THE FA FAMILY NEWSLETTER

Newsletter Number 9 January 1991

A semi-annual newsletter for families affected by Fanconi anemia, caring physicians and research scientists

Published by Fanconi Anemia Research Fund, Inc. Editors: Dave and Lynn Frohnmayer
2875 Baker Blvd. Eugene, Oregon 97403 Phone: (503) 686-0434

SECOND FA SCIENTIFIC WORKSHOP FURTHERS RESEARCH COLLABORATION: A PROGRESS REPORT

Our second annual scientific workshop on Fanconi anemia was held in Portland, Oregon on November 10 - 11, 1990. Approximately two dozen scientists and observers from six nations participated actively and commented on research in progress.

The workshop was sponsored by the Fanconi Anemia Research Fund, Inc. Financial support was generously provided by several Oregon-based foundations, the Pennsylvania-based Fanconi Anemia Research Foundation (established by Dr. Michael Greenberg), and by a donation from Dr. Vicki Athens.

INSIDE

PLEASE COMPLETE AND RETURN TO DR. VICKI ATHENS

Evaluations from virtually all scientists in attendance were extremely positive. New collaborations were established and previously unpublished research information was subjected to peer review. Several scientists have begun new projects. Progress is encouraging enough to justify repeating the workshop at least annually.

The workshop material is highly technical. We include a summary separately as Appendix 2 to this newsletter. Even though the project descriptions come primarily from "lay reader summaries" prepared by researchers themselves, the topics are often difficult for anyone but modern molecular biologists to understand.

The summary is attached so that FA families and those assisting in fundraising will know that their research dollars are assisting sophisticated efforts on the frontiers of scientific discovery.

As this newsletter goes to press, we are hopeful that several participants will summarize workshop proceedings for publication in one or more scientifically respected professional journals.

GMCSF TRIAL CONTINUES

Dr. Eva Guinan of the Dana Farber Cancer Institute and Children's Hospital in Boston is currently enrolling FA patients in a GMCSF clinical trial. She is attempting to stimulate the bone marrow function of patients using this colony stimulating factor. Patients who may be eligible for this study are FA patients under age 18 who have never responded or have stopped responding to androgen therapy or have had to stop an effective androgen therapy due to complications.

Patients must have had a recent bone marrow test which shows no evidence of clonal abnormality suggesting a preleukemic condition. Patients will be treated on an outpatient basis in Boston. The average length of treatment will be nine weeks. A variety of housing options is available.

If you feel your child may meet the above criteria, please have your physician call Dr. Guinan's secretary, Lisa, or her nurse practitioner, Karen, at 617-732-3315.

FA RESEARCH FUND, INC. GIVES FINANCIAL REPORT

Funds raised by FA families and friends in 1989 totaled $319,085. This amount does not include monies raised prior to the incorporation of the Fund, nor does it include money raised by families to offset their own extraordinary medical needs. In 1990, funds raised totaled $261,722.

Linda Solin, our FA Research Fund, Inc. coordinator, provided the following breakdown concerning expenditure of 1990 funds. Administrative expenses (rent, staff, printing, telephone, equipment and furniture), $18,933; fundraising expenses, $6,189; research grants, $147,995; FA Symposium, $23,628; FA Newsletter, $1,090 for a total of $197,835 in expenditures.

The amount spent on administrative expenses represents only 7% of funds raised in 1990. Our part-time coordinator worked on a paid basis for only six months in 1990 so this amount will increase in 1991. Nonetheless, compared to other charitable organizations, this is an astoundingly low figure.

MEDICAL REFERENCE MATERIALS ON FA AVAILABLE

Michael Greenberg, M.D. makes the following generous offer to FA patients and their physicians:

"I have available...a bibliographic listing of almost 600 medical and scientific articles about FA from the National Library of Medicine computer. These articles are highly technical and may be of only limited use to the lay person. However, they can, at the very least, provide an excellent 'reading list' for the pediatricians and/or hematologists caring for FA patients and families. I will supply this listing free of charge to anyone who requests it. Write for it at:

The Fanconi Anemia Research Foundation
Suite 300
900 East 8th Ave.
King of Prussia, PA 19406"

COMPLIMENTARY ROOMS OFFERED

Westin Hotels have offered complimentary rooms for cancer patients who must travel for treatment. Stays are limited to six weeks and are on a space available basis only. For reservations or additional information, contact the American Cancer Society in the city where the patient is to be treated.

LINDA SOLIN WILL HELP WITH YOUR FUNDRAISERS

Families wishing to begin fund-raising efforts can contact our coordinator, Linda Solin (503) 687-4658. She will provide sample letters, brochures, and helpful ideas on how to proceed.

Your letters to potential contributors should inform donors that our administrative expenses are kept to an absolute, bare minimum. The vast majority of funds raised go directly to FA research.

Fanconi Anemia
Research Fund, Inc.

66 Club Road Suite 390
Eugene, Oregon 97401
(503) 687-4658
FAX 503-484-0892

January 7, 1991

To FA Families:

The last newsletter suggested that FA patients who develop chicken pox be treated with Acyclovir. We would like the FA families to know this suggestion is not universally accepted.

This drug is used in patients with a primary immune deficiency, which is not the primary problem in FA. Acyclovir has not been adequately tested with regard to its effect on chromosome breakage. It has also not been evaluated with regard to possible bone marrow suppression in FA. Acyclovir can also cause kidney damage.

We suggest that FA families with exposure to chicken pox contact their physician immediately. Zoster immune globulin (antibody to chicken pox) can be given to prevent or ameliorate the subsequent development of chicken pox. Further measures must be considered on an individual basis.

Yours sincerely,

Blanche P. Alter, M.D.
Mount Sinai Medical Center
New York, NY

Yours sincerely,

Nasrollah Shahidi
University of Wisconsin
Madison, WI

FA FAMILIES CONTINUE TO GENERATE BADLY NEEDED FUNDS

Throughout this past year, FA families continued to make extraordinary efforts to generate funds for medical research. We are proud of you all, and deeply grateful for the many hours of hard work these numbers represent. The following amounts include only those deposits made by December 31, 1990. Some families are just beginning their fund-raisers.. We will report on their efforts in the next newsletter.

Phyllis Cafaro, aunt of FA patient Jimmy Lucarell, raised $106,615 in 1990. This represents over 40% of all funds raised by our organization this past year. We are enormously grateful to Phyllis for her hard work, dedication and determination to impact this illness.

Since we last reported on their efforts, Sandy and Marc Weiner have raised $23,704 for a total of $28,099. Vicki and Andrew Athens have raised $33,232 for a total of $35,232. Linda and Robert Scullin raised an additional $3,785, and have now raised $40,691 for our Fund. Bill and Jackie Lucarell raised $9,281 for a total of $38,979. Dottie and Richard Day who just joined our support group have already raised $3,360.

Fredi and Ron Norris raised $3,825 in 1990 for a total of $4,825. Gayle Licari contributed a most helpful $700 to our Fund. Margaret and Brian Curtis raised another $525 for a total of $5,795. David and Lynn Frohnmayer's efforts brought in $41,457 for a two year total of $235,677.

Leardon Keleher has just begun her fund-raiser and had raised $150 by the end of 1990.

We commend these families for a tremendous amount of hard work. Because of their consistent efforts, we are now funding eight research projects and have held our second annual international symposium on FA. Our deepest gratitude to each and every family willing to forego privacy and precious family time to work on behalf of this Fund. Tons of thanks to all of you!!

Funds have also been contributed to the FA Research Fund following the death of a precious family member. Funds have been contributed on behalf of Rebecca Dodd, Nancy Nicholson and Dennis Oster. We are grateful for these contributions but deeply, deeply saddened by the tragic losses which inspired them.

WORLDWIDE FA GROUPS ORGANIZE

Parents and scientists around the world have organized groups to provide support and facilitate medical research into FA. Appendix 1 identifies the names, addresses and purposes of these FA organizations.

MEET OUR BOARD

The Board of Directors of FA Research Fund, Inc. represents a wide variety of backgrounds and talents:

Dennis L. Solin, President of the Board, is a Certified Public Accountant and managing partner of Solin and Associates. Mr. Solin donates his professional services to our foundation as well as much of his staff time and equipment.

Joyce Owen, Ph. D. is a professor of biology at the University of Oregon. She also has a record of distinguished research in molecular biology.

Marla Rae Watson is Secretary to the Board of Directors. Ms. Watson is Executive Assistant to the Oregon Attorney General and has a background in public affairs and broadcasting.

