



FA FAMILY NEWSLETTER

#33

A Semi-annual Publication of the Fanconi Anemia Research Fund, Inc.

Spring 2003

Fanconi Anemia Scientific Symposium

The Wyndham Franklin Plaza Hotel in Philadelphia was the site of the Fourteenth Annual Fanconi Anemia Scientific Symposium held from December 2-5, 2002. One hundred fifty-eight researchers attended this meeting to hear oral presentations from 46 scientists regarding the results of their research into Fanconi anemia. In addition, 26 scientists detailed their research through poster presentations. Countries represented by participants in the Symposium were Brazil, Canada, England, France, Germany, Israel, Italy, Japan, Mexico, The Netherlands, Spain, Turkey, and the United States.

Topics covered five areas: Overview, Gene Discovery, and Stem



Cell Differentiation; Cancer and Leukemia; Functions of FA Proteins in DNA Repair and Hematopoiesis; Novel Therapies; and Bone Marrow Transplantation.

Evaluations by the participants rated this meeting as outstanding. Highlights included presentations on *continued on page 24*

Annual Family Meeting: Mark Your Calendar

The Fanconi Anemia Research Fund has reserved Camp Sunshine from August 8–12 for the Annual Family Meeting. Camp Sunshine, on Sebago Lake in Casco, Maine, has an outstanding program for children and parents alike. The FA Research Fund complements this program by inviting physicians and researchers who specialize in Fanconi anemia to discuss their treatment programs and/or research protocols. The Family Meeting is invaluable to parents who would like to talk with experts in a relaxed atmosphere, hear comprehensive information about FA treatment, or just relax with other FA parents. A scholarship program is available for FA families who need assistance in traveling to Maine.

Camp Sunshine provides free lodging and meals. Suzanne Lauck, Family Support Coordinator, will send information in the late Spring regarding Family Meeting registration. ♦

HIGHLIGHTS

Oral Cancer in FA Patients.....	2
Clone with Subtle Abnormality on Chromosome 3 Predicts MDS, AML in FA Patients.....	3
Model Presented for Understanding Head & Neck Squamous Cell Carcinoma.....	3
The FA Research Fund Solid Tumor Initiative.....	4
Family News.....	11
Fundraising	20

Singh Discusses Oral Cancer in FA Patients

Bhuvanesh Singh, MD, Memorial Sloan-Kettering Cancer Center, New York City, addressed our recent Scientific Symposium, providing new, potentially very helpful insight into the cancers that affect FA patients. Singh noted that 39 FA patients have developed squamous cell carcinoma (SCC) among the 754 in the International Fanconi Anemia Registry. Of these carcinomas, 47% are cancers of the head and neck. The cumulative incidence of SCC in FA patients is 19% by the age of 40.

FA patients develop SCC at an earlier age than the non-FA population. Surgery is the primary therapy, since FA patients do not tolerate radiation or chemotherapy well.

Singh noted significant differences between FA patients with head & neck squamous cell carcinoma (HNSCC) and this same disorder in the general population. Use of tobacco and alcohol is associated with more than 85% of the non-FA

head and neck cancers, but only 16% of these cancers in FA patients. Among 19 FA patients with HNSCC, 10 (or 53%) developed a recurrence of the tumor within ten months, and 63% developed two or more cancers during their life span. Comparable rates are far lower in the general population.

Singh was able to study 24 tumor samples from FA patients with head and neck cancer. While mutations of the p53 gene are found in 36% of non-FA head and neck cancers, Singh's group found no p53 mutations in the FA tumors. Of special significance, 83% of the FA tumors were positive for human papilloma virus (HPV), compared to 28% in the non-FA population. These data suggest that HPV may play a



Bhuvanesh Singh, MD

significant role in SCC development in FA patients.

Singh concluded that there is an urgent need to develop new ways of treating and preventing this complication in FA patients. ♦

Post-transplant Complications in France

Eliane Gluckman, Hôpital Saint-Louis, Paris, France, reported on post-transplant complications in FA patients transplanted in France from 1981 through 1996. She compared 37 FA patients to 73 non-FA patients in terms of incidence and severity of graft-versus-host disease (GVHD), and GVHD resistance to cortisone therapy. In all categories, FA patients did worse than non-FA patients.

continued on page 10

FA and Breast Cancer Risk

At the December Scientific Symposium, Arleen Auerbach of The Rockefeller University, New York, presented data on the risk of breast cancer in FA patients and carriers. Of 367 female patients in the International Fanconi Anemia Registry (IFAR), only three have had breast cancer. These patients were ages 29, 40 and 42 at the time of breast cancer diagnosis. Auerbach believes this represents a significantly increased risk of breast cancer in FA patients compared to an age-matched non-FA population; twenty times the expected number of breast cancers was observed in FA females. However, of the 754 patients (males and females) in the recent analysis of the IFAR data, 60 developed AML (2,314 times the number expected based on an age-matched normal population) and 19 had squamous cell carcinoma of the head and neck (500 times the expected number). Thus, while the risk of all cancer is significant for FA patients, these patients are not especially predisposed to breast cancer relative to their extraordinary risk for AML and squamous cell carcinoma, particularly of the head and neck.

Auerbach is also conducting an extensive study of FA carriers. The risk of cancer in carriers is unknown at the present time. However, carriers of the three most common FA genes (*FANCA*, *FANCC* and *FANCG*) do not appear to have an increased risk of breast cancer. ♦

Clone with Subtle Abnormality on Chromosome 3 Predicts MDS, AML in FA Patients

Heidemarie Neitzel, PhD, Institute for Human Genetics, Charité, Berlin, reported that a particular chromosomal abnormality, defined as gains of the chromosomal segment 3q26q29, represents an ominous finding in FA patients.

Bone marrow from 54 FA patients was tested using three methods: conventional cytogenetics, comparative genomic hybridization (CGH), and fluorescence *in situ* hybridization (FISH). Twenty-eight patients had no chromosomal abnormality, while 26 patients had clonal aberrations. Of these 26, 19 had abnormalities on the long arm of chromosome 3, indicating a significant overrepresentation of 3q aberrations in these FA patients. Neitzel's laboratory observed a considerable

increase in this clone over time, suggesting that this abnormality confers a proliferative advantage to these cells.

Neitzel compared the clinical course of FA patients without the chromosome 3 abnormality and those with this aberration. Patients without abnormalities of chromosome 3q did significantly better. Only one of these patients developed MDS and one leukemia. In the 19 patients with an abnormal 3q, however, 13 developed MDS and 4 leukemia. These data reveal that 3q abnormalities are strongly associated with a poor prognosis.

Neitzel concludes that detection of 3q aberrations is imperative and can be achieved by screening FA bone marrow and FA peripheral



Heidemarie Neitzel, PhD

blood with interphase FISH. Ideally, blood should be screened every 3 months. **Neitzel advises that patients with this abnormality should strongly consider bone marrow transplantation before this clone evolves further.** ♦

Model Presented for Understanding Head & Neck Squamous Cell Carcinoma

Ruud Brakenhoff, PhD, Department of Otolaryngology, Vrije Universiteit (Free University) Medical Center, Amsterdam, proposed a novel model for understanding the development of head and neck squamous cell carcinoma (HNSCC) in the general population. He noted that 10-30% of non-FA HNSCC patients develop local recurrences in spite of tumor-free margins after surgery, suggesting the presence of undetected cancer cells or precancerous lesions related to the tumor. Based on research to elucidate the basis of this clinical problem, researchers gained novel insight into the process of HNSCC carcinogenesis.

Brakenhoff described four biological states that characterize the

evolution of these tumors: 1) the switch from a normal epithelial stem cell to a genetically altered stem cell; 2) the switch from a single genetically altered stem cell into a large precancerous field of genetically altered stem cells; 3) progression of a clone in the field into invasive carcinoma; and 4) development of metastatic carcinoma.

A critical event that influences cancer risk is the development of genetically altered fields, which displace the normal mucosa and can extend up to 10 cm in diameter. When a malignant tumor is removed, the remaining pre-cancerous field can give rise to new tumors.

Understanding the critical molecular steps in this progression model



Ruud Brakenhoff, PhD

could lead to early diagnosis and treatment of these precursor lesions. Currently, non-invasive methods for detecting these fields, as well as strategies for treatment, are being developed. ♦

The FA Research Fund Solid Tumor Initiative: A Progress Report

The FA Research Fund has taken a number of actions in the last year to advance research into the solid tumor malignancies for which FA patients are at extremely high risk in their late teens and adulthood. These tumors include squamous cell carcinoma of the head and neck, esophagus, gastrointestinal tract, and gynecological system, all of which respond extremely poorly to standard cancer treatment.

