura and eleven-year old Chris Byrka from Connecticut, asking for support of the National Neurofibromatosis Foundation. The PSA's are scheduled to run in the fall on 300 television stations throughout the United States. Mark Chmura has been an enthusiastic NNFF supporter (pledging dollars for every catch he makes next season) and has made the Foundation his "official NFL Charity".

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#### Heroes in the fight against NF are honored in New York

At the annual luncheon of the NNFF Board of Directors and Chapter Council, the Foundation honored individuals who distinguished themselves in the fight against NF. NNFF Council of Fellows member Debbi Honorof (Plandome Manor, NY) received the NNFF Medal of Merit for her many years of service as a volunteer, National Board member and Foundation employee, Ms. Honorof already is the recipient of the Foundation's highest award, The Lynn Courtemanche Award. Deanna Miyamoto (Mill Creek, WA) received the 1997/98 National Volunteer of the Year Award for her contributions to the Foundation's Public Education efforts. Maryanne and Arthur Ward (Tallahassee, FL) received the 1997/98 Chapter Volunteers Award for their tireless and effective service with the NNFF Florida Chapter, especially in the area of public education.

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#### NF Profile:

##### Susan Goldfinger: A Winning Attitude

"You can overcome anything". You can either laugh or cry. When you cry you loose. When you laugh you win". That is the motto of Susan Goldfinger.

Diagnosed with learning disabilities in the third grade, Susan fell far behind her classmates and was held back in fifth grade. At the time she thought it was a disaster, but it turned into a positive situation. The extra year enabled Susan the extended time she needed to mature and improve upon the skills she would need for high school, college and beyond. Teachers told her she should consider a vocational education rather than finish high school and continue on to college. But she was

determined. Susan graduated Wright State College in Dayton, Ohio with dual Bachelor of Arts degrees in history and religion. During her last year there she was designated "Senior Leader of the Year". "Every time I was told I couldn't do something, I proved everybody wrong, both physically and scholastically", says Susan proudly. Twenty-nine year old Susan is currently studying at Xavier University and expects to receive a Masters degree in Montessori Education next year.

From her earliest years, Susan has vivid memories of very severe physical pain which still plagues her body today. She lost count, but thinks she has had about 40 surgeries to correct bladder, kidney, orthopedic and brain problems.

Susan says that her NF has taught her several important life lessons. The most important are tolerance and compassion. By working within the Ohio NF Chapter, she has reached out to patients and encouraged, particularly the younger members because she feels that "everyone wants to know that someone else has felt a little of their problems. That is one of the main reasons that the Internet is so popular. We must all learn to validate the feelings of those around us."

The Ohio NF Chapter is an integral part of the lives of the entire Goldfinger family. Susan's mom, Dolores is Chapter President, and serves on the NNFF Board of Directors. Her father, Gerry is the Chapter Treasurer. Her younger brother and older sister, also work diligently to give support to the Ohio constituents via referrals, newsletters and fundraisers.

"Life has been a struggle of wits and skills", says Susan. "I have had many challenges and they have been on several levels, including physical, emotional and educational. But with the strong support of my family I have been able to overcome them. I love to learn and make new discoveries all the time. I hope that I am able to pass on this excitement about learning to all the children whose lives I touch."

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#### Testifying before Congress

NNFF President Peter Bellermann testified in April before the House Appropriations Subcommittee for Labor, Health and Human Services and Education. In his testimony Bellermann hailed the National Institutes of Health (NIH) for their role in the fight against NF. He especially praised the NIH for their cross-institutional collaborations on behalf of NF1 and NF2. He asked for increased overall funding for the NIH, calling investments in basic research the most effective long-term healthcare policy for the United States. Bellermann also encouraged increased funding for NF research, pointing to the rapid progress achieved during the past decade and to the potential of NF research for work in cancer and learning disabilities.

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#### New Webmaster for Foundation's Website

The Foundation's popular website has a new webmaster in Dr. Sjouke Zwanenburg, who has taken on his assignment "pro bono publico". Dr. Zwanenburg is a member

of the Foundation's Council of Fellows. He serves as a genetic toxicologist and as the Head of Planning and Laboratory Services, Toxicology/Pathology, Europe, at the giant Swiss pharmaceutical firm Novartis Pharma Ltd in Basel. Jonathan Tann and his company Agency.com continues to house the website as a public service.