Bruce Strimling, MD, is a pediatrician experienced in treating FA patients. He has also served on a variety of health related boards at the local, county and state levels.

Kathy Marzano, MS, is a medical rehabilitation counseling therapist with her own private practice in medical and general counseling. She focuses on the treatment of pain, stress and depression in medical patients.

Phyllis Cafaro is a shareholder in The Cafaro Co. She is also a civic volunteer with a great humanitarian commitment to our cause. She has effectively raised substantial funds and continues to seek financial commitments from public and private sources for our research.

A LETTER FROM OUR INTERN

Hi! I am new to the FA Research Fund, Inc. My name is Geri Young, and I am a student doing a six month placement through the University of Oregon. I am excited to be part of an effort which will hopefully find a cure for Fanconi anemia.

I have recently learned about The Hole In The Wall Gang Camp, which is a year-round center for children, their families and health care professionals coping with cancer and serious blood diseases. It is an Old West style camp located on 300 acres in the beautiful hills of northeastern Connecticut and surrounds a 44 acre lake - full of fish. In the summer, it offers an old-fashioned camp experience for children and young people and provides a safe and healthy environment in which fun, excitement and joy abound.

Medical care is provided by on-site physicians and nurses with special training in hematology/oncology. The fully-equipped health care dispensary is staffed 24 hours a day. Necessary laboratory studies and prescribed therapies, including administration of chemotherapy, can be performed at the camp. Wheelchairs and walkers are welcome.

In the months when the camp is not in operation, it is used as a resource center where counseling sessions are held for families who have lost their children because of these illnesses. The center accommodates seminar groups of physicians who convene for the purpose of understanding and improving oncological treatment of children.

The Hole in The Wall Gang Camp was founded by Paul Newman and is in its third year of service. It is generously supported by Newman's Own food companies but heavily depends, as well, on private and public donations. All summer programs are offered completely free of charge. Parents must only provide transportation for their children.

Children with active cancer or blood disease get preference in admission, but children who have been in remission long enough to be considered cured are also welcomed at The Hole In The Wall Gang Camp. Children spend a week at camp interacting with other children who have similar problems. They experience the joy of life in a safe, yet exuberant environment. Sounds exciting to me!!!

For more information, please write: The Hole In The Wall Gang Camp
565 Ashford Center Road
P.O. Box 156
Ashford, CT 06278
(203) 429-3444

Or call me at the FA Research Fund, Inc. (503) 687-4658

Kids,
I would love to have your pictures in my office. And if you want to draw me a picture, that would be very special! Geri

Are there any kids out there who would like a pen pal? Yes?? Write me a letter to let me know. Send your name, age, address and your favorite thing to do. Geri

OHIO REPORTS EARLY SUCCESS IN PERFORMING FA TRANSPLANTS

Dr. Richard Harris, Director of the Bone Marrow Program at Children's Hospital, Cinncinnati, Ohio, reports that his center has performed four sibling matched bone marrow transplants on children with Fanconi anemia. The first was performed in September, 1987, the second in January, 1989 and two were done in the spring of 1990. One transplant (Eric Miller's) was from perfectly matched sibling cord blood. All four transplants were successful. Two additional FA patients will be transplanted immediately using matched sibling donors.

The Children's Hospital in Cincinnati has done bone marrow transplants since 1981 and now performs approximately forty-five each year. To date the center has only performed matched sibling transplants with FA patients. In the near future, however, Dr. Harris plans to transplant an FA child with marrow from a perfectly matched, unrelated donor. Dr. Harris collaborates closely with Arleen Auerbach, PhD, and uses the protocol developed by Dr. Gluckman in Paris.

The Engle family from Colorado Springs wrote recently of the happy progress of their grown FA son:

"Forrest is now 38 years old. In September of 1989, he and his dad went to New York. Forrest had many tests done there (for research), and one of the suggestions made was to reduce the prednisone gradually. He had been taking 20 mg and is now taking 5 mg every other day. His liver function test in September showed a marked improvement which his doctor attributes to the prednisone decrease. His platelet count is stable (for him). He has a wonderful appetite and generally feels quite well."

We are delighted to learn of Forrest's long-term stability!

NEWS NEEDED

We hear repeatedly that parents appreciate hearing from other families affected by this illness. How you are coping with this difficult diagnosis, how your child or children are doing, results of different therapies, words of encouragement for others are all deeply appreciated. If you have lost a child to FA we will include a remembrance or whatever you feel is appropriate. Please send your editors whatever you are willing to share with the support group. So much of this newsletter depends on your contributions.

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Dear David & Lynn,

We have some wonderful news to report to you and other other FA families. On April 17, 1990, our 6 year old son, Eric, underwent the first bone marrow transplant in the U.S. using cord blood from his 6 month old brother, Ethan.

The procedure was done at Children's Hospital Medical Center in Cincinnati, Ohio, under the direction of Dr. Richard Harris, at the request of the International Fanconi Anemia Registry, using the Paris protocol.

On June 7, 1990, Eric was released from the hospital, and on August 27th he started first grade! His hemoglobin is now 12.0, platelets 170,000 and white blood count averages 2500.

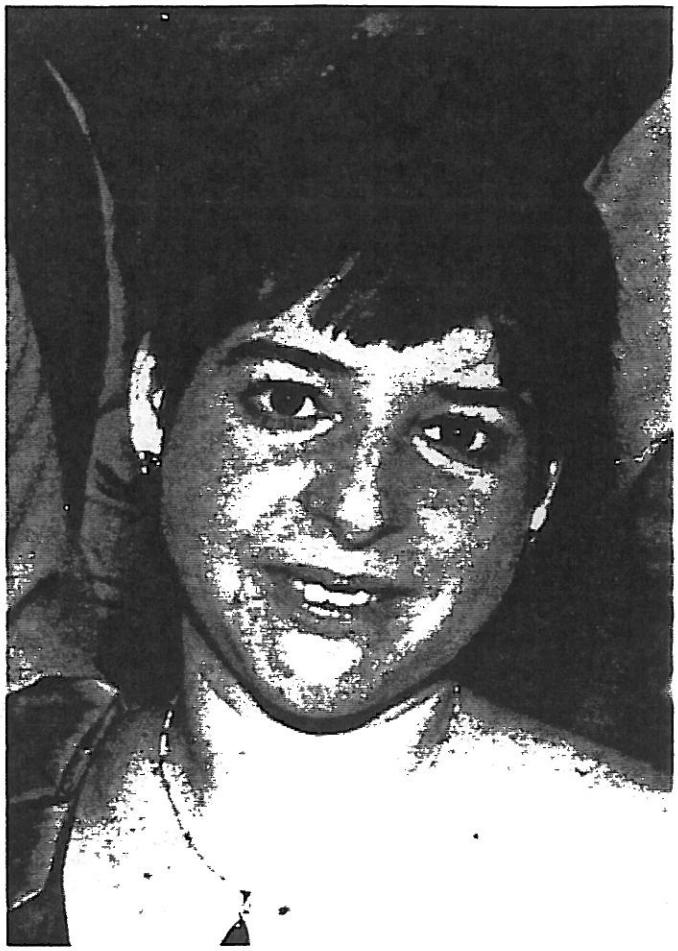
Needless to say, we are very thankful and pleased with his amazing progress. Not only were we blessed with an identical match, we were also fortunate to have a tremendously devoted staff at Children's Hospital during the 2 month stay.

Dr. N.T. Shahidi continues to follow Eric at the University of Wisconsin Hospital and Clinic. Should any of the FA families desire more information, please do not hesitate to call us at (608) 838-8775.

With warmest regards,

John & Barbara Miller
5109 Summer Trail
McFarland, WI 53558

On January 7, 1990, Nancy Nicholson passed on from complications of FA. She was 33 years old. Nancy's loving parents, Alice and Robert Nicholson, asked that we include the following poem together with special words of remembrance.



Do not stand at my grave and weep;
I am not there. I do not sleep.
I am a thousand winds that blow;
I am the diamond glints on snow.
I am the sunlight on ripened grain;
I am the gentle Autumn's rain.
When you awake in the morning's hush,
I am the swift uplifting rush
Of quiet birds in circled flight.
I am the soft star that shines at night.
Do not stand at my grave and cry.
I am not there; I did not die.

Author Unknown

"In memory of our loving and beloved Nancy, Gift of God, whose life blessed us for 33 years."

December 8, 1990

Alice Nicholson shared these lovely words in a recent letter:

"We have a special thing in our family that has been such a sweet reminder of Nancy. About a week before she died, while Susan (her sister) was visiting for Christmas, we were sitting around the kitchen table and I was remarking on how much we enjoyed the hummingbirds that came to our feeders in the back yard. Susan said she didn't like them because they remind her of big bugs (and she hates bugs). Nancy said - "Watch out, Sue, because when I die I'm coming back as a hummingbird." A week or so later she died but since then our hummingbird visits have taken on a new specialness. Susan now has a feeder attached to her apartment balcony and just loves her hummingbird visits. Have given several feeders to family members - just a little way to bring Nancy to thought."

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Monday Morning, December 17, 1990

Staff Photo by Kevin O'Connor

Rich and Dottie Day pose in front of the family Christmas tree with 3½-year-old son Adam, who has a rare hereditary form of anemia.

Prescription: Apply Love and Hope

By KEVIN O'CONNOR

CLARENDON — When he isn't driving a truck, Adam Day is an aspiring train engineer, dabbling sculptor and Ninja Turtle warrior whose plastic sword lies ready in the middle of the living room floor.

Adam is 3½ years old, a scant but sturdy 18 pounds and one of approximately 200 children in the world known to have a rare hereditary form of anemia that usually leads to death before adulthood.

That sentence usually silences people. One woman started to cry when she saw a photograph of Adam displayed by his parents, Rich and Dottie Day.

"If they can find a cure for this, it's going to cure a lot of problems."

Dottie Day

"I basically comforted her," Dottie says.

But enough of that. Adam has overturned a basket of clean laundry onto himself, adding to the scattered Matchbox cars and train track that temporarily halts foot traffic in the family's Clarendon apartment.

Rich and Dottie Day have their hands full. But with good family, good friends and good health insurance, they aren't looking for sympathy or financial support.

Instead, the Days are trying to raise research money for a disease that, because of its rarity, lacks celebrity spokesmen, star-studded telethons and charity galas.

Last month, the couple received a letter from the Oregon-based Fanconi Anemia Research Fund. "We write with a great sense of urgency," it began. The good news: A doctor has identified the chromosome of a gene that causes the disease. The bad news: There isn't enough money to continue research for more than a year.

And so between his day job, her evening job and the holidays, the Days are working to raise awareness and money as

(See Page 6: Adam)

Adam

Continued from Page One

part of a 175-family grass-roots support network.

Their cause promises to reach further than those afflicted with Fanconi anemia, a progressive illness in which a missing gene limits the body's production of platelets and red and white blood cells.

Although the disease is rare, discoveries about it relate directly to a better understanding of birth defects, leukemia and other cancers.

"If they can find a cure for this, it's going to cure a lot of problems," Dottie Day says.

Adam was diagnosed less than two month ago. But he was born with warning signs. He had a duplicate left thumb that was removed at nine months of age. One shoulder is lower than the other. And his hazel eyes are closely set.

After his first birthday, Adam began to weigh and measure less than other children his age. Rich and Dottie began a two-year battery of tests. They discovered their son's ailment by accident when a technician mistakenly ran an exhaustive blood examination rather than a simple one as requested by a doctor.

By this time, the couple had traveled with Adam to hospitals in Rutland, Burlington and Boston. To cope with the diagnosis, they joined the support network and began to read anything and everything about the disease.

"As far as we know, we're the only people in the state," Rich says.

But they are receiving an increasing amount of local assistance. Since starting their campaign, the couple has raised more than $2,000.

Friends are planning a bake sale and quilt raffle Saturday at the Rutland Mall. Employees are raising money at Howard Johnson's restaurant, where Rich takes Adam for an occasional dinner when Dottie works evenings. And the couple is investigating more formal fund-raising efforts with the assistance of First Vermont Bank.

Telling such a personal story publicly isn't always easy. Dottie says that the woman who cried was one of the first persons she encountered in her efforts.

"I told Rich, 'I'm not going to be able to handle this.'"

But they have — with strength and straightforwardness. And so the couple talks to reporters, bankers, passersby at a shopping center. They scan a 2-inch-thick medical dictionary to explain another term. They peel the Silly Putty mustache off the small upper lip of Adam, their biggest inspiration.

Says Dottie, "The only thing we can do is raise funds."

And Rich, "If we can save some other little boy's or girl's life, so be it, we will."

Contributions to the Fanconi Anemia