To address this issue, the Fund has done the following:

- Convened the first *FA and Cancer Conference* in Chicago in April, 2002. Twenty leading researchers and treating physicians were invited to attend this conference to advise the Fund in addressing the issue of solid tumors. As a result of this meeting, a number of researchers are now investigating FA.
- Funded a recent research project to study mouth cancer in FA patients.
- Published a newsletter entitled *Fanconi Anemia: A Cancer-Prone Disease* to acquaint solid tumor researchers with the Fund and with Fanconi anemia.
- Staffed the Fund's display booth at the American Association of Cancer Research (AACR) conference, at the American Society of Clinical Oncology conference, and at the Sixth Research Workshop on Head and Neck Cancer to interest researchers in studying FA-related cancer.
- Invited Steven Engroff, MD, University of Maryland, to speak with FA parents and adult FA patients about head and neck cancer at the Fund's Regional Meeting in Columbia, MD, in June 2002. Similarly, Dr. Engroff spoke with FA parents at the FA Family Meeting, Camp Sunshine, Maine, in August, 2002. Blanche Alter, MD, MPH, National Cancer Institute, also presented information regarding FA and cancer epidemiology at both meetings.
- Invited cancer researchers to the FA Scientific Symposium held in Philadelphia in December. This outreach resulted in a separate session on solid tumors and the presence of a number of cancer researchers new to Fanconi anemia research.
- Sent a letter to all major cancer institutes in the United States, Canada, and Europe regarding the high incidence of solid tumors plaguing FA patients to acquaint institute researchers with the need for research into the disease and the ability of the Fund to sponsor that research.
- Developed the *FA Courier* to encourage FA patients to donate research materials (including tumor samples) so that researchers studying FA solid tumors will have sufficient material for research projects.
- Organized a Standards for Clinical Care Conference for March, 2003, which will include development of a chapter on squamous cell carcinoma of the head and neck for the next edition of the *Fanconi Anemia: Standards for Clinical Care* handbook. ♦

FDA Halts Certain Gene Therapy Trials

On January 14, 2003, the FDA halted 27 gene therapy trials after learning that a second child with severe combined immunity disease, treated in France, had developed leukemia. Three trials were previously halted after the first child developed this complication.

All 30 trials involve attempts to insert a retroviral vector into a blood-producing stem cell. Only 15% of 200 gene therapy trials in the US were affected by this ruling. Trials involving other gene-delivery vectors and targets other than blood stem cells are not affected.

The possibility that a retroviral vector could lodge near a cancer-causing gene and turn it on, or within a tumor-suppressor gene and turn it off, has always been a theoretical concern. Until these two cases, however, the risk was considered quite low. There have been 40 or 50 similar trials in the US involving 100 patients. Most had limited or no success, but none has caused a cancer-like complication. Gene therapists wonder if there is something about this specific disease and this specific trial that caused these two unfortunate outcomes.

Nine children have benefited considerably from the French trial. Scientists must balance risks against benefits in deciding how next to proceed. ♦

Researchers Explore Novel Therapies for FA

At our recent Scientific Symposium, researchers presented their work on novel therapies that have the potential to correct FA bone marrow cells (or epithelial cells) without stem cell transplantation.

- **Catherine Verfaillie**, University of Minnesota, discussed her ongoing work with multipotent adult progenitor cells (MAPC). These cells can be isolated from the bone marrow, grown in large quantities, and can differentiate into a variety of different cells and tissues. Because of these traits, they may be ideal cells for treating both blood and epithelial cells of FA patients.
- **Francesco Galimi**, Laboratory of Genetics, The Salk Institute, uses a lentiviral vector to transduce stem cells. This vector has the advantage of transducing non-dividing stem cells and can reduce the *ex vivo* (outside of the body) gene transfer time from days to hours. Using this vector, Galimi is able to cure the bone marrow of FA mice. Galimi is now testing the capability of lentivectors to correct the Fanconi gene defect in cells derived from FA patient marrow and cord blood. Because of the difficulty in isolating a large number of stem cells from FA patients, early results have been disappointing.
- **Christopher Walsh**, Mount Sinai Hospital, says the fact that only a small number of CD34+ cells (a type of stem cell) can be isolated from the marrows of FA patients has hampered early gene therapy experiments. A rare, alternate stem cell population called SP (side population) cells might provide a better target for gene therapy. FA patients with good blood counts have an almost normal number of these cells. As blood counts decline, so does the population of SP cells. Gene therapy experiments with FA mice, using SP cells and a lentiviral vector, have produced promising results.
- **Marcus Grompe**, Oregon Health and Science University, discussed the drawbacks of current methods of gene therapy that rely on viral vectors to carry genes into cells. One characteristic of FA is

the loss of stem cells; it is hard to isolate the necessary number of these cells and even harder to transduce them with a normal gene. A further complication is the need to manipulate these fragile cells *ex vivo*. Grompe believes that gene transfer methods which could be applied directly in the patient (*in vivo*) might be preferable. He is currently working on two separate methods of gene transfer that do not use viruses and allow for insertion of naked DNA into the genome. One technique uses a gene delivery system called “*Sleeping Beauty* transposon” and the other a method called “integrase.” Early experiments in mice have produced very promising results: FA group C blood stem cells have been corrected directly *in vivo* and without using a gene therapy virus. ♦



John Wagner, MD, asks questions of the presenters in the Novel Therapies section of the Scientific Symposium.



Arleen Auerbach, PhD and Farid Boulad, MD at the Fanconi Anemia Scientific Symposium.

Results of Transplants at Memorial Sloan-Kettering

Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center, New York, reported on nine FA hematopoietic stem cell transplants performed at his center between May 1998 and May 2002. Two patients had aplastic anemia, six had myelodysplastic syndrome, and one acute myelogenous leukemia at the time of transplant. Seven patients were heavily transfused, and seven had received treatment with oxymetholone prior to transplantation. Four patients underwent related mismatched donor transplants with respective matching at 4/6(7/10), 4/6(8/10), 5/6(8/10) and 5/6(9/10) HLA-antigens. Five patients underwent unrelated donor transplants with respective matching at 5/6(7/10), 5/6(8/10), 5/6(8/10), 5/6(9/10) and 6/6(10/10) HLA-antigens.

The preparatory regimen included single dose total body irradiation, fludarabine, and cyclophosphamide. Seven patients received peripheral blood stem cells, and two received bone marrow; all were T-cell depleted.

All 9 patients engrafted. With a median follow-up of 18 months, 7 of 9 are alive and 6 of 9 are alive disease-free. Two patients with a significant history of infection died of pulmonary infection. One patient relapsed with MDS 8 months post transplant. This patient is presently in remission, 3 months following a second transplant after receiving high dose busulfan and fludarabine.

All patients experienced rapid engraftment, early immune reconstitution, and no or minimal GVHD. Given the severity of disease prior to transplant and the degree of donor mismatch, these results are extremely promising. ♦

Transplant Results from Germany

Wolfram Ebell, MD, of Humboldt University, Berlin, stated that there are 149 FA patients in the German registry. Since the 1980s, 84 German patients have received stem cell transplants.

Ebell presented data on 20 patients recently transplanted in Germany. For specific details the reader can request the abstract of this presentation via the enclosed form. Ebell does not use irradiation, but rather a protocol consisting of fludarabine, busulfan (for most patients), and pre/post immunosuppression. He does not T-cell deplete marrow or peripheral blood. Thirteen of these 20 patients, or approximately 60%, survive. Ebell noted several trends:

- Patients with aplastic anemia only did better than patients with myelodysplasia (MDS). Patients with frank leukemia had the poorest survival rate.
- Younger patients (0-10) did better than older patients (11-20).
- Patients given bone marrow did better than those receiving peripheral blood stem cells.
- Patients without prior androgen usage did better than those with prior androgen usage.
- Abnormal clones alone (in the absence of progression to MDS or AML) do not predict a poorer outcome.
- Patients with a subtle clonal abnormality on chromosome 3 do poorly without a transplant, suggesting that these patients might be good candidates for immediate stem cell transplants. (See article on page 3 entitled "Clone with Subtle Abnormality on Chromosome 3 Predicts MDS, AML in FA patients.") ♦



Wolfram Ebell, MD

Transplant Outcomes in Minnesota

John Wagner, MD, University of Minnesota Medical School, Minneapolis, reviewed recent transplant outcomes at his center. Just three years ago, only 18% of FA patients survived unrelated donor transplants. Patients experienced high levels of toxicity from the preparatory regimen, graft rejection, graft-versus-host disease (GVHD), and opportunistic infection. Today, many of these problems have been overcome and outcomes have improved dramatically. The probability of survival in standard risk patients is 100% for FA patients with an HLA identical donor (N=7), and 81% for FA patients with a matched unrelated donor (N=25).