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May was NF Awareness month

For years Foundation members have recognized May as NF Awareness Month. This year INFA, the International Neurofibromatosis Association, enlarged on the idea and proclaimed May as NF Awareness Month worldwide. NNFF Chapters successfully petitioned mayors and governors to issue proclamations. Special public awareness activities were featured by Chapters from Hawaii to New York and by lay organizations outside the United States from Belgium to Australia.

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Your Turn

Perspectives, Questions and Comments from Patients and Families

Many patients receive superb care from competent and sensitive medical professionals. Some Foundation members are not so fortunate however, the following is one mother's frustrating experience:

"It Only Takes A Minute...." "I think you just aggravated nearly all the Physicians in this room." My husband's comments stunned me. The National Conference on Neurofibromatosis included a session emphasizing the doctor-patient relationship at which I was asked to speak. I did not mention any hospital or physician by name. My emphasis was on the importance of humanizing a medical diagnosis.

Jeane-Marie was born with a palm-size growth on her back and many café-au-lait spots. Her pediatrician came to my hospital room and inquired if I had any large freckles. I was a redhead, naturally I had freckles. Seven months later, the Pediatrician confided he had suspected Jeane-Marie had NF the day she was borne but elected not to inform us. It was incurable. He suggested a baseline regimen which took nearly a week to complete. During this time I asked the neurologist if Jeane-Marie should have annual X-rays. He replied, "Don't become a hysterical mother over this. The X-rays will do more damage than good." The genetics counselor shared that his melanoma was in remission, NF isn't even a malignancy, we should be grateful. Never having dealt with physicians, I was incredulous by the consumer-producer mentality of our appointments.

When Jeane-Marie was four years old, I noticed her rib cage was dramatically asymmetric. Upon reviewing her X-rays, the radiologist was bewildered why they had not referred our daughter for surgery. She had idiopathic scoliosis which they could have detected earlier with an annual X-ray. The orthopedic surgeon decided spinal fusion and insertion of C-D rods were needed. During this operation, the neurosurgeon would remove a neurofibroma near the spine. When asked the size of the neurofibroma, he said, "Old ladies die and never even know they had a tumor."

We haven't a clue what that meant. When asked what we should expect post-operatively, the thoracic surgeon told us not to worry, she's in good hands. Why do physicians confuse "worry" with the right to know? The frustrations continued the following year when they removed the C-D rods and Jean-Marie was having breathing difficulties. They told us her recovery was slower this time. Six phone calls and three weeks later when Jean-Marie could no longer walk, they discovered her back had never fused. The next months consisted of halo casts, lead weights and extensive surgery to repair the damage. Sensing our frustration, the head nurse said "If you are expecting an apology, you'll never get one." All we wanted was direction regarding Jean-Marie's future.

I ended my presentation to the room full of physicians by stating that I have a Ph.D. in Molecular Genetics. In all those years, never did I tell a physician my background. A mother should not have to give her academic credentials to be treated with respect and dignity. Immediately following the meeting, a physician approached me and said, "These doctors are good at what they do. You might as well ask them to change the color of their eyes than to change their bedside manner." Another excused the profession by saying most of the patients are indigent and they're just grateful to have care, no questions asked. The message that day may apparently have been lost.

I am a firm believer that a patient's mental state and rate of surgical recovery are closely linked. It is extremely important that a physician understand the power in providing not only exceptional medical support, but also emotional support through informed care. Neurofibromatosis is a complicated and frustrating disease and maybe why physicians find it so difficult to communicate with the families. Once I asked a physician why he wouldn't tell me which of Jean-Marie's vertebrae had been fused. He simply said, "Do you want the best physician for this job or a physician with good bedside manner?" This comment still does not make sense to me. The answer is obvious, "Why can't I have both?"

Although early I allowed physicians to exclude our family from becoming involved with Jean-Marie's care, over the past four years we have found superior surgical teams with a kind and caring presence. Families that need to ask questions, should ask again if the answer is not forthcoming. This process should not be difficult. It only takes a moment. - Cecilia Crouse, West Palm Beach, FL

#### NF1 vs. NF2

I have been trying to find out the differences between NF1 and NF2. My mother, sister and brothers and myself all have NF1 and my newborn son is scheduled for genetic testing. Can a person with NF1 pass along NF2 to their child? - C.M., West Orange, NJ

NF1 and NF2 are genetically two distinct disorders. The gene for NF2 is found on chromosome 22, while the gene for NF1 is on chromosome 17. People with one cannot pass along the other to their offspring, unless of course, in the case of a spontaneous mutation in the offspring.

