# FA family newsletter

#17 A Semi-annual Newsletter on Fanconi Anemia for Affected Families, Caring Physicians and Research Scientists Winter, 1995

*Scientists gather at FA symposium*

## Scientific Progress Charted at FA Symposium

Dramatic panoramas of the spectacular Columbia River Gorge provided the setting for the Sixth Annual Fanconi Anemia Scientific Symposium. The FA Research Fund brought together nearly sixty scientists from seven nations and three continents at the newly opened Skamania Lodge, Stevenson, Washington to share the latest research results.

Evaluations of this exciting conference by participating scientists were extremely positive. Researchers reported on the following topics:

- Clinical progress in marrow transplantation for FA
- Progress in gene therapy strategies for FA-C patients
- Studies of the function of the FA-C gene protein
- The identification of a fifth complementation group, FA-E
- The discovery that of 23 European FA patients analyzed so far, 15 belong to complementation group A (FA-A), five to FA-C, two to FA-D, one to FA-E and none to FA-B. The prevalence of FA-A may exceed 55%.
- Numerous laboratory efforts to identify the FA-A gene
- Use of mouse, yeast and fruit fly models to explore the nature of FA defects or to discover new FA genes

*For further information, please read the "lay summaries" in the Scientific Supplement, and the informal review summary on p. 2.*

## Family Meeting: Reserve Dates and Make Plans Now!

Last year's FA family meeting was especially successful, thanks to the generosity of Dr. Larry Gould and his wonderful staff at Camp Sunshine, Lake Sebago, Maine.

Our fifth annual meeting will be held late this spring at Lake Sebago once again. You should have received a special mailing by now. Please join us! Last year's evaluations were incredibly enthusiastic. Don't just take our word

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### HIGHLIGHTS

# MEDICAL NEWS

## Scientific Meeting: Informal Review Summary

*We are indebted to Rich Gelinas, PhD, of ICOS Corporation and the University of Washington, who provided an extensive review from which this summary is drawn.*

### I. Clinical Developments: Marrow Transplantation and Gene Therapy Approaches

Researchers presented many exciting clinical developments. The outcome of bone marrow transplantation for younger children with FA who received marrow from perfectly matched sibling donors has been excellent, especially since 1990 (Richard E. Harris, Cincinnati, Ohio). Arleen D. Auerbach described a rapid method for identifying persons with mutations in the FA-C gene. The method, which can detect the most common defects of the FA-C gene, has been used for clinical testing and genetic counseling in a group of Jewish families in New York City.

Perhaps the most exciting news was from two groups which have been working on gene therapy for FA-C. These groups showed that the growth and DNA repair properties of FA-C defective cells could be restored to normal levels after transfer of the normal FA-C gene with the aid of a retroviral vector (Johnson Liu, Bethesda, Maryland & D. Wade Clapp, Indianapolis, Indiana). It was encouraging to hear how the efficiency of gene transfer has been improved, as well as the preparation of target stem cells. The first test of gene therapy for FA-C could take place in 1995. The patients and the medical team headed by Liu are ready, but the trial can begin only after all federal approvals have been secured. (See related story on page 3). Nasrollah Shahidi described a third gene therapy approach using a novel "gene gun".

### II. Gene Discovery

Many groups reported progress toward identifying the genes for FA complementation groups A or D (FA-A and FA-D). Based on important complementation studies of Hans Joenje and his colleagues, mutations in the FA-A gene seem to be the most frequent cause of this disorder. Positional cloning, which makes use of an automated fluorescent approach to linkage analysis, is closing in on the FA-A gene (Rachel Gibson, London, England). DNA or chromosome transfer methods represent two more mapping approaches that are underway in the laboratories of Margaret Zdzienicka (Leiden, The Netherlands) and Markus Grompe (Portland, Oregon). Other labs are trying to clone the FA-A gene by introducing collections of cDNAs into FA cells, and isolating the ones that restore normal properties of growth and DNA repair. Two different laboratories reported discovery of genes that show some of the properties expected for the FA-A gene. Both laboratories emphasized that more tests were needed (Robb Moses, Portland, Oregon and Stephen Meyn, New Haven, Connecticut).

Since at least five laboratories are working hard to isolate the FA-A

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## THANKS TO OUR SPONSORS

Our scientific conference could not have succeeded without the extraordinary support of caring and generous sponsors. Please join us in saluting our benefactors:

**Phyllis Cafaro - The Cafaro Company (Ohio)**
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**Skamania Lodge (Washington)**
**The Samuel S. Johnson Foundation (Oregon)**
**Ortho Biotech (New Jersey)**
**The Rose E. Tucker Charitable Trust (Oregon)**

We are deeply grateful for the advancement of FA science which these donors made possible.

## Useful Article Reviews FA Science

Families and physicians may wish to consult a very complete review article on recent developments in FA science. Johnson Liu, MD, Manuel Buchwald, PhD, Christopher E. Walsh, MD and Neal S. Young, MD collaborated to produce this summary and analysis entitled *Fanconi Anemia and Novel Strategies for Therapy*, in the December 15, 1994 issue of *Blood* (vol. 84, No. 12, pp 3995-4007).

Several physicians have recommended this article to your editors. We pass the recommendation on to you. *Blood* is a major medical journal which should be available in the library of your local hospital or nearby medical school.

## NIH Gene Therapy Trial for FA Nears

As this newsletter goes to press, NIH researchers Johnson Liu and Christopher Walsh had just submitted their gene therapy protocol for complementation group C patients to the Food and Drug Administration (FDA) for approval. Drug company approvals for use of important growth factors in this experiment have been secured from Sandoz Corporation and Amgen Corporation. Genetics Therapy, Inc. of Bethesda, Maryland has worked tirelessly to produce the cloned normal FA-C gene that will be used in this trial. If the FDA approves this trial, it could begin the spring of 1995.

## Indiana University Receives Gene Therapy Grant

Researchers at the Indiana University School of Medicine have just received a $6 million grant from the National Institutes of Health to develop gene therapy protocols for inherited blood diseases. The five year grant will fund efforts to find better ways to insert normal genes into bone marrow stem cells.

Among the diseases being studied under this grant are Fanconi anemia, severe combined immunodeficiency and chronic granulomatous disease. The project will involve more than a dozen researchers in several departments at the School of Medicine.

Researchers use certain kinds of viruses to carry genes into cells. This grant will fund the development of a new laboratory to produce these viruses under conditions required by the Food and Drug Administration.

***Scientific Meeting Summary***

*continued from previous page*

gene, the feeling at the meeting was that this gene will be cloned or at least localized to a chromosome before next year's Seventh Annual Symposium.

### III. New FA Complementation Group Identified

The discovery of a fifth FA complementation group, FA-E, was reported by Hans Joenje (Amsterdam, The Netherlands). This advance was made possible in part by EUFAR, (European Fanconi Anemia Research). EUFAR helps identify patients with FA, works out pedigrees in FA families, and has now established a collection of cultured cells from each of the different FA complementation groups. Like the FA cell repository located at Oregon Health Sciences University, EUFAR disseminates these materials to other researchers in Europe, including those scientists conducting the linkage mapping studies mentioned above.

### IV. Drosophila (fruit fly) and Yeast Studies Related to FA

Some researchers believe that a core problem in FA is the inability to repair DNA damage. Similar defects have been noted in other organisms including the common fruit fly (drosophila) and in yeast. Ken Burtis (Davis, California) reported the cloning of a drosophila gene that is altered in flies that are unusually sensitive to DNA crosslinking agents. Burtis is actively exploring the possibility that the human counterpart of this gene could be responsible for one type of FA. Amanda Paulovich of Lee Hartwell's lab (Seattle, Washington) discussed how previous studies in yeast may suggest

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how a defect in DNA repair could cause the poor cell growth and perhaps even the predisposition to leukemia which are characteristics of human FA cells.

### V. FA Protein Studies: Protein Location, FA Mouse Models and Relationship of FA to DNA Damage

Following the cloning of the gene responsible for FA-C in the laboratory of Manuel Buchwald (Toronto, Canada), several groups are now trying to learn more about the cellular role of the protein encoded by this gene. Evidence from several laboratories suggests that this protein is found in all cell types in the body, not just cells derived from the bone marrow. A finding that generated extended discussion is that the protein seems to reside largely in the cytoplasm, rather than in the cell nucleus, the expected location for a protein involved in DNA repair (Hagop Youssoufian, Boston, Massachusetts).

Proteins that associate closely with the FA-C protein are under study in the laboratories of Alan D'Andrea (Boston, Massachusetts) and Maureen Hoatlin (Portland, Oregon). These proteins should provide clues about the molecular basis of FA and perhaps suggest the identity of other FA genes.

In the developing mouse embryo, the FA-C gene product can be readily detected in cells that are the sites of calcification in growing bones (Manuel Buchwald, Toronto, Canada). Unexpected was the preliminary finding that mice that were bred with two copies of a disrupted FA-C gene appear to be normal.

Finally, extracts prepared from FA-A cells were shown to be defective both in their ability to recognize that damaged DNA exists and to start the process of removing the damaged DNA (Muriel Lambert, Newark, New Jersey). While our picture of the FA defect is still incomplete, the diversity of approaches now focused on this problem will soon lead to major advances.

### VI. Relationship of the FA-C gene to Leukemia

The D'Andrea laboratory in Boston reports that some non-FA adults who develop leukemia are found to have lost the function of the FA-C gene, implying that the normal FA-C gene acts as a tumor-suppressor gene. D'Andrea's studies have expanded to include intensive study of the relationship of FA to leukemia (see *Scientific Supplement*).

## Caution Urged About Marrow Transplant and Gene Therapy "Cures" for FA

*by Blanche P. Alter, MD*
*Chief, Division of Pediatric Hematology/Oncology*
*University of Texas Medical Branch, Galveston, TX*

### Life after Bone Marrow Transplant (or Gene Therapy)

One of the hardest conversations I had occurred when an FA patient was discharged from the hospital following a successful BMT. The patient announced: "I don't have FA anymore." Wrong! The statement should have been: "I don't have FA in my bone marrow anymore." BMT (or gene therapy using hematopoietic cells) may cure aplastic anemia, myelodysplasia, or leukemia, and may reduce the risk of those events occurring subsequently. Hematologic cure means the patient may also live longer, long enough now to be at risk for the complications of the older FA patient. Women may experience irregular periods, infertility, and early menopause, with associated osteoporosis. FA patients also have an increased risk of malignancies of the reproductive system, mouth and throat, digestive system, and others. The risk of malignancy may be increased even more in transplanted patients because of the immunosuppression used as preparation for the BMT.

Surveillance for possible malignancy might include gynecological examinations and Pap smears every 6 to 12 months for females past puberty, frequent skin examinations, upper endoscopy and esophageal biopsies for patients with difficulty swallowing, tests of liver funct every few months, and annual abdominal ultrasound examinations, particularly in those who have undergone androgen therapy.

These concerns are by no means raised to discourage BMT or gene therapy, but just to remind everyone that these procedures will not provide total cure for FA. Understanding the nature of the primary defect in FA remains critical for long term care of these patients.

# FAMILY NEWS

## The Murnane-Byrne Family Copes with FA

**Two Children with FA**

by Des Murnane, Kilmacanogue, Ireland

We thought that we had three "normal" healthy children until Friday November 26, 1993. At 4pm that day we heard the news that changed all that. Just as people of my generation remember what they were doing when they heard that JFK was shot, I remember that I was at my desk at work when Mai rang me at that time. Our son, Ben, was nine then; our daughters, Ruth and Jess were five and three respectively. Mai had been worried about Ben at the time—he had recently finished a course of antibiotics for an ear infection but was still abnormally pale and listless. Mai had recently listened to a radio program about childhood leukemia during which an oncologist had emphasized that early diagnosis was important—symptoms to watch for were excessive pallor, easy bruising, listlessness. Call it maternal intuition or parental paranoia but that Friday, Mai decided to have a blood test done for Ben. About 4 pm, the doctor rang to say that Ben's blood counts were very low; although it was too early for any diagnosis, leukemia was one of a number of possible illnesses and he had booked a bed in Crumlin Hospital in Dublin to facilitate further tests. Hearing this over the phone at the office, I tried to hold myself together but the memory of that radio program made us fear the worst while hoping for an innocent explanation. To us then, leukemia was the worst—we had not heard of FA.

That first weekend in the hospital was hell while we waited for the results of supplementary blood tests. Mai and I were in a state of semi-shock, trying not to think of leukemia and remain upbeat for Ben's sake. To make matters worse, Ben had again developed a bad ear infection and was going through a lot of pain. Hospitals were pretty alien places to us. Although Ben had spent one night in the hospital when he was three, our children had enjoyed relatively good health and neither Mai nor I had ever been an in-patient. On Monday we were told that it was not leukemia and a sense of relief set in. We thought that anything else had to be better. Now that we knew what it wasn't we had to find out just what it was that was wrong. During the ten days that Ben stayed in Crumlin initially he underwent a number of surgical procedures—for the extraction of

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## Brass Ring Society Update

In a special insert to our last *Family Newsletter* (#16), we advertised a generous invitation from "The Brass Ring Society." This organization invites families of children with life-threatening illnesses to fulfill a child's dream.

Ray Esposito, the President and Founder recently wrote the following request:

"The Society cannot fulfill a dream for a child who has already had a dream fulfilled by another wish granting organization. That would be unfair to children who are waiting for their first dream.... Having said that, I again want to encourage all FA families who have NOT had a dream fulfilled to call for an application."

Many thanks, Ray!

For information or applications, write or call:

**The Brass Ring Society**
**National Headquarters**
**551 East Semoran Blvd., #E-5**
**Fern Park, Florida 32730**
**(407) 339-6188**
**1-800-666-WISH**

## The Kwon-Kim Family

**Two sons recently diagnosed with FA**

*by Sejin Kwon, Ulsan, South Korea*

It was early morning of 28 Dec, 1994. Michael (3 years 2 months old), my younger boy, had been hospitalized the previous afternoon for osteopathic surgery on his congenitally deformed right thumb. Because the bone surgery requires a general anesthesia, doctors had ordered blood testing the night before. But in the morning, they wanted one more sample of his blood. They mentioned the low number of platelets in his

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## We Welcome New Families Who Have Joined Our Support Group

**Teresa & David Baber**
Rt. 2, Box 199A
Wallingford, KY 41093
(606) 876-4321

**Sarah Baker**
403 Turnstone Trail
Queensboro, NC 27455
(910) 545-8771 (H)
(910) 373-7250 (W)

**Johnnie & Debra Byrd**
2117 Jefferson St.
Two Rivers, WI 54241
(414) 794-8840 (H)
(414) 793-3629

**Susan Combs**
335 Ward Ave.
St. Joseph, MI 49085
(616) 983-5857

**Carol & James Dillon**
126 Chase Ave.
Lowell, MA 01854
(508) 970-0814

**Melodie & Gary Ganz**
140 Windsor Drive
Vernon Hills, Il 60061
(708) 362-9189

**Diana Hume**
206 Buckingham Drive
Evansville, IN 47715
(812) 477-8062

**Jeff & Beth Janock**
17 Midway Ct.
Rockaway, NJ 07866
(201) 627-8323

**Shirley Johnson**
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33-7569 4314 (W)

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**Maria & Juan Olivas**
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Belen, NM 87002
(505) 864-9026

**Bryan & Amy Price**
16B Bradshaw Drive
Clinton, MO 64735
(816) 885-8631

**David & Karen Russo**
12018 Mandarin Rd.
Jacksonville, FL 32223
(904) 284-4200

**Glenn & Maureen Russo**
281 Pomeroy Ave.
Pittsfield, MA 01210
(413) 442-0438 (H)
(413) 499-9368 (W)

**Lorne Shelson & Annette Waxberg**
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Toronto, M5N 2L2
Canada
(416) 489-5502 (H)
(416) 869-1571 (W)
(416) 869-1735 (FAX)

**Donna & Gary Touchstone**
40114 Bahm Road
Franklinton, LA 70438
(504) 839-2991

**Tanya Wright**
PO Box 370
Jenkins, KY 41537
(606) 832-4502

*"In this sad world of ours, sorrow comes to all, and it often comes with bitter agony. Perfect relief is not possible, except with time. You cannot now believe that you will ever feel better. But this is not true. You are sure to be happy again. Knowing this, truly believing it, will make you less miserable now. I have had enough experience to make this statement."*

~ Abraham Lincoln

**The Murnane-Byrne Family**

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bone marrow samples for testing and for the insertion of a triple lumen Broviac catheter to facilitate blood testing—three general anesthetics in all. Severe aplastic anemia was diagnosed and it was thought that it was acquired rather than genetic, as Ben did not exhibit any obvious physical characteristics usually associated with the latter. We were told that while aplastic anemia could sometimes correct itself, it was likely that Ben would need a bone marrow transplant, and preferably a sibling transplant. While the hospital proceeded to test the compatibility of our girls with Ben he was allowed to go home and we started to get ready for Christmas.

This was a difficult time for all of us—for Mai and myself trying to normalize the abnormal circumstances, not knowing what lay in store, with every waking moment dominated by Ben's illness; for Ruth and Jess taking on board the little lifestyle adjustments—Ben's liquid soap, paper towels, special mouthwash and the inability to have many people in the house together because Ben's low counts left him prone to infections; and not the least for Ben himself whose normal world was turned upside down—he was to miss four and a half months of school and live in semi-isolation during that period, seeing little of his friends. We went to sleep fretful and woke up even more so, hoping some day we would wake up to find out that it was all a bad dream—our emotions ranged from fear to bewilderment, but always anxious. We got to know the thin line between hope and despair.

The period immediately after Christmas brought some more knocks. The compatibility tests showed that while Ruth and Jess matched each other, they were not a match for Ben, and the search for a matched unrelated donor began. In the meantime, Ben was to be admitted to Crumlin in mid-January for drug therapy as the first alternative. The day he was admitted, the results of the chromosome breakage tests came through—Ben's anemia was not acquired, but FA. The proposed drug therapy was abandoned as inappropriate and Ben was discharged while being put on oxymetholone (androgen therapy) to boost and maintain his counts. We were advised that, in the absence of a sibling donor, the prognosis for Ben was guarded, given the risks associated with matched unrelated donor transplants and prolonged use of steroids. Once the genetic connection was established, Ruth and Jess were tested for FA, and at the end of January we discovered that Jess also had FA, although her counts were normal. This was our lowest point—the realization that two of our three children had FA was almost too much pain to bear. You ask what did our kids do to deserve this? Our hopes and dreams lay shattered.

In the past year we have tried to adapt to living with FA, and much has improved since. Ben was on 75 mg of oxymetholone daily for almost six months—his weight increased from 55 lbs to 85 lbs in that period; his voice deepened and he went through premature puberty. Although he became more cranky, too, he adapted to these changes much better, I think, than

*Ben, Jess and Ruth Murnane*

most adults would. He returned to school last April and has missed relatively little of it since. His routine with friends and leisure activities have resumed as before except that he does not indulge in contact sports or swimming; computer games have filled these gaps. This term he was placed first in his class in English and is consistently in the top three in most other subjects. A prize-winning poem which he wrote for an environmental project on whales was featured in a public exhibition in Dublin which attracted much publicity. In the last six months his dosage of oxymetholone has been steadily reduced so that now his counts are maintained on 3 mg per day.

Jess' counts remain normal. Ruth and Jess have probably grown closer and are best friends—most of the time! In July last, a donation of bone marrow (or "bow and arrow" according to Jess) was taken from Ruth, at our request, to be kept under liquid

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**The Kwon-Kim Family**
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blood. It struck me like lightning. I demanded indefinite postponement of the surgery and asked to see a pediatrician. After consultation with him, I arranged for David (4 years 10 months) to fly to Seoul which is about 500 miles from our home in Ulsan. David flew by himself with the help of the flight attendants. Waiting for him in the airport, emotion overwhelmed me. I couldn't grasp the reality. Of course I didn't quite understand what FA is by then. But a few words like higher risk of leukemia and indefinite treatment were enough to make me tremble. They put us in a pediatric cancer ward. The other ward was for children with infectious diseases. It seems that the doctor wanted to let me know what to expect if the close examination turns out positive.

Actually the crisis began two months ago, when David and my wife Jee-Ai made a trip to the hospital in Seoul for David's annual check up. Since David was born with various minor anomalies at the University of Michigan Hospital while I was an engineering PhD student in Ann Arbor, we have brought him to a major hospital once a year even after we returned to Korea. His congenital anomalies included low birth weight, one absent kidney, microphthalmia, malformed left thumb. At this year's examination, his osteopathic surgeon who was also aware of Michael's right thumb problem suggested seeing a pediatrician specializing in hormones and birth defects. The pediatrician suspected David looked like an FA patient whom he saw while he was visiting a US. hospital, and recommended a detailed examination. My wife was quite upset and called me in Ulsan. I had never heard of anything like Fanconi anemia; I thought it was a poor diagnosis of an overzealous young doctor. David had some anomalies. However, he wouldn't be so active and playful if he had an anemia. It can't be. He's just small and has a renal malformation which is not life threatening. That's it. All we have to do is to take him to a big hospital once a year to make sure he has no infection in his renal system. On the other hand, if it's true that he has a hereditary disease due to a genetic disorder, I didn't believe medicine had any cure for it. David as well as we will suffer whatever it may be. As a trained scientist myself, I thought I know too well there's insurmountable limit in what man can understand from God's creation. So I told her to comfort her over the phone. And discredited the doctors. Then we completely forgot about it.

Now, knowing Michael's abnormal blood count, I realized that I cannot deny it anymore. While we were awaiting the test result of blood and bone marrow, I read several papers about FA, which the doctors gave me. As I read the articles one by one, I began to realize the seriousness of the disease is beyond my imagination. Numerous anomalies I can find from my boys were listed as FA symptoms, including the blood count. It didn't require a trained doctor to diagnose them as having FA. Most shocking was that fatality was 80% by age 12 before there was treatment. [See editor's note.] I knew it was almost impossible. But I hoped somehow the BM test result would turn out negative. It didn't. You may well understand the ensu-

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*Nancy Williams, at a Virginia Federal Campaign Fair*

Nancy writes: "This is one way to raise awareness and funds for FA. I plan to do the same at our local malls."

*Wonderful work, Nancy. Many thanks! (eds.)*

**The Kwon-Kim Family**
*continued from page 8*

ing pain Jee-Ai and I suffered. We ply belong to different world and culture from yours. But the agony of having FA-inflicted children should be universal. I briefly considered killing myself and the whole family. Or quit my career as an assistant professor at the University of Ulsan, to be around with the kids while they are with us. Coming back home from the hospital, we were completely shattered and exhausted. Everything loses its meaning. Man shall not understand God's will. But, is it also God's will that innocent ones suffer? I was lost and blank. I didn't know what to do except for just waiting. Then Jee-Ai challenged me not to quit but to fight. To find and do whatever we can to help the boys, while we have time. I gathered my strength and called that there was a support group listed on one of the papers doctors gave me. It had no street name, phone number, etc. Just 'Fanconi Support Group, Eugene OR' was all I had. Sarah, my sister living in Greensboro, NC was so eager to find out and contact you. She wanted to do anything to help us.

From then, I read several books on medicine including a textbook of hematology. Until 1989, BMT treatment was inconclusive due to FA patients' sensitivity to immune-suppressing agents and GVHD. I found the research was unusually active, although it is a rare (you called it orphan) disease. I needed more up-to-date material. One librarian mentioned Medline, which is a CD-ROM data base of medicine. It contained abstracts from all the major medical journals up to October 1994. I learned about recent advances in BMT and G-CSF. One of the interesting therapies was about using blood cells from a sibling umbilical cord as stem cells of recipient. We have no other child than these two boys who are affected by FA. As I am in my mid- and Jee-Ai is in her early thirties, we can have another child as a donor. I do not know if it is morally correct. But I would like do whatever is in my power to save the children.

God bless you.
Sejin Kwon, Jee-Ai Kim*
David and Michael Kwon

**note: women retain their family name.*

## The Ganz family

**Teenage Daughter Recently Diagnosed with FA**

*Elizabeth Ganz*

The Ganz family, Gary, Melody, Nathan and Elizabeth, live in Vernon Hills, Illinois. Their 13 year old daughter Elizabeth was diagnosed with FA in November, 1994, when her new pediatrician noticed her reduced platelet count of 80,000 and the presence of enlarged red blood cells. Elizabeth was born with narrow ear canals. An extra finger on her right hand was removed surgically at age 2. Her only treatment currently is taking the ACES vitamins.

Elizabeth is a 7th grader who has been on the honor roll and student council for four years. She takes baton, enjoys babysitting and loves her English Springer Spaniel, Patty. Gary is a trader for Ace Hardware, Melody is a Special Education Teacher and Nathan is a 15 year old high school student.

*Editor's note: According to cases reported to the International Fanconi Anemia Registry, the average life expectancy is approximately 22 years.*

## Pen Pal Requested

Jaime Alcazar, age 7, would like to have a pen pal friend who also has Fanconi anemia. If you would like to be Jaime's pen pal, please write to her at:

**3524 Edward Dr.**
**Crete, Il 60417**

Jaime is looking forward to hearing from you!

## The Lewis Family

**Dylan's first fifteen months**

*by Mike & Myra Lewis, Darrington, Washington*

A week before I was due to deliver our second child, I had some light bleeding. Although I had placenta previa early in my pregnancy, which may cause some bleeding, my doctor sent me to the hospital for an ultrasound.

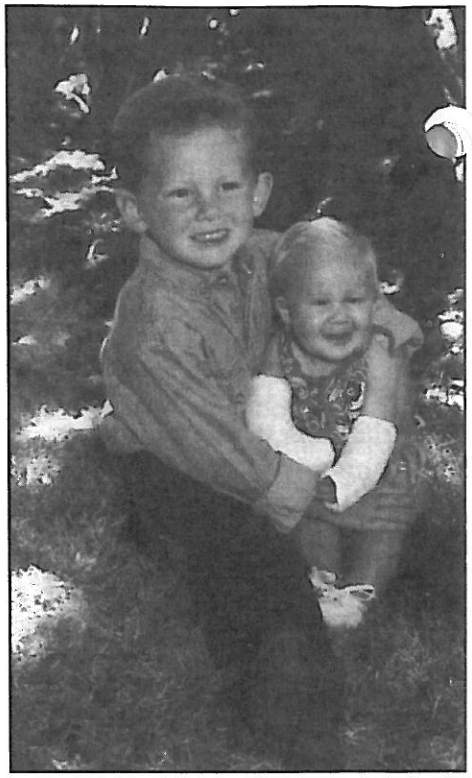
The ultrasound seemed unusual in that people were coming and going and really spending an unusual amount of time trying to determine if my placenta had possibly detached itself. They sent me home (30 miles away) and when I walked into my house, a message was waiting from my physician. He wanted us to come to his office immediately. He sent us to Seattle for a more thorough ultrasound and evaluation because it appeared our unborn child weighed only three pounds. We just couldn't imagine this; it had been a textbook pregnancy.

Several specialists were involved in my evaluation once I was at the University of Washington Medical Center. They told us that they suspected a chromosomal abnormality. We were certain that there was some mistake because we had a very normal four year old at home. They wanted to deliver me the next day because they felt they could better care for the baby on the outside.

Dylan Charles was born the next afternoon weighing 3 lb. 8 oz. He had missing radial bones in each arm, missing thumbs, three fingers on one hand and four on the other, fused kidneys, duodenal atresia (stomach not attached to intestine), and a very low platelet count. These were things that were revealed within the first few hours of life. With each discovery we kept saying, "Okay, we can deal with this, it can't possibly get worse," but each time it did.

Dylan had been transferred to Children's Hospital that first evening, and spent his first month there. We had no idea what the diagnosis was going to be. Of course, the doctors didn't want to go into any possibilities. They wanted to know for certain before discussing anything. Truly, we didn't know if he was even going to survive. When Dylan was nine days old, they had confirmation of chromosomal breakage testing. I'll never forget that consultation as the doctors tried to explain what FA meant for our precious new son. It was heart wrenching. I was even willing for God to take him then, to spare him and us the pain that was sure to engulf our lives. There were so many emotions that we were feeling all at once. It's still painful to recount them now.

But that was then; this is now. We have a 15 month old son with the sweetest spirit ever given to a child. Because of Dylan, we have been given the gift of really knowing what is important in life. Our character has been given an overhaul! Life's little curves don't even phase us—we often find ourselves saying, "In the scope of things it's really no big deal." Dylan is so special to us and all of our family. We thank God for giving him to us to care for and love unconditionally.



*Chase and Dylan Lewis*

To date, Dylan has suffered through three surgeries. It amazes me still how resilient children are. We know we have many battles ahead of us, but right now, we feel strong and choose to live in each beautiful day, not what the future has to deal us. We still thank God daily that Chase, our older son, does not have FA. We feel so much for those of you who have the extra burden of not having any healthy children. Our hearts are full of compassion for you.

There is so much more that I could share with all of you, but I will close by saying that although I am sorry that we share this common thread, I am grateful to be in such a committed and faithful group with such strong leadership. You'll never convince us that God doesn't have a master plan.

*The Dudarenko family from the United Kingdom sent us a touchingly special "1994 Diary". It reviews the uncertainties, hopes and fears which so many of us experience with FA. We thank the Dudarenkos for their permission to reprint this honest diary, and for giving their concluding advice. We found their observations to be both wise and hopeful.*

# 1994 - A Year With Fanconi Anemia

*by Rick Dudarenko*

## JANUARY

My daughter, Natasha, had lost a little blood from the bowel and was seen by our GP. A subsequent blood test showed some abnormalities—leukemia was suspected.

Further tests at the Royal Manchester Children's Hospital confirmed that Natasha did not have leukemia but was probably suffering from a rare inherited genetic disorder. The precise diagnosis would take a further 2 to 3 weeks.

Since the illness was thought to be of genetic origin, samples from my son Alexander were also sent for testing.

Natasha was 6 years old and Alexander 9 years old at this time.

## FEBRUARY

The laboratory tests were now complete. In both my children's cases, we were told the diagnosis was the same—FANCONI ANEMIA.

### What is Fanconi Anemia?

Fanconi anemia is a very rare genetic illness. We were horrified to hear that FA typically results in severe bone marrow failure and that kids with FA are at high risk to develop leukemia and other forms of cancer. They are prone to infections, bruising and bleeding. Doctors told us the prognosis for children with FA was very bleak.

### What Treatment Was Available?

Our consultant hematologist told us that there were only two options available at this time:

*1. Oxymetholone*

This is an androgen (corticosteroid) which often stimulates the bone marrow of an FA patient into production of blood cells. It can have some serious side effects:

a) It could cause liver problems (tumors).

b) It could cause virilization (masculine features).

c) It could cause personality changes (aggression).

d) It is usually effective for only a short time (5 years or so).

*2. Bone Marrow Transplantation*

This process replaces the patient's bone marrow with that of an adequately matched donor. We were told that this procedure was more effective the earlier it was done.

At this time the children's blood counts did not require boosting and it was decided that no treatment was appropriate for now.

A nurse at the Manchester Royal Children's Hospitals told us about a support group for FA sufferers and their families in England: F.A.B.U.K.

We contacted David Westmoreland at F.A.B.U.K. He and his family have been a great source of friendship, support and information in our search for a greater understanding of FA.

F.A.B.U.K. sent us a copy of a book published by the Fanconi Anemia Research Fund, Eugene, Oregon, USA, authored by Lynn and Dave Frohnmayer: *Fanconi Anemia: A Handbook for Families & Their Physicians.*

This is an excellent source of practical and accurate information for FA families AND their doctors.

## MARCH

We spoke at length to David Westmoreland and his wife, Christine. They gave us the kind of detailed information and support that can only come from parents who have lived and coped with FA for a long time. For this, we are very grateful.

David made me aware of an upcoming meeting in Paris, France. This was to be a gathering of FA support groups from around Europe. Its purpose was to set up a European organization to consolidate family support and fund raising activities throughout Europe. I decided to attend. Colleagues at work rallied to help finance the trip.

The meeting was held at the Hôpital St. Louis in the offices of Professor Eliane Gluckman who is Europe's foremost bone marrow transplant physician

for Fanconi anemia patients.

Parents (Support Group Leaders) attended from France (Alain Silverston), Germany (Ralf Dietrich), the Netherlands (Ron Baas), and Italy (Giovanni Pagano), as well as my brother, Henryk and I.

We started by discussing our experiences with this illness and exchanging practical information. For me, as a "novice", this dialogue was invaluable.

Because of the rarity of this disease (around 200 known sufferers throughout Europe), the only real source of ACCURATE, PRACTICAL information is from people directly affected by, and dealing with, Fanconi anemia. We agreed to create a European Fanconi anemia group, and named it E.L.F.A. (European Link for Fanconi Anemia).

The meeting concluded with a trip to a reunion of bone marrow transplant patients. At the reunion, I had a chance to meet parents, children and doctors who had experience of this difficult medical procedure. I learned many (often harrowing) FACTS about bone marrow transplantation in Fanconi anemia patients.

I urge all parents of children with FA who are considering BMT to research the subject very thoroughly. I have discovered that there are many difficulties with BMT for FA patients.

We also registered our names with the Fanconi Anemia Research Fund in the USA. It was founded by Dave and Lynn Frohnmayer who have children with FA.

My children's blood counts were low, but stable. No medication given yet.

**APRIL**

From a Fanconi Anemia Research Fund Newsletter, we learned that there was to be a meeting of FA families and researchers at Camp Sunshine in Maine, USA. We considered this an opportunity not to be missed and decided to go.

My children's blood counts had dropped a little but their hematologist recommended that there be no treatment yet.

**MAY**

With the help and generosity of friends and work colleagues we managed to go to Camp Sunshine.

The purpose of the trip was to meet families who have experience with Fanconi anemia, find out about the latest research/treatment and let my children meet other children suffering from Fanconi anemia.

Camp Sunshine is located on the shore of Lake Sebago, southwest of Portland, Maine, USA. Families live in large "trailers" (mobile homes) located in a pine forest on the lake shore. The Camp has dining and entertainment facilities. Camp Sunshine is financed by the generosity of the owners and contributions from charities and the public. It is staffed by volunteers and students.

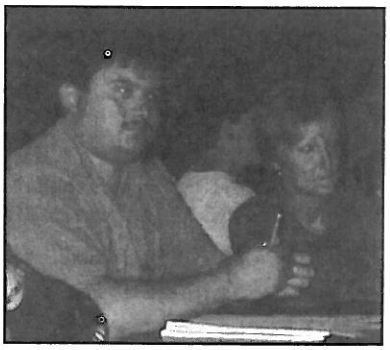
The organizers had devised a program which was extremely entertaining and educational for both adults and children. The children were put into groups based on age. These groups were looked after by counselors (students) who were responsible for the children for the duration of our stay. The children were taken on nature rambles, fishing, sailing, camping, etc. *They had a great time!* They also had a unique opportunity to discuss their problems with other children who could really understand them.

The Camp Sunshine experience was invaluable in terms of my children learning more fully about their situation.

For the parents, this was a unique opportunity to meet and talk with many others who had practical experience of living and dealing with Fanconi anemia on a day-to-day basis. Fanconi anemia is an extremely rare disease. There is very little documented (or accurate) advice or information available. Some of the advice given to me literally has life or death implications (e.g. bone marrow transplantation).

*I will be forever grateful for having found accurate information, based on practical experience, in time to make qualified judgments on behalf of my children.*

A number of FA researchers attended Camp Sunshine and gave presentations on their latest research findings. Although many of their findings reinforced the gravity of the situation, there was much hope for the future in the areas of related bone marrow transplants, locating and decoding the remaining FA genes, extending the scope and effectiveness of hormone treatments and developing new drugs. I was impressed and touched by the accessibility and openness of all the medical



*Rick and Ann Dudarenko*

researchers and counselors who gave up their free time to attend. This gathering of FA expertise has made Camp Sunshine an annual "mini-medical symposium" for all interested parties.

Evenings were much lighter—magic shows, clowns, costumes and games for the children. Music, dancing and comedians for the parents gave all of us a much needed chance to unwind among understanding friends. We made many new friends at Camp Sunshine. We hope to keep in touch and help each other in the times ahead.

Camp Sunshine was organized by the Fanconi Anemia Research Fund of Eugene, Oregon, USA, founded and run by David and Lynn Frohnmayer and a wonderfully dedicated staff. My family will be eternally grateful to them.

## JUNE

We returned from Camp Sunshine with a much greater understanding of Fanconi anemia and its treatments.

A very loud and clear message from FA parents was "be careful, double-check any information you are given by your physicians—they probably have little or no experience of FA. In reality, you have to become your own FA expert." We were told this time and time again.

Natasha had some nose and gum bleeds. Both children had little energy and were feeling tired. The children's hematologist decided to start treating Natasha and Alexander with oxymetholone.

**Natasha** - 50 mg / 25 mg on alternative days

**Alexander** - 50 mg per day

We were told that the oxymetholone may not have any positive effect for up to six months after starting treatment.

## JULY

Both children had nose bleeds and were feeling very tired. Regular blood tests showed that their counts had not improved but were stable. The oxymetholone had not had any effect at this time.

## AUGUST

No nose or gum bleeds this month.

Regular blood test showed that Alexander's blood counts (haemoglobin and platelets) had slightly improved. Natasha's counts were more or less the same.

## SEPTEMBER

Both Alexander's and Natasha's blood counts had started to improve. Alexander's counts had gone up by a good margin. Natasha's were up but not by as much.

Natasha's appetite was improving. Alex was also eating well.

## OCTOBER

The oxymetholone had started to produce good results. Alexander's blood counts had improved again. Natasha's counts had improved considerably over the previous month, especially the platelet count.

| Counts at this time | Hg | White | Platelets |
|---|---|---|---|
| Alexander | 8.8 | 3.9 | 112,000 |
| Natasha | 7.1 | 3.7 | 54,000 |

On the down side, some of the side effects had started to show. Alexander was becoming more aggressive and argumentative while Natasha had some signs of acne on her face. Body hair had started to develop on both children.

We heard about the Fanconi Anemia Research Fund Scientific Symposium which was scheduled for the second week of November in the Pacific Northwest of the United States. I decided to try and attend.

## NOVEMBER

With my brother Henryk, I managed to attend the Fanconi Anemia Research Fund Scientific Symposium. The symposium was very well attended by clinicians, researchers and observers—around 60 people from 7 countries.

The symposium started with presentations from clinicians on bone marrow transplants and trials of G-CSF (a growth factor).

Regarding BMT for FA patients the message was clear:

*If the donor is a well matched sibling (brother/sister), the results are quite encouraging.*

*If the donor is a non-sibling, the results are very discouraging.*

The results of the G-CSF trial in America have been very encouraging with at least some improvements in the blood counts of many patients.

These findings were followed by presentations

from geneticists researching FA.

Due to the highly technical nature of the presentations, I found much of the content very difficult (if not impossible!) to follow. I have never seen so many PhDs per square metre before! And I was heartened to see how many highly motivated, dedicated scientists have taken a keen interest in Fanconi anemia.

One of the researchers at the symposium is now awaiting final permission from the FDA to start a gene therapy trial on FA-C children. Parents and patients eagerly await the results.

I managed to discuss my children's treatment with Dr. Nasrollah Shahidi who is a world authority on the use of oxymetholone for the treatment of FA. He suggested that we reduce the amount of oxymetholone that Alexander was taking.

I discussed my USA trip with the children's hematologist. He agreed to lower Alexander's dose of oxymetholone. Both Alexander and Natasha's blood counts were still improving. The side effects described earlier were about the same.

The whole family went to Guys Hospital, London to give blood samples for research. This effort will assist work being done by Dr. Chris Mathew and Rachel Gibson. Some of the blood was sent to Dr. Hans Joenje in Amsterdam who is researching FA gene complementation groups.

## DECEMBER

We received a letter from Guys Hospital informing us that the children were NOT in FA complementation group C. This was disappointing because FA-C is the only FA gene that has been isolated so far. To determine the children's complementation group will take 3-4 months.

Alexander and Natasha are looking forward to Christmas. They have been to the Royal Manchester Children's Hospital Christmas party and look forward to a "Santa Flight" from Manchester Airport on Christmas Eve.

Considering what they have gone through this year they are, at present, in pretty good shape.

### A Few Thoughts and Observations

- Fanconi anemia is very rare. As such, the vast majority of doctors have never seen an FA patient or know anything about the illness.
- If a treatment is advised, please research it thoroughly.
- Check how much experience your doctors have of any particular type of procedure or treatment.
- Beware of statistics on Fanconi anemia and terms such as "survival rates." What do they REALLY mean?
- Contact other FA families.
- Listen to advice from FA families. They are some of the very few people who truly understand the practical side of dealing with FA.
- Gather as much information as possible from anyone/anywhere you can.
- Contact researchers and, if possible, donate samples to help their research.
- Collect all statistics (from blood and liver enzyme tests, for example). Compile your own tables and graphs. Few hospitals tend to do this. Information, presented in these formats, is very useful when seeking second opinions and other medical advice.
- You will, after a time, become an FA "expert". Do not underestimate your "gut feelings." They will probably be a good guide.
- Register with a support group(s). They will supply you with the kind of information that is simply not available anywhere else.
- If possible, try and raise money for research.
- Appreciate what you have today. Do not dwell on what could have been tomorrow.

### And Finally...

Life has changed dramatically, values have changed. Many things that were once considered important have been shown to be trivial.

It is difficult for others to comprehend the magnitude of our situation. The children look okay—are they really that ill? If it were only that simple!

I am always amazed at the resilience of FA children. Whenever I feel down I look at my children's (mostly) smiling faces. This puts many things into perspective.

## PLEASE NOTE

*All opinions expressed are those of R.M. Dudarenko & Family and are NOT to be considered as precise medical advice or fact. Always check with a physician and then get a second opinion.*

# FUNDRAISING

## Quilt Offer

Debby Slater has made an incredibly generous offer to help raise funds for FA research. With two months notice, she will make a quilt with 600 squares, which could be raffled off at the workplace, a church, crafts fair or any community gathering attracting many people. Debby suggests selling 600 raffle tickets before a winner is drawn. The FA Research Fund will pick up shipping costs.

Please call Debby at 518-370-5539 if you are willing to raffle one of her quilts. Thanks, Debby, for your wonderful offer!

$1,000 was given in memory of Sylvia McFall, precious grandmother of Hannah McCarty.

## Family Fundraising

From June 20, 1994 through December 31, 1994, forty-five families raised $167,454 for Fanconi anemia research. We are deeply grateful for each and every effort! Without your help, we would not be able to support the laboratory research which brings us ever closer to an understanding of this disorder.

We hope you share our commitment to continue these crucial efforts. It is hard for all of us to ask for help. But we have made enormous strides because of our

*Continued on next page*

## Debby Slater Shares Creative Fundraising Ideas

Debby Slater continues to amaze us with her creative fundraising ideas. In just the past few months, Debby has raised crucial dollars for research in the following ways:

- At Halloween, with the help of the Elks Club and the Women's Auxiliary, she organized a "Haunted Halls" event for children. A minimal admission charge raised $450.

The Women's Auxiliary then surprised Debby by holding two fundraising dinners which brought the total raised to $900.

- Debby made and auctioned off a patchwork Christmas tree skirt, netting $588.
- A garage sale brought in $1,000.
- Debby organized "Niska Day" or a play day for children, held at a local high school. Children were charged 25 cents a game, and could choose among a duck pond ring toss, a beanbag toss and a pickpocket lady. Eight hundred children enjoyed the day and won prizes, and $200 was raised.
- Debby asked her parents to make donations to FA research in lieu of Christmas gifts to her. The idea spread to members of the extended family, and all agreed to participate. Instead of buying gifts for each other, Debby's family contributed $1,300 to our research fund. Debby stated that everyone was very enthusiastic about this, and they all plan to continue this tradition. Debby added "There was no work, no shopping, we just wrote checks!"

We are immensely grateful to Debby and her wonderful family for their incredible selflessness, generosity, and tireless efforts!

## We Honor Our 1994 Grantors and Corporate Contributors

Georgia Pacific Corporation
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Chiles Foundation
Oregon Community Foundation: Edwin and June Cone Fund and Bowerman Fund
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Rose E. Tucker Charitable Trust

### *Family Fundraising*

*continued from previous page*

hard work, and our progress must continue. Please, do whatever you can to help us raise funds for research. Our children and adult FA patients are depending on us.

We list only those amounts deposited in our account by December 31, 1994. Many of you were in the middle of a fundraiser, had sent us funds which we had not yet deposited, or made a contribution in memory of a loved one. Our next newsletter will report on these special gifts.

We thank all of the families listed for their courage and tireless efforts.

**Over $90,000**

Lynn & Dave Frohnmayer

**$10,000 - 15,000**

Deane Marchbein & Stuart Cohen

**$5,000 - 10,000**

Phyllis Cafaro
Jennifer & Robert Kiesel
Mike & Myra Lewis

**$4,000 - 5,000**

Chick Deeks
Debby & Jeff Slater
Karilyn & John Kelson

**$3,000 - 4,000**

Des Murnane
Marc & Sandy Weiner
Robert & Linda Scullin

**$2,000 - 3,000**

Carol & Jim Siniawski
Neil & Iris Frank
Therese & Terry Robertson

**$1,000 - 2,000**

Alfred Leontic
Alison & Steve McClay
Dottie Day
Ron & Fredi Norris

**$500 - 1,000**

Bill & Jackie Lucarell
Bill & Pat Danks
Bob & Andrea Sacks
Lynnette Chandler
Mark & Susan Trager
Mary & Pat DiMarino
Matt & Diane Senatore
Michael & Pam McCoury

**Up to $500**

Aaron & Jean Randolph
Alice Nicholson
April Benton
Brian & Margaret Curtis
Carol Ceresa
Carol Dillon
Irene & John Kalman
James Galvin
Janice & Richard Thomas
Johnnie & Debra Byrd
Kenny & Lisa Myhan
Linda & Mark Baumiller
Joe & Lynn Linsenman
Nathan & Ann Eckstadt
Jack & Pam McCarty
Rene & Peg LeRoux
Robin & David Paulson
Teddi Matlack

Contributions were received in loving memory of Mike Lucarelli, Michael Elzinga, Avi Weiner, Alex Norris, Christopher McCoury, Jason Randolph and Hugh Deeks.

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### The Murnane-Byrne Family

*continued from page 7*

nitrogen in the event that it will be required by Jess, if and when her counts deteriorate. The girls have a full social diary—partaking in gymnastics and swimming, Irish dancing and lately, ballet. Mai, who coaches them in a gymnastics club, sees promising signs of talent emerging and swimming badges are being collected like stamps!

It is fair to say that Mai bears much of the day-to-day burden of coping with FA—the weekly trips to Crumlin with Ben for counts and monitoring, the twice weekly cleaning of the Broviac catheter, etc. These recurring chores have been eased somewhat by the practical support of family and friends, together with the positive attitude and ceaseless caring of the medical staff at Crumlin Hospital. In recent months Mai has even found the energy to organize a series of small fundraising events to benefit both Crumlin Hospital and FARF. The most successful of these was a wine and cheese party held in our house, which attracted about sixty people! Ben designed a program and tickets, and he and his friends acted as doorman and waiters. The girls, resplendent in party dresses, acted as coat-check attendants and hostesses. A good time was had by all!

FA has made us appreciate more what we have today. Last summer we had some of our best times together, holidaying on an island off the west coast of Ireland, and then spending a few days with friends in London. We make an effort to do things together—going to the movies, puppet theater, walks and picnics on forest trails near home. We try not to look too far ahead, because this brings anxiety, fear, and uncertainty. We are more comfortable coping with the present.

# FOR YOUR INFORMATION

## For Helpful Reading

*by Nancy C. Williams, FA Parent*

I would like to recommend reading the book *A Window to Heaven* by Dr. Diane Komp, of Yale University. Dr. Komp was the physician of my daughter, Donna, many years ago at University of Virginia Medical School in Charlottesville, Virginia.

Dr. Komp explains what it means to believe in God when life's tragedies tend to undermine our faith. This wonderful book is about life and death in which our children are our teachers. It gives us hope for tomorrow, amidst the storms of life.

Two other books written by Dr. Komp are *A Child Shall Lead Them* and *Hope Springs from Mended Places: Images in the Shadows of Life.*

### *Family Meeting*

*continued from page 1*

for it—read the "1994 Diary" of the Dudarenko family (p. 11)!

Most of our scientific and medical presentations, plus small group discussion meetings, will occur over the weekend of May 19-21, 1995. We made this change so that those who have work or school obligations can minimize disruptions and still attend. Those who can stay through Friday, May 26 may extend their wonderful Camp Sunshine experience. It includes parent discussion groups, exercise and relaxation, fabulous children's programs, and additional scientific and medical presentations. And, until the onset of Memorial Day weekend, lodging and food are without charge to the immediate FA family. Adult FA patients and families who have lost an FA child are warmly welcomed. We are deeply grateful to Dr. Gould and his staff for reaching out to us.

A final note: travel expense to Portland, Maine, may prove a difficult barrier for your family. Last year, a creative mother approached local businesses and professional offices and obtained donated airline tickets. With plenty of advance notice, you may well be able to do the same. Our office will also be working with Dr. Gould to obtain free airfare for a few families. It is too early to know if these efforts will be successful. If you have exhausted local resources and airfare remains the sole barrier to attending Camp Sunshine, get in touch with our office as soon as possible.

*"Never doubt that a small group of thoughtful committed citizens can change the world. Indeed, it's the only thing that ever has."*

Margaret Mead

## Bone Marrow Recipient Eager to Share Experience

Two years ago, Clay Eubanks, now 19, received a bone marrow transplant from an unrelated donor at the University of Minnesota Hospital. Clay's experience was a very positive one. He is eager to talk with any Fanconi anemia patient who is contemplating a transplant.

Clay can be reached in Florida at 904-574-0444 between 9 am and 12 pm Eastern time, and also on the weekends. Thanks for the thoughtful offer, Clay!

### EDITORS' NOTE AND DISCLAIMER

Statements and opinions expressed in this Newsletter are those of the authors and not necessarily those of the editors or sponsoring 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.

# BULLETIN BOARD

## *Biotechnology-Based Therapy Is Found Effective Against Leukemia in Mice*

By ELYSE TANOUYE
*Staff Reporter of* THE WALL STREET JOURNAL

Researchers have developed a biotechnology-based therapy that was effective against a type of leukemia in laboratory mice, opening the way for testing in cancer patients later this year.

The experimental drug uses a genetically engineered antibody that homes in on leukemia cells and delivers a compound that kills the cells. The drug eliminated virtually all the detectable leukemia cells in mice, according to a study reported in today's issue of Science by scientists who created and own the therapy at the University of Minnesota.

Because treatments that produce promising results in animals often don't work in humans, the new drug's usefulness won't be known until it's given to cancer patients later this year, said Fatih M. Uckun, the lead researcher of the study and professor of therapeutic radiology and pediatrics at the University of Minnesota.

The drug, called B43-Gen, was tested against B-cell precursor leukemia, the most common form of childhood cancer and second most common form of adult acute leukemia, according to the researchers. Conventional chemotherapy cures about 75% to 80% of children and half of adults afflicted with the disease, said Dr. Uckun, a pediatric oncologist. Development of B43-Gen grew out of the researchers' search for a treatment for those 5,000 patients each year who fail chemotherapy and die of the disease.

### Strategy of Blocking Enzymes

The drug grew out of researchers' theory that cancer cells can be killed by blocking enzymes called tyrosine kinases, necessary for important cell functions such as division and repair. But kinases also exist in normal cells, and researchers in the past have been stumped by the difficulty of getting kinase-inhibiting drugs only to cancer cells.

The Minnesota researchers attempted to solve the problem by attaching a known kinase inhibitor, Genistein (or Gen), to a monoclonal antibody that targets a specific protein on the surface of leukemia cells. Monoclonal antibodies are engineered versions of antibodies used in the immune system to seek out and destroy foreign invaders such as viruses or bacteria.

Monoclonal antibodies are enjoying a research revival after failing to live up to initial hype in the biotech business as "magic bullets" against cancer. Early versions of the monoclonal antibodies were scientific duds because they were too big to penetrate tumors, Dr. Uckun said. But the B43 monoclonal antibody was built smaller than the original version, enabling it to penetrate the cell with the Genistein, a steroidlike substance derived from soybeans, he said.

### Survival of Mice

All the mice that received the B43-Gen treatment lived for the 120 days of the study, while most mice treated with standard chemotherapy died. The mice didn't suffer any side effects, according to the researchers. An examination of tissue from the mice showed the drug had killed virtually all of the cancer cells.

The B43 monoclonal antibody attached to another cancer-fighting compound, called pokeweed antiviral protein (or Pap), also fared better than standard chemotherapy in the study, although not as well as the B43-Gen combination. The Minnesota researchers have begun testing B43-Pap in cancer patients who failed previous chemotherapy, according to Dr. Uckun.

The disease went into remission in one-third of the patients treated with the drug, enabling them to undergo a bone-marrow transplant, he said.

From the **Wall Street Journal** February 1995

# Finding to help in gene therapy

**■ Research:** An easier way has been found to isolate all-important human stem cells.

By The New York Times

Researchers reported Thursday that they had found a simple way to isolate human stem cells, the elusive progenitors of all the body's red and white blood cells.

The method could quickly replace the current cumbersome methods and facilitate studies of these pivotal cells, which are needed for gene therapy and bone marrow transplants.

The trick, discovered by Dr. David Scadden and his colleagues at New England Deaconess Hospital in Boston, was to exploit the fact that stem cells are quiescent and do not grow in circumstances when other marrow cells do.

Scadden's group forced those other cells to grow and, as soon as they started to divide, forced them to commit suicide, leaving behind mostly stem cells.

About 1 in 5 cells was a stem cell with this method, whereas other methods typically ended up with a soup of marrow in which just 1 in 50 or 1 in 100 cells was a stem cell.

The new method, reported in the journal Science, comes on the heels of decades of efforts by researchers throughout the world to find a way to fish the tiny stem cells out of the huge pool of marrow cells where they live.

Although human marrow contains about 10 billion cells at any one time, just 100,000 of them are stem cells, Scadden said.

They are of immense interest because they form a pool of immortal cells that develop when needed into red or white blood cells.

Some stem cells will multiply and transform themselves into colonies of these specialized cells; others will divide and remain stem cells, replenishing the stem cells that were lost.

Researchers want to isolate stem cells to understand how blood cell production is regulated and to use them for gene therapy.

On a basic science level, investigators said, the stem cell system is awesome. For example, Scadden said, stem cells routinely send enough of their members down the path to become a type of infection-fighting white blood cell that ingests bacteria — to create 1 billion of these white blood cells, or neutrophils, each day.

Each neutrophil lives just 7 to 10 hours. Normally, the neutrophils circulate in the blood and percolate through the tissues as a sort of surveillance force.

When an infection begins, the stem cells go into overdrive, developing into neutrophils so quickly that at least 10 billion a day are made, Scadden said.

Because stem cells are immortal — in contrast to most cells, which undergo a fixed number of divisions and then die — they are the targets for many gene therapy studies in which the goal is to add new genes that will last a lifetime.

Scadden and others, for example, want to add genes to stem cells that would make them resistant to the human immunodeficiency virus, which causes AIDS.

Others are trying to add genes to healthy stem cells of cancer patients, to make them resistant to chemotherapy. Still others want to treat diseases like sickle cell by adding genes to marrow stem cells.

For all those theoretical and practical reasons, said Dr. Jerome Groopman, a hematologist at Deaconess who was not part Scadden's group, "there has been a very, very intense concerted effort to devise strategies to isolate stem cells."

From the **Register Guard**

Eugene, Oregon

January 1995

*Bob and Andrea Sacks share with us a beautiful poem by Dawn Hallman. This poem has brought them great comfort, as it will many of us. Our sincere thanks to Bob and Andrea.*

# *It Does Matter*

***It Does Matter That You Were Here....***
*Your courage and fight will never be forgotten.*
*We will always remember with pride the bravery it took to carry on in the face of overwhelming odds.*
*We will continue to be inspired by your example.*
*We will never forget all you taught us.*
*You are an example of true courage.*

***It Does Matter That You Were Here....***
*In fighting this disease you taught your doctors and nurses something new and put us one step closer to the cause and cure of this disease.*
*The legacy of medical research will always owe you a part of its knowledge.*

***It Does Matter That You Were Here....***
*You touched our lives. We are forever different for having known you. We will always carry the memories of joys and sorrows; laughter and tears; humor and pain; silliness and sadness. The light of those memories will forever burn in us and light our days and comfort us through the darkness of the nights.*

***It Does Matter That You Were Here....***
*Because of how you lived your fight, you encourage us to fight the obstacles in our lives.*
*Your fight inspires us to live our lives with courage and humor and laughter and joy. Your life inspires us to be honest with ourselves and others about our loss, our pain and our sorrow.*

***It Does Matter That We Are Here....***
*We will never forget. You are a part of us forever.*

*~Dawn Hallman*
*in honor of my daughter, Sashaw*

FA family newsletter

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**Newsletter Published by:**
Fanconi Anemia Research Fund, Inc.

**Medical Advisor for Newsletter**
N.T. Shahidi, MD

**Editors:**
Dave & Lynn Frohnmayer and Joyce Owen

**Layout and design:**
Tanya Harvey

**Printing donated by:**
Shelton-Turnbull Printers

**Distribution Support donated by:**
Amgen, Incorporated
The Edwin & June Cone Fund of the Oregon Community Foundation