However, patients with one or more high risk features have a statistically lower probability of survival. Factors associated with survival are younger age (patients 18 or younger do better than older patients); absence of leukemic blasts; HLA matched marrow or HLA 0-1 antigen mismatched umbilical cord blood; and absence of systemic infection. High risk patients have a 33% probability of survival (N=11).



John Wagner, MD

As a result of these findings, Wagner recommends that standard risk patients should be considered for transplant with the onset of marrow failure and prior to administration of therapies such as androgens and transfusions. High risk patients, however, should delay transplant and consider options such as androgen therapy. Other approaches are being explored for these patients.

Infection remains the primary cause of death. Wagner noted that 18% of high risk patients developed an aspergillus fungal infection, compared to 5% of standard risk patients. ♦

Cincinnati Modifies Protocol for Alternate Donor Transplants

Richard Harris, Children's Hospital Medical School, Cincinnati, Ohio, described a new trial using T-cell depleted peripheral blood progenitor cells (PBPC) from unrelated or related mismatched donors, in an effort to decrease graft-versus-host disease (GVHD). Harris reported on eight FA patients transplanted with this protocol. The preparatory regimen included total body irradiation, cyclophosphamide (Cytoxan), ATGAM, and fludarabine. Four patients had a major HLA-A or -B mismatch donor, while four were completely matched. Six were heavily transfused; three had been on androgens.

Engraftment was rapid in all patients. Five remained engrafted. However, three experienced major engraftment problems. One patient relapsed with myelodysplasia, was re-transplanted, and died of aspergillus fungal infection. A second was re-transplanted, again lost the graft, and is transfusion dependent. A third received donor lymphocyte infusions and is presently 100% engrafted.

Harris concludes that heavily T-cell depleted PBPC from alternative donors results in a very low risk of GVHD in FA patients. Long-term engraftment is a major problem. Harris has modified this protocol to increase the dose of cyclophosphamide and fludarabine, in the hope of preventing graft failure. ♦



L to R: Wolfram Ebell, MD, Farid Boulad, MD, Eliane Gluckman, MD, Richard Harris, MD, and John Wagner, MD, respond to audience questions during the Bone Marrow Transplantation session of the Scientific Symposium.

Fanconi Anemia Research Fund Honors Researchers

Five exceptional researchers were honored for their work on FA during the 14th Annual Scientific Symposium. Dave Frohnmayer, vice-president of the Board of Directors of the FA Research Fund, made the awards on behalf of the Fund during the Presenters' Dinner.



Dave Frohnmayer and Eliane Gluckman, MD

Eliane Gluckman, MD, Hôpital St. Louis, Paris, received the *Lifetime Achievement Award*. Frohnmayer highlighted the exceptional contribution that Gluckman has made to the field of FA research and to the clinical care of FA patients. The Board of Directors noted her exceptional work as a pioneer in cord blood transplants, in FA bone marrow transplants, and in FA research in Europe. Frohnmayer cited Gluckman's leadership and outreach to the FA medical and scientific community regarding FA solid tumors as a catalyst for the FA and Cancer Conference hosted by the Fund in early 2002.

*We are what we repeatedly do.
Excellence, then, is not an act,
but a habit.*

-Aristotle



Dave Frohnmayer and John Wagner, MD

John Wagner, MD, University of Minnesota, Minneapolis, received the first *Pioneer Award for Therapeutic Advancement* bestowed by the Fund. The Board of Directors acknowledged Wagner's outstanding contribution to the science relating to stem cell transplantation of FA patients. Frohnmayer noted that Wagner's pioneering work, including the use of fludarabine, has increased dramatically the odds of FA patients surviving a transplant, especially from an unrelated donor. Frohnmayer also acknowledged Wagner's exceptional leadership in pushing FA science forward.



Arleen Auerbach, PhD

Arleen Auerbach, PhD, The Rockefeller University, New York, received the *Lifetime Achievement Award*. Frohnmayer acknowledged the exceptional contribution that Auerbach has made to the field of FA research by establishing the premier FA diagnostic center in the world at The Rockefeller University. Frohnmayer also expressed the Board's profound appreciation for Auerbach's tireless dedication to FA research and for her compassion in helping countless families understand the genetics of the disorder.

Fanconi Anemia Research Fund Honors Researchers

continued from previous page

To conclude the ceremonies, Frohnmayer bestowed the *Award of Merit*, the highest award given by the Fund, on two outstanding researchers, **Markus Grompe, MD**, Oregon Health & Science University, Portland, and **Alan D'Andrea, MD**, Dana-Farber Cancer Institute, Boston. Only two other researchers, Manuel Buchwald, PhD, Sick Children's Hospital, Toronto, and Hans Joenje, PhD, Free University, Amsterdam, have received this honor since the inception of the Fund in 1989.

Frohnmayer acknowledged the exceptional contribution that Grompe has made to the field of FA research through the discovery and

elucidation of *FANCD2*. Because of Grompe's accomplishment, FA has been vaulted out of the realm of an orphan disease into a much broader and faster-paced scientific arena. Frohnmayer expressed profound appreciation for Grompe's dedication and long-term commitment to FA patients and FA research, from establishing the FA Cell Repository at Oregon Health & Science University to continuing innovative research.

In presenting the *Award of Merit* to D'Andrea, Frohnmayer acknowledged the remarkable contribution that D'Andrea has made to the field of FA research by unlocking the secrets of the FA protein pathway, and through the discovery that the *BRCA2* gene is identical to *FANCD1*. Frohnmayer expressed the gratitude of the FA Research Fund that D'Andrea has consistently been



Alan D'Andrea, MD and Markus Grompe, MD

a leader in FA research, setting the pace, taking risks, and pushing this science forward. ♦

Standards for Clinical Care Consensus Conference

The FA Research Fund is sponsoring a Standards for Clinical Care Consensus Conference at the O'Hare Hilton Hotel in Chicago from March 6 - 8, 2003. The purpose of the workshop is to develop an updated consensus regarding clinical care for FA patients.

Eva Guinan, MD, Dana-Farber Cancer Institute, who moderated the first Consensus Conference in 1998, will moderate this conference as well. The physicians in attendance will develop consensus regarding optimal standards of care for FA patients in their areas of expertise. The FA Research Fund will publish the results in an updated edition of the 1999 *Standards for Clinical Care* handbook.

The 1999 edition will be expanded by the inclusion of chapters

entitled Hand and Arm Anomalies (chaired by Scott Kozin, MD, Shriners' Hospital, Philadelphia); Diagnosis and Treatment of Gastrointestinal Abnormalities (chaired by Sarah Jane Schwarzenberg, MD, University of Minnesota); Diagnosis and Treatment of Gynecological Abnormalities (chaired by Pamela Stratton, MD, National Institutes of Health); Experimental Therapies (chaired by Bruce Blazar, MD, University of Minnesota); and Squamous Cell Carcinoma of the Head and Neck (chaired by Bhuvanesh Singh, MD, Memorial Sloan-Kettering Cancer Center).

The 1999 chapters that will be updated and the chairs of those sessions include Diagnostic Work-Up (Blanche Alter, MD, MPH, National Cancer Institute); Treatment of

Hematologic Abnormalities (Akiko Shimamura, MD, Dana-Farber Cancer Institute); Diagnosis and Treatment of Growth Failure and Endocrinopathies (Michael P. Wajnrajch, MD, Cornell Medical Center); Matched Sibling Donor Hematopoietic Cell Transplantation (Richard Harris, MD, Cincinnati Children's Hospital); and Alternate Donor Hematopoietic Cell Transplantation (John Wagner, MD, University of Minnesota). ♦

Risks of Radiation Therapy in FA Cancer Patients

Blanche Alter's article on "Radiosensitivity in Fanconi's anemia patients" was published in *Radiology and Oncology* (62:345-347, 2002). Alter describes literature reports of 14 FA patients with squamous cell carcinoma who were given radiation therapy. Three of these patients had received a bone marrow transplant; eleven had not. Possible toxicity was reported in six of these 14 patients: 1/1 with vaginal cancer, 4/10 with head and neck or esophageal cancer, and 1/3 with oral cancer following bone marrow transplant.

Most of the patients whose cancers were treated with radiation therapy died shortly thereafter (at 3 months for the patient with vaginal cancer, 3-12 months for eight of the untransplanted ten patients with head and neck or esophageal cancer, and 3-6 months for all three of the post-BMT oral cancer patients). The only survivors were two untransplanted patients with oral cancer who were alive at 3 and 10 months following radiation therapy.



Blanche Alter, MD, MPH

Alter notes "although radiation therapy may be blamed for the outcomes, the poor survival may be a reflection of the advanced stage of the tumors for which definitive surgery was inadequate and radiation was required."

Alter concludes that it would appear prudent to use surgical interventions as much as possible. Her article stressed the importance of using careful surveillance in an effort to detect precancerous lesions. ♦

Mutations of *FANCA* Found in Non-FA Patients with Aplastic Anemia or Myelodysplasia

Johnson Liu, Mount Sinai Hospital, New York, reported that several non-FA patients suffering from aplastic anemia (AA) or myelodysplasia (MDS) had mutations in *FANCA*. His laboratory studied 80 non-FA patients with AA or MDS. Three of these patients had a disease mutation in *FANCA*. These are either inherited

or acquired mutations. These findings suggest that FA carriers might be at risk for the development of AA or MDS, following a second genetic "hit" or an environmental toxic exposure. ♦

Post-transplant Complications in France

continued from page 2

Eighty-seven percent of the FA patients had acute GVHD, and most of these patients went on to develop chronic GVHD. Sixty-two percent developed Grade II-IV GVHD.

Although FA and non-FA patients had a similar 10-year outcome, FA patients resistant to cortisone therapy experienced an additional cluster of lethal events beginning at 5 years post-transplant. This late mortality, restricted to FA patients, was closely related to head and neck carcinomas. These cancers did not appear in the first five years post-transplant, but the cumulative incidence of cancer was 20% in transplanted FA patients after ten years, and 53% after 15 years. Gluckman concludes that the impact of acute GVHD on survival is not limited to the early post-transplant period and is a major risk factor for head and neck cancer. Prevention of GVHD is crucial. (Eds. Note: Recent transplant protocols have greatly reduced the incidence of GVHD in FA transplants.) ♦

Editors' Note and Disclaimer

Statements and opinions expressed in this newsletter are those of the authors and not necessarily those of the editors or the Fanconi Anemia Research Fund. Information provided in this newsletter about medications, treatments or products should not be construed as medical instruction or scientific endorsement. Always consult your physician before taking any action based on this information.

Chris Byrd: Life After Transplant

It has been three years since my unrelated bone marrow transplant, and I am very proud to say that my life has never been so normal. While I have struggled with what some have called chronic graft-versus-host disease, my platelets, hemoglobin, and white count have been perfectly normal since I came home to Orlando, Florida from Minneapolis in February of 2000. Problems that I have faced since transplant have included chronic lung and sinus infections as well as problems gaining and maintaining weight. Although these problems are serious since my immune system is still getting stronger, the majority of the problems have been treated with normal medical practices without the need for immune suppressants and/or

steroids. The chronic infections have not been a problem since November 2002, when I received my first flu shot since my transplant. Since then I have been perfectly healthy, and I haven't even experienced normal cold symptoms.

I am currently a junior at the University of Central Florida pursuing a double degree in Legal Studies and International Political Science. I enjoy staying active in my university community: I am currently the vice-president of the United Nations Association of UCF, the Treasurer for Phi Alpha Delta Law Fraternity International, and a founding father of Sigma Nu Fraternity International. I have been working for Sears Heating and Cooling for the past two years, and I am looking forward to establishing an

internship with a local law firm this summer. I enjoy scuba diving and the beach, although I have to wear T-shirts and a ton of sunscreen to protect my sensitive skin from the sun due to full body radiation.

My advice to anyone considering an unrelated bone marrow transplant is to keep a positive attitude and to look forward to all of the new and exciting opportunities that wait in a life free from the blood-related aspects of Fanconi anemia. I would like to encourage anyone who has any questions or would like to know about my life and experiences to contact me, preferably by e-mail at CTB90@aol.com. As you can see, I am usually very busy but I will do my best to respond as soon as possible. Stay positive and God bless. ♦



Will Lackey

“Where There’s a WILL, There’s a Way”

by Kayla Lackey, Charlotte, NC, www.willpowerfund.org

William Tyler Lackey—“Will” to all who know him—is a 4-year-old little boy who was diagnosed with FA on September 25, 2002. Like everyone else, we have a story, a story that speaks of fear, anger, hope and love.

Our story begins with the week prior to September 25th when Will was seen by a pediatric hematologist to whom we were referred after we discovered that Will’s platelets were a little low at 115,000. That was the first time I’d ever heard of Fanconi anemia. I was forewarned to prepare myself for the test results to come back positive and was told that Will “fit the profile.” Results were due to

be back in two weeks.

The next week was spent learning. I read everything I could find on Fanconi anemia. I surfed the web until the wee hours of the morning. I was determined to “be ready.” I e-mailed Suzanne at the FARF and asked for access to the e-group, a request that was denied at the time, because we were not yet diagnosed. We exchanged e-mail several times during that week, and she was wonderful at guiding me in the right direction, even though I was still an outsider—an outsider who hoped she would never be accepted.

continued on page 23

Fighting FA

by Erik,
e-hansse@online.no

“We think Johan (then age 11) has leukemia. He should go to a hospital in another city in Norway next week.” So said the voice in a telephone call I received at work on a Friday in 1995. That call became the local 9/11 in our family and was the start of a long journey. Some days later, the diagnosis was rescinded, but the doctor did not know what caused Johan’s low haemoglobin level of 10. Johan was later given the diagnosis of aplastic anemia.

FA is really a dramatic disease. For parents getting the diagnosis for their newborn baby, there is no time to rest. It becomes an uphill fight from day one. How these parents work for their children! Anyone who hasn’t experienced it will never know. Our situation was different. The first 6-7 years of Johan’s childhood were lovely, and my wife Turid, our daughter Ragnhild, Johan, and I had a very fine time together. Then our son became more and more “lazy” when we were exercising together. As good parents, we fought much with Johan over that topic. Had we only known about his low haemoglobin (hgb) level we could have avoided lots of tears and bad parental feelings later!

The next years became a really hard time. Johan’s hgb fell to 6.0 in 2000, and he required bi-weekly blood transfusions. My task was to tell my teenager every quarter that the hgb had dropped slightly, and then the question came: “What will happen if this continues?” My response that the best doctors in Norway were involved was countered by “This is what scares me. I would be calmer if it were the doctor on the corner who is treating me.”

Our “problem” was that no blood



Johan skiing in Norway, Easter 2002

sample was tested for FA. In all these years we had to see doctors, motivate Johan, discuss with the frustrated teacher who claimed that Johan was difficult and unmotivated at school (although his situation was known), calm the grandparents, and work with our own feelings. An overwhelming agenda. Personally, I felt it very difficult to combine intense business work with phone calls to doctors discussing vital issues for my son. In hindsight, I see that our family had a really hard time in all these years. But apparently, this became a “project” for my wife and myself, and it brought us closer together. On the other hand, it did also put tension into our relationship because the maturing of our own feelings was not aligned. Being a manager, I had to be open at work about my situation, while Turid working at home needed more time to work with her feelings. I also learned that we as parents needed to absorb the bad news ourselves some days before we could communicate it to Johan and others.

In our situation we struggled with much uncertainty because we didn’t know the enemy: what was the

disease? We discussed for hours whether it was the food, the house, the air, the previous medicine, the...?? We arrived, of course, at the same conclusion every time—nobody had a clue.

After “waiting” for five years, things started to happen in 2000. At Easter, a blood sample was sent to London to test for FA. Positive! Again, I got the message by phone on a Friday. I searched the Internet immediately and found the FA handbook and much other information at www.fanconi.org. During the weekend I read all the information and became really scared. The doctor didn’t know much about FA and couldn’t tell us much. As we finally found the diagnosis, we hoped for a treatment, but the hope was turned into horror. It was hard to tell a 16-year-old boy about FA. And how much and when should you tell? After a couple of months, the haematologist told us that no treatment was available and Johan had to rely on blood transfusions in the future.

Every family experiencing FA goes through lots of dramas and

continued on page 13

Fighting FA

continued from previous page

dilemmas. Johan's objective during his teenage years was to "be just a normal kid." Nobody should know that he had FA. As parents, however, we had to decide who needed to know about Johan's situation and what should be told when.

The turning point came in the summer 2000. I had a cold, had to stay in-house, and surfed the Internet again. Then I read about the upcoming Family Meeting at Lake Geneva. Immediately I decided to join, although I found it crazy to travel from Norway to Wisconsin for the weekend. I overcame those obstructions and travelled. I had no expectations, but I felt that the camp was the last effort to be tried. How the hopes for the future changed during my stay! When I came there, I met other parents of FA children for the first time. I learned a lot about the disease and oxymetholone (Oxy) treatment. It was really an emotional chaos. I met so many nice parents, kids, doctors and FARF staff. We are not used to praying for each other in Norway, but it was good to know that many people were praying for our family in the US!

Things happened fast when I came back to Norway. Johan was put on Oxy in October. It worked very well, and he had his last blood transfusion in November 2000. Johan has today a normal hgb level and is by all means very active. His motivation and interest for schoolwork have improved significantly. Last Christmas, Johan and I had a real speed skating contest over a quarter mile at a lake. I was beaten, but both the winner and the loser were ecstatic!

To sum up, every FA family could write books describing their hopes, sorrow and anger. Living this "roller

Mark Your Calendars: Regional Meeting in Minneapolis

The Fanconi Anemia Research Fund is sponsoring a regional meeting in Minneapolis, Minnesota on Saturday, May 17, 2003. John Wagner, MD, and Margaret MacMillan, MD, from the Blood and Marrow Transplant Program at the University of Minnesota Medical School, have arranged an outstanding program for FA parents and FA adults.

The preliminary program will address the basic understanding of Fanconi anemia, as well as novel treatment strategies. The speakers and their topics will include:

Margaret MacMillan, MD: Blood and Marrow Transplantation for FA

Betsy A. Hirsch, PhD: Interpreting the Cytogenetic Report

Phuong Nguyen, MD: Marrow Aspirate Findings in FA

Frank Ondrey, MD: Head and Neck Cancer in FA

Sarah Jane Schwarzenberg, MD: Feeding Intolerance and Abdominal Problems in FA

Anna Petryk, MD: Diabetes and Hormonal Problems in FA

John Wagner, MD: Preimplantation Genetic Diagnosis to Prevent Disease and Select for HLA

Catherine Verfaillie, MD: Future Applications of Adult Stem Cell and Gene Therapy

In addition to these presentations, the day will include a reception at the Science Museum of Minnesota, workshops with cytogenetics and hematology, tours of the local housing facilities used by families during treatment, and tours of the Fairview University Medical Center Bone Marrow Transplant Unit and Bone Marrow Transplant Clinic. Depending on the number of parents who will be able to arrive early on Friday, May 16, 2003, Dr. Wagner has offered to arrange a possible excursion to the National Marrow Donor Program.

Regardless of whether you live in this particular geographic region, we hope you will join us at this meeting. It is open to all FA parents and adult FA patients. The FA Research Fund has a scholarship program to which you can apply if you need financial assistance to attend. If you are interested in attending or have questions about the meeting, please contact the Fund office by April 16 at info@fanconi.org, by fax at 1-541-687-0548 or by phone at 1-800-828-4891. ♦

coaster life" is much more intense than any "normal" family could ever understand. It is good therapy for parents to learn more about FA. The worldwide network of skilled people is vital whenever you need it, especially for those of us living in small

countries with only a handful of FA patients. The FA camp is "a must" for all parents to establish the network and get updated on FA research.

Enjoy the good moments, gain energy, and fight FA! ♦

In Memory of Alex Eddy

by Sharon Swanson

Woo Hoo!! That was the send-off we gave Alex on the day he departed this world. It was one of Alex's favorite expressions (being the diehard *Simpson's* fan that he was). Saying goodbye to Alex was hard, yet joyous. He is now free of a body that limited him, free of invasive tubes, free of pain. He can now be more "real" than any of us can imagine and can only hope for.

Alex was a unique child from the day he was born, December 22, 1987. The 22nd, the day after the Winter Solstice, is the day light begins returning to the earth. So, I called him my "Child of the Light," and it was true: he always carried a light within. Adults in particular were drawn to Alex and his inner "light." Alex was quiet and gentle in nature, caring and affectionate. Everything Alex undertook, he did with a passion. Whether he was the best or even good at what he did was not as important as experiencing the "activity" to the fullest. He loved many things: baseball, fishing, nature, playing card games (*Pokemon* and *Magic the Gathering*), collecting anything and everything, playing the tenor sax, and doing anything that allowed him to be part of a group, whether it was being on a team, cub scouts, or attending a family gathering. Alex was a disciplined student who excelled in school, but hated busywork. He had dreams of one day attending a college like Harvard.

Alex was not diagnosed with FA until he was 6 years old. He had always been extremely thin as a child, had some *café-au-lait* spots, and slightly "different-looking" thumbs, but no other physical anomalies. A blood test taken when he had the flu led to his diagnosis. From that day

forward our world came crashing down around us, but over time we learned to live with the disease. In fact, while Alex was on oxymetholone, our life was almost "normal." The disease was more of a nuisance, with only hints of its life-threatening qualities lurking in the background.

In October 2001, we traveled to Fairview University Medical Center (FUMC) in Minneapolis, met with Dr. MacMillan, and had Alex's annual bone marrow biopsy. The biopsy showed there were very few cells left in Alex's bone marrow and that, as a result, oxymetholone would not be effective much longer. Dr. MacMillan recommended that we proceed to transplant, given the success rate of the latest protocol and since a matched unrelated donor had already been identified. After much research and soul searching, we determined that the transplant was Alex's best chance for securing a longer life. We scheduled his bone marrow transplant for June 2002, allowing Alex to finish the 8th grade, get his braces off and, most important to him, finish his last season of baseball.

We drove from Shreveport, Louisiana and arrived in Minneapolis on June 8; the transplant date was June 25. While it was tough, Alex did quite well through transplant and was discharged on day +25. But that's when Alex's luck ran out. Alex was admitted to the hospital 7 more times in the following months for repeated fevers, Grade 2 graft-versus-host disease, changes to his medications and, finally, for adenovirus. During our last admission, Alex suffered seizures, followed by a loss of ability to oxygenate, which required him to be put on a ventilator. He also developed kidney failure, requiring



Alex Eddy

peritoneal dialysis. Six long weeks later, with his lungs having further deteriorated, Alex was removed from ventilator support. He quietly passed away on December 13, just 9 days short of his 15th birthday. What I know is that the doctors and nurses at FUMC all fought hard for Alex, as did we, but in the end we were doing more to him than for him, and so we set him free.

We are so grateful to Alex for the time he blessed our life and the things he taught us. He's the one who showed us that this disease did not define who he was. He approached it with a Zen-like attitude: never giving in to it, yet never fighting it. He taught us how to be present in the moment, something he practiced daily. During transplant he even mentioned that he never worried about what tomorrow would be like, that he couldn't do anything about it anyway, so he might as well just stay focused on today. Alex was happy and good-natured and laughed easily, especially when watching inane movies (*Dumb and Dumber*, *In Search of the Holy Grail*). He was loyal and loving with a strong sense

continued on page 17

Lessons in Life

adapted by Joanne Cacciatore for bereaved parents

I've learned people don't care how much you know until they know that you care.

I've learned to avoid judging others so I think what I say, not say what I think.

I've learned that it's taking me a long time to become the person I want to be.

I've learned that a child who has lived just moments can be your greatest teacher.

I've learned that you can keep going long after you think you can't.

I've learned that we are responsible for what we do, no matter how we feel.

I've learned that heroes are people who do what needs to be done, regardless of their personal circumstances.

I've learned that learning to forgive takes a lot of practice.

I've learned that friends can become strangers, and strangers can become friends.

I've learned that ignorance isn't an excuse for the lack of compassion.

I've learned that ignorance begets ignorance.

I've learned that some people will never, ever 'get it.'

I've learned some people love you dearly, but just don't know how to show it.

I've learned that true love continues to grow, even over the longest distance.

I've learned that the community of sorrow is the strongest of all.

I've learned that it isn't always enough to be forgiven by others. Sometimes you have to learn to forgive yourself.

I've learned that no matter how bad your heart is broken, the world doesn't stop for your grief.

I've learned that your life can be changed in a matter of minutes.

I've learned that writing, as well as talking, can ease emotional pains.

I've learned to trust myself.

I've learned that the people you care most about in life are taken from you too soon.

I've learned that you should always leave loved ones with loving words. It may be the last time you see them.

I've learned that love isn't measured by the amount of time you have with someone.

I've learned that some sorrow is so deep that it has no words. But so is love.

What has your child taught you?



In Loving Memory

Jeremy Brand
5/30/95 - 10/16/02

Alex Eddy
12/22/87 - 12/13/02

Jordan Farris
1/16/85 - 9/20/02

Carlotta Frontani
7/8/92 - 11/4/02

Henry Strongin Goldberg
10/25/95 - 12/11/02

Clifton Langhorne
9/13/75 - 1/13/02

Jason Masters
5/5/95 - 1/18/03

Haley Race
7/20/00 - 11/13/02

Erica Seiford
9/4/85 - 1/5/03

Heavenly Sheldon
4/22/99 - 8/30/02

Tian Sheldon
7/28/95 - 11/26/02

Guillermina Villegas
7/26/00 - 11/8/02

With Love, From Mom

This eulogy was delivered by Laurie Strongin Goldberg for her son, Henry

On October 25, 1995, Henry made me a mom and a better person. Before he could even smile or talk, Henry taught me what was important and what just didn't matter at all; and he taught me to savor each moment, to love, to laugh and to dwell in possibility.

And together as a family we have done just that, packing more smile and laugh-producing times together in seven years than many do in a lifetime. We have lived and loved as though we could one day lose Henry, while simultaneously pushing love and science to their limit to ensure that we would have him in our lives forever. Henry has driven a tractor, fallen in love, danced with 10 women at one time, and laughed until he fell over. Just two days ago, Henry finally got the biggest, baddest Swiss Army knife, which he held onto 'til the very end. We have lived every day with Henry to its fullest. We have had ice cream for dinner; transitioned from the hospital to running a lemonade stand in a matter of minutes; gone to Cactus Cantina seven nights a week; and acquired every single *Pokemon* figure made. At last count we had 188. He met President Clinton, Cal Ripken, Batman, the entire Minnesota Twins, and more significantly, they got to meet him. We did all those things because at that moment in time we could and because, though we always hoped things would get better, we knew enough to go when the going was good. Just in case.

As I'm sure all of you know, Henry just made everything better. He was wise well beyond his years, and he was so much fun. It's almost as if all the good things in life were created with Henry in mind. No one

had greater appreciation for Disney-world, Funland, Sullivans or any of the other fun things in life than Henry. He was a great lover of music and could sing "Brick House" and dance with the best of them. I will cherish my memories of Allen and Henry dancing together in our home.

It is such a privilege to be Henry's mother, and I am thankful every day that Allen and I found one another and created such a wonderful, love-filled family.

It's no surprise that Henry has had an ongoing fascination with superheroes. He put on a Batman costume for Halloween when he was two and didn't take it off until we left for Minnesota two and one-half years later. Henry didn't need it anymore since he had received sufficient training and, at that point, he had achieved superhero status in his own right. As my brother Andrew said, "Batman should wear a Henry shirt."

My dad used to tell me that a day without me was a day without sunshine. Now I know what he was talking about. Sweetie, you are everything enjoyable in life. You are a lemonade stand on a hot summer day. You are the first piece in a box of Godiva chocolate; kite flying on the beach; the final encore at a Springsteen show; s'mores at a campfire; a *piñata* at a birthday party; fireworks on the Fourth of July; a ride on a Ferris wheel; the glow of candlelight during a thunder storm; finding a sand dollar on the beach; penny candy; class outside; the last ski run of the day; meeting your child for the first time. The loss of you drenches my heart in sorrow.

One nightfall, the evening before we left for Henry's transplant, Henry



Henry Strongin Goldberg

and Jack were taken by the magic of fireflies and started to run around our yard, catching one after another. Each catch was a victory and was met with curiosity and excitement. Some of those bugs sacrificed their lives at the clumsy, but curious, hands of these three- and four-year-old boys.

I watched and let myself feel what it's like to be a kid, filled with curiosity and wonder about the world. At some point I noticed that Henry had disappeared, so I went inside to see what had become of him. I went upstairs and slowly opened his bedroom door and heard a whisper telling me to come in quick and to shut the door. I found Henry lying on his back watching the fireflies, which he had brought upstairs one-by-one and set free, light up his room.

I'm not sure how Cactus Cantina or Max's Ice Cream will survive without you, and I sure wish that Daddy, Jack, Joe and I didn't have to. I miss you so, so much already, honey. Our job now is to ensure that everything is better because of you. So, like you, we will draw our swords, but don't expect the same resiliency. You set the bar high. Give us a while, and we will make you proud, my son.

So today we say farewell to your body, and every day from now on we will cherish your soul and spirit, for they live within us now. Goodbye, Henry. ♦

Identical Twins Grow Up with FA

by Kari Doctor

My identical twin sister, Alissa, and I were diagnosed with Fanconi anemia 26 years ago at the age of 3 months. After a brief explanation, my parents were told that if we developed the anemia, the only possibility of a “cure” was a very experimental bone marrow transplant and that we would probably not live past the age of 10.

Alissa was born without thumbs and a shorter left arm, which is missing the radius bone. She had surgeries to rotate, shorten and move her index fingers into position as thumbs. Alissa has incredible dexterity and loves to crochet, make jewelry, and quilt. She also had several surgeries to straighten her left arm and stabilize her wrist. The Shriners’ doctors investigated lengthening her arm, but found that it would not be feasible. I, Kari, had surgery at the age of 15 months to correct a renal problem. As a result of scar tissue blockage in the ureter tube, I lost that kidney.

We underwent blood counts every 3-6 months as we were growing up, which were always within the normal range. When we were 13, the doctor called and told our mother that she no longer needed to bring us in because everything looked like it was going to be fine. That was a welcome message, but not a surprise. When we were three years old, God gave our mother the assurance and peace that we were going to be okay. We were not aware of the seriousness of our diagnosis until we were teenagers.

Growing up was much more of a challenge for Alissa because kids teased her because of her birth



Kari Doctor and her twin sister Alissa Burk

defects. But I feel God has blessed our lives and used our situations to develop our character for His purposes. Alissa has an incredible empathy and love for children. She has worked with children for 9 years now, volunteered at a handicapped mission in Mexico for 3 months, and earned her degree in early childhood education. I have my own business as a graphic artist.

Neither of us has ever developed any blood-related problems associated with Fanconi anemia. However, my husband and I sought genetic counseling last year before trying to start a family and have since gone through testing of skin (fibroblast) samples that has confirmed the diagnosis and, also, blood samples that show that our blood has been “cured.” Those tests were performed on Alissa with the same results. We feel God has given us a promise in *Jeremiah 29:11*, “‘For I know the plans I have for you,’ declares the Lord, ‘plans for welfare and not for calamity to give you a future and a hope.’” ♦

Alex Eddy

continued from page 14

of right and wrong, particularly when it came to how you treat others. He often became indignant at both friends and adults for their behavior. He never tried to be popular, almost shunning that, wanting to be stubbornly true to who he was.

I have no regrets about our choice to go to transplant or the care we received at FUMC. People facing a similar decision should feel confident that they would be in the best of hands. During my stay, I saw many FA children (and even one adult) go through transplant and return home. I maintained a web page as we went through this experience, which was extremely therapeutic. More important, it opened us to an extended community of family and friends, both old and new (which included many of you) who joined us and supported us on this journey. This community transformed this very difficult experience into one of beauty and love; into one of many gifts, not just of loss; into a future of hope, rather than despair. For that, I humbly thank you. ♦

Elma Dueck's Journey with Fanconi Anemia

by Kenneth Dueck, her husband

On December 23, 1970, Elma was born in a remote region in Mexico, hours from the nearest paved roads. After migrating to the USA (Oklahoma) in 1979, she worked on her family's dairy farm, milking, and gardening.

Soon after we married in 1991, one of her sisters had complications during pregnancy (Elma had 6 sisters and 4 brothers). After CBCs on other siblings, it was discovered that several others had low blood counts or odd platelets. Elma was one of them.

In 1992 Elma and I pursued the issue some and had a bone marrow biopsy. While results were not normal, doctors didn't pinpoint the problem as Fanconi anemia.

Our oldest daughter was born by C-section in 1993. In 1996 our son was born naturally. In 1998, while pregnant with our third child, Elma's blood counts dropped lower, and she had to have a blood transfusion.

After a natural delivery, her counts did fine again. About a year later, in October 1999, she discovered that her blood counts had dropped significantly. After that, she had to have 3 units of blood approximately every 5 weeks. Elma's blood work was sent to The Rockefeller University in New York in January 2000. The result came back positive for FA.

A bone marrow transplant was recommended, but we weren't at all ready for it, as Elma's double cousin's child had a bone marrow transplant for FA in Canada and did not survive. Eventually it seemed that her only choice was a bone marrow transplant, as oxymetholone didn't do much for her.

We chose Minneapolis as the transplant center. They seemed to

have the most experience with adult FA bone marrow transplants. Bone marrow transplant was urged as soon as possible, but they needed 1/5 of a million dollars up front. That seemed an impossible amount.

But God had a way. Our church pitched in tremendously and, in a couple of months time, we had sufficient funds to go ahead. God also provided a 6/6 match in one of Elma's sisters who doesn't have FA. Three of her sisters and one brother (two of whom are now deceased) also were diagnosed with FA.

On January 4, 2002 we arrived in Minneapolis for the work-up and transplant. Our 3 children and my sister were with us. The children came to visit their mom practically every day in the hospital. The doctor recited a long list of complications

that could happen, but nobody got them all (Elma got a good bit of them though!). On January 24, Elma went into the hospital where she received four days of chemotherapy and one of radiation. The transplant was on January 31, 2002. On February 10, the white blood cells started to come in. By the 20th, she was released from the hospital.

Except for a seizure soon after transplant, things went pretty much as expected with mouth sores, not eating and hair loss. On day +21 the bone marrow biopsy showed 100% donor, which has remained that way. Then the GVHD (graft-versus-host disease) set in! Itchy rash from head to foot (she was reminded of Job in the *Bible*), plus diarrhea and nausea, which responded well to steroids.

continued on page 19



Elma Dueck (second row on right), her siblings, and her parents

Elma Dueck's Journey with Fanconi Anemia

continued from previous page

But, the itch didn't, so she had to have a course of ATG. It took 3 courses of ATG to subdue the GVHD. In the meantime, CMV (cytomegalovirus) flared up.

In early May Elma was hospitalized to treat the CMV. So, on Day +100 she was in the hospital instead of on the way home. While in the hospital, we discovered that she had aspergillus fungus in her lung, for which she is still taking medicine. Then her mouth and esophagus got so sore, she could hardly swallow water. Finally, after about ten and one-half weeks in the hospital, Elma was released. Things seemed to be on the mend.

Soon we noticed that she was getting weaker, and the therapist set to work. However, Elma was then diagnosed with Guillain-Barré syndrome. When dealing with Guillain-Barré syndrome, more than therapy is



Elma Dueck with her three children

needed, so into the hospital she went. She came out three weeks later. She still couldn't turn on her side in bed by herself, but grew stronger steadily, if slowly. We returned home in January 2003. We were welcomed back by our very supportive church (after

2 months, they still show up almost every evening with a meal!).

Elma's older sister Frieda Martens (who had FA) got aplastic anemia, some severe infections, and passed away in December at age 42. Five weeks later her brother Larry Plett, who had FA and was sick with leukemia, died at age 37.

The transplant with its complications has been much more difficult than we anticipated. The bone marrow appears to be working, although there are a number of ongoing complications. God is faithful! He has given grace and strength as needed. Also, you realize how many friends you have and what they are worth in a time like this. The facilities, doctors, nurses and staff at Fairview University Medical Center were excellent! ♦

Fundraising Assistance

Did you know that 85 percent of the donations to the FA Research Fund are raised by FA families?

The staff of the Fund stands ready to assist you with your fundraising efforts. We'll help you write or edit your fundraising letter; photocopy it; provide the postage; and mail it from our office, using your mailing list. If you're going to hold a fundraising event, we'll provide similar help.

The FA Research Fund asks FA parents to make certain that any event they hold is covered by liability insurance. This insurance for a one-time event is often available through a family's homeowners insurance as a relatively inexpensive insurance rider. Please contact the Fund if you need assistance obtaining or paying for this required insurance.

When a donation is received, we'll send a letter of thanks from the Fund with a tax receipt, and we'll notify you that a donation has been made in your name. One request: Please ask your donors to write their donation check to the "Fanconi Anemia Research Fund."

Our sincere thanks go to all of you for your efforts to raise funds to combat this devastating disease.

FUNDRAISING

Getting Started with Fundraising

by Andrew & Jennifer Gough

Our daughter, Shannon, was diagnosed with FA two years ago. This year we sent out fundraising letters for the first time. We had thought about doing it last year, with a custom letter we would write and send out ourselves. However, life's normal time pressure and some concerns over asking friends and relatives for money resulted in the project never getting started.

This year we decided that having FA is far worse than any possible social embarrassment from asking for donations, so we decided if our daughter can live with FA, we can help raise money for research. The research sponsored over the past 14 years by FARF has already helped our family, and the Fund is currently sponsoring research that could help Shannon directly.

To make sure the project got done this year, we decided to take the Fund up on their standing offer to do the administrative work—the printing and mailing of the letters. We decided that it didn't matter that much exactly what the letter said as long as it covered the basics (what is FA and how the research supported by the Fund has helped), so we created a letter by slight modification to a template provided by the Fund. In the end, it is only important to give others the opportunity to donate, not exactly what is said. We prepared a mailing list of the addresses of our parents, other relatives, our friends, and friends of our parents. Once the letter and mailing list were ready, we e-mailed it to one of the employees at

the Fund, who prepared all the letters and had them mailed out in one day. So far the fund has received donations of several thousand dollars from our letter.

We urge you all to give the people you know the opportunity to donate by sending out fundraising letters. The Fund office staff is enthusiastic to help you. Any amount your letters raise will help expand the amount of research that can be funded—as there are more great research proposals than there are funds for them. ♦



Shannon Gough

FA Families Increase Fundraising Efforts

by Mary Ellen Eiler

I am pleased to report that many FA families stepped up to the plate during 2002 to raise money for FA research and to decrease the dependence of the Fund on the fundraising efforts of only one family, the Frohnmayers. While the FA Research Fund faced the same disheartening decrease in donations that affected other non-profit organizations due to the poor economy, we were heartened that donations decreased by only 18% from the previous year.

The excellent news is that while the Frohnmayers raised 54% of the total funds donated during 2002, the remaining FA families increased their percentage of funds raised from 31% in 2000, to 43% in 2001, to a whopping 46% in 2002! Clearly, the trend is in the right direction, and I'm extremely grateful for your efforts.

Even better was the news that, whereas 40 FA families raised \$1,000 or more in 2001, 53 families did so in 2002. That is a tremendous accomplishment, as we continue our urgent effort to assist the Frohnmayers in raising funds for a cure for FA.

Of the FA families in the United States, 118 made a donation or raised funds for FA research in 2002. If you have not yet participated in raising funds, we urge you to do so, as we all work together to beat this unrelenting and devastating disease.

Thanks to all who were active partners with the Fund in raising money for our critically urgent cause during 2002! ♦



Vicki and Andrew Athens, with Fabrizio, Antonino, and Marie DiMercurio at the Downriver Dash.

The Athens and DiMercurio Families Sponsor the Downriver Dash

FA parents Vicki and Andrew Anton-Athens and Marie and Antonino DiMercurio of Michigan sponsored the *Second Annual Downriver Dash* on September 14, 2002, to raise funds for FA research. The race, a 5K run/walk, also included a *Kids Dash*. Through registration fees for the run, this event raised \$7,000

in the last two years. The *Downriver Dash* is an occasion of fun and exercise for all, as well as a wonderful way to make a community aware of Fanconi anemia and to raise money for research. Thanks go to the Athens and DiMercurios for this excellent effort! ♦

Harley Raffle Raises Funds for FA Research

The Board of Directors of B Positive, a non-profit organization started by FA parents Mark and Dianne Pearl in Chesterfield, MO, donated \$15,000 to the FA Research Fund after a very successful raffle in their community. The Bourbeuse Valley Harley-Davidson dealer in Villa Ridge, Missouri, sold B Positive a Harley at cost, and the members of group then sold 1,500 raffle tickets

for \$10 each. On top of that success, the gentleman who won the Harley donated the bike back to B Positive, resulting in \$15,000 of total proceeds! Buoyed by this success, members of B Positive will hold the 2nd Annual Harley-Davidson raffle in 2003! Our thanks to this great group! ♦

A Scary Way to Fundraise

Steve Holmes and Kerry Robinson of Sammamish, WA, were looking through the alumni bulletin of the University of Oregon when they saw an article about the Frohnmayer family and how Fanconi anemia had affected them. Touched by the loss of Katie and Kirsten Frohnmayer and by the efforts of Lynn and Dave to defeat FA, Steve and Kerry decided to act. Their children suggested holding a haunted house as a fundraiser. They have done just that for three Halloweens now, raising funds for FA research. One of the guests who attended the haunted house even secured a matching grant from Microsoft!

Steve and Kerry's neighbors helped with the effort, transforming a garage into the haunted house. They constructed a plastic labyrinth of walls inside and dressed up in scary costumes (but not too scary, in deference to the little ones who attend!). Last year the house included a torture chamber, a "nut" room, a graveyard, a mad surgeon's operating room and an insane fortuneteller. Cookies, candy and apple cider are also part of the attraction of this very creative event. ♦

Credit Card Donations

Credit card donations can be made to the FA Research Fund via *PayPal*. Look for the *PayPal* button below the *Donations* line on the home page of the FARF web site (www.fanconi.org).

Family Fundraising Efforts

From July 1 through December 31, 2002, FA families raised \$441,673 for Fanconi anemia research. The Fund also received \$9,079 from the United Way and the Combined Federal Campaign. Our thanks to all of you who have worked so hard to raise critically-needed research dollars.

\$30,000 and up

Dave & Lynn Frohnmayer
Pat & Mary DiMarino

\$10,000 - \$19,999

Laurie Strongin & Allan Goldberg
Christie & Randy Kelley
Deane Marchbein & Stuart Cohen

\$5,000 - \$9,999

Vicki & Andrew Anton-Athens
Joseph Chou & Frances Wang
Andrew & Jennifer Gough
Jeff & Judy Hoffman
Charles & Katy Hull
Lorraine & Kevin McQueen
Leighsa & Stephen Perlsh
Jack & Lisa Nash
Andrea & Bob Sacks

\$1,000 - \$4,999

Mark & Linda Baumiller
Randy & Nancy Bloxom
Chris & Susan Collins
Brian & Margaret Curtis
Bill & Pat Danks
Donna DellaRatta
Ed & Janice Duffy
Beth & Jeff Janock
John & Karilyn Kelson
Gregory & Lynette Lowrimore
Steve & Allison McClay
Gil & Peggy McDonnell
Dianne & John Ploetz
Randy & Stephanie Race
Erik & Lori Salo
Bryan & Karen Siebenthal

Mark & Susan Trager
William & Mary Underriner
Michael & Beth Vangel
Marc & Sandi Weiner

Up to \$999

Ken & Jeanne Atkinson
Richard & Sharon Atwood
Lily & Keith Baggett
Cherie Bank
Audrey & John Barrow
John & Francene Berglund
John & Elaine Beyer
Roel & Diane Brand
Ed & Barbara Brookover
Donald & Danielle Burkin
Joelle & Joachim Carvahlo
James Colon
John & Kim Connelly
Charles & Dahne Deeks
Carol & James Dillon
Marie & Antonino DiMercurio
Brian & Jennifer Dorman
Gene & Lynn Eddy
Paige Ellis
Ezat & Laila Faizyar
David & Mary Ann Fiaschetti
Pat & Maria Gleason
Jack & Tina Greer
Alan & Rachel Grossman
Mitchell & Tirzah Haik

Roger & Eleanor Herman
Ronnie Hickman
Robert & Jennifer Kiesel
David Kwon
Ayala Laufer
Peg LeRoux
Gayle Licari
Eric & Beth Losekamp
Cecelia Meloling
Andrea & Matthew Morris
Sheila Muhlen
Bob & Alice Nicholson
Robert & Mary Nori
Luis & Lucina Perez
Brad & Lisa Pitts
Hal & Bobbie Porter
Lynn & Shirley Quilici
Jan & Lucia Rasmussen
Marcia Reardon
Lynn & Rick Sablosky
Bill & Connie Schenone
Jim & Carol Siniawski
Jeff & Debby Slater
Karen Steingarten
Greg & Brandi Stuart
Paul & Debra Sundsvold
Richard & Janice Thomas
Waldo & Michell Valenzuela
Kim & Michael Williams

Use of Logo

This is just a reminder to our FA families: please use our logo or letterhead only after you have consulted the staff of the FA Research Fund and received their approval. This is necessary to be sure our messages are accurate and consistent. It also helps to avoid legal complications. We are happy to collaborate on fundraisers and mailings.

Where There's a WILL, There's a Way

continued from page <None>

To my surprise, it did not take two weeks—it was only one week to the day that I got that terrible call that changed my life forever. I was home from work early that day. Will was sent home from day care because of a fever. It was 2:30 p.m. when the phone rang—it was our doctor. Our conversation was very brief: “The test results confirmed FA. We will meet in one week to discuss.” End of conversation.

I felt like I had been hit with a ton of bricks. My body fell to the floor, screaming in pain. I couldn't think, I couldn't talk, and I couldn't believe it—my son, the light of my life, was going to die from a dreadful disease that I couldn't even understand. WHY?!?! I called my best friend, and I couldn't speak. I was crying into the phone, “He has it, he has it!” We then cried together. This was our worst day in over 20 years of friendship.

My second call was to Suzanne at the FARE. Although I'd never met her, I knew she was the one person I needed to talk to on that terrible day. I was right. We talked for about an hour and, even though my heart was still shattered into a million pieces, I hung up that phone with a new sense of hope and understanding.

It has been four months since that terrible day. I know more about FA than I ever wanted to. I have learned so much in such a short time, and I have to say “thank you” to the staff at FARE. They have been so helpful. I came to them at my lowest point. I had already given up, and they inspired me to make a difference. I started a nonprofit organization called WILL POWER in honor of Will. Our slogan is “Where there's a

WILL, there's a way.” Although Will is probably at least 2 years away from transplant, we wasted no time. We held 3 bone marrow drives before the end of 2002 and added 118 names to the list of donors. Many of those have also gone on to give blood and platelets. We appeared on the local news, and we have raised awareness in our community regarding FA and the importance of marrow donations.

I still have my fair share of days when I wonder WHY, but now I know that I am not in this alone. To those of you in the FA family that I have spoken with, THANK YOU. There have been many days that those conversations with other parents were what carried me through. This is not an easy disease to deal with. Thank God there are friends out there who understand. ♦

Your FA Research Dollars at Work in 2002

Investigator: Hans Joenje, PhD, Free University, Amsterdam
Title: *Complementation Analysis in Fanconi Anemia*
Amount: \$58,707

Investigator: Catherine Verfaillie, MD, and Uma Lakshmiathy, PhD, University of Minnesota, Minneapolis
Title: *FANCC Gene Correction by Homologous Recombination in Multipotent Adult Progenitor Cells*
Amount: \$105,500

Investigator: Bruce Blazar, MD, and Jakub Tolar, MD, University of Minnesota, Minneapolis
Title: *Multipotent Adult Progenitor Cell Effects on Tissue Repair after Bone Marrow Transplant in Fanconi Anemia*
Amount: \$70,000

Investigator: Catherine Verfaillie, MD, and Balkrishna Jahagirdar, MD, University of Minnesota, Minneapolis
Title: *Transplantation of Adult Stem Cells for Treatment of Fanconi Anemia*
Amount: \$107,737

Investigator: Maureen Hoatlin, PhD, Oregon Health & Science University, Portland
Title: *Development of a Xenopus Model for Fanconi Anemia*
Amount: \$59,751

Investigator: Maureen Hoatlin, PhD, Oregon Health & Science University, Portland
Title: *Retroviral Expression Cloning of FANCI and FANCI*
Amount: \$54,360

Scientific Symposium

continued from page 1

the function of the FA proteins; the relationship of FA to DNA repair and homologous recombination; research regarding the relationship of human papilloma virus to the squamous cell carcinoma that affects FA patients; novel methods of possible gene therapy; and the ongoing efforts by transplanters to increase the success rate for FA patients undergoing bone marrow transplants.

Included as an insert in this newsletter is a listing of the Symposium presentations, giving the name of the presenter and the title of his or her presentation. If you would like a copy of one or more of these abstracts, indicate your request on the enclosed form and return it to the FA Research Fund office. ♦



1801 Willamette St., #200
Eugene, OR 97401
phone: (541) 687-4658
(800) 828-4891 (USA only)
FAX: (541) 687-0548
e-mail: info@fanconi.org
web site: www.fanconi.org

Newsletter Editors

Lynn & Dave Frohnmayer
Mary Ellen Eiler
Joyce Owen, PhD

Layout and Design

Tanya Harvey, Wild Iris Design

Staff

Executive Director:
Mary Ellen Eiler
Family Support Coordinator:
Suzanne Lauck

Board of Directors

Barry Rubenstein, JD, President
David Frohnmayer, JD, Vice President
Ruby Brockett, Secretary/Treasurer
Deane Marchbein, MD
Kevin McQueen
Mark Pearl
Robert D. Sacks
Michael L. Vangel
Peter von Hippel, PhD
Joyce Owen, PhD, Director Emeritus
Lynn Frohnmayer, Advisor to the Board

Scientific Advisory Board

Grover C. Bagby, Jr., MD, Chair
Manuel Buchwald, PhD, OC
Richard Gelinan, PhD
Eva Guinan, MD
Hans Joenje, PhD
Christopher Mathew, PhD
Stephen Meyn, MD, PhD
Raymond J. Monnat, Jr., MD
Maria Pallavicini, PhD
Leona D. Samson, PhD
Kevin M. Shannon, MD
Neal Young, MD

Printing

Image Masters Printers



The Fifteenth Annual International FA Scientific Symposium

OCTOBER 16-19, 2003

Renaissance Houston Hotel Houston, Texas