#### Neurofibromas and Pregnancy

Both my wife and daughter age 6 have NF1. My question regards the risks of further pregnancies. During her only pregnancy, existing skin-surface fibromas increased in number, size and in some cases, became reddened. Subsequent to the pregnancy,

the "new" fibromas remained and where possible, were successfully removed. Is there evidence that a second pregnancy might produce substantially more fibromas than the first, or cause existing ones to react in a radical manner? - Mark Schwartz, South Africa.

The medical literature includes many anecdotes indicating that the symptoms your wife experienced do occur frequently. Examples include instances where neurofibromas become larger or appear for the first time during pregnancy. Neurofibromas that grow larger during pregnancy may, in some cases decrease in size after the baby is born. This is most likely a function of the general swelling and fluid accumulation that naturally occurs during pregnancy. Other neurofibromas that grow may remain large indefinitely. Clearly there is an element of risk that symptoms may grow worse during pregnancy, but this does not happen in every pregnancy. Currently, we do not know if hormonal changes are indeed the cause of these phenomena.

#### Creating Public Awareness

I was feeling helpless because I wasn't doing enough to help to find a cure for NF. I am on disability and don't have many social contacts. I plan on participating in the California chapter's Bowl-A-Thon, but didn't feel that I could raise much money through sponsors. It occurred to me to contact our community newspaper - which has always been receptive to the community's needs - and see if they would be receptive to doing a story on NF. They said yes! I am very nervous about the interview, but very excited to have this opportunity to raise public awareness about NF. I hope this will help reduce the number of people who ask "neuro-what? or what's NF?". I've printed out a lot of information from the NNFF web pages and also have their literature, so I think I am well prepared. One week later: Something great happened this morning! A gentleman from Chino called and said that he read the article. He has NF and has never met or spoken to anyone with NF. He didn't know about the NNFF or the CA chapter. I told him about all the Foundation - what it is doing to find a cure and all it does to provide information and support. So I think the article has helped! That was my hope, I figured if even one person was helped then it was worth doing. - Debbie Holgate, Chino Hills, CA

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Stories Wanted: The National Neurofibromatosis Foundation is seeking compelling stories about the experiences of patients and their families with NF. These stories will make a valuable contribution to the Foundation's Public Education Programs by enabling us to distribute them (like this writer did) to local and international media organizations, as well as newspapers, magazines, television and radio. Please send your stories to: NNFF; Public Ed. Dept.; 95 Pine St; 16th Fl.; NY, NY 10005.

#### Coming to Peace with Myself

At times I felt the only season in my soul was winter. I felt alone, cold and full of anger. It has taken me a long time to learn to live with my NF. Now most of the time I feel like summer. I have learned to look at things in warm, loving and bright light. Perhaps the hardest thing is learning to come to peace with NF. A lesson each of us must learn in our own way and our own time. I hope this might help someone. - Bobbie Milton, Sioux Falls, SD

Pen Pals

I have NF1 and so does my 10 month old son. - Elizabeth Gordon; 2880 Nickells Valley Rd.; Centerville, TN 37033.

I'm 17 and will write to anyone who needs a friend. - Allyson Wilson; 32186 Meadow Brook; Livonia, MI 48154

My husband and I are deciding whether to have children. I have NF. We'd like to hear from others who have had to deal with this issue. - Kim Dunn; 11051 Royal Ascot; Baton Rouge, LA 70816

I'm 35 and would like others with NF to write to me. - Lucretia C. Denson; 1381 NW 95th Terr; Miami, FL 33147

Jessica, my 13 year old has NF. Would you be her penpal? Her screen name is MABSinger@aol.com

Looking for penpals. - Lisa Mohler; 255-42 74th Ave; Glen Oaks, NY 11004

My 2 sons and I have NF. Please write. - Regina Werth; 1426 Summit Ave; Racine, WI 53402

I'm 41 and would like penpals. - Cameron Sheeleigh; 30 Elm St.(J); Summit, NJ 07901

There must be NF Chicagoians - Write to: John Harris; 2032 W. Jarvis; Chicago, IL 60645

I enjoy guitar, piano, tennis. I am 14 and have NF1. - Jonathan Armstrong; 789 Danbury St; Salinas, CA 93906

I'm 33 and mother of 4. I'm seeking penpals so we can encourage one another. - Valerie Slininger; 311 Eastham Rd; Pt. Pleasant, NJ 08742

55 year old female would like to hear from others with NF1. - Carole Sergerson; 1308 Rollins (#1); Cheyenne, WY 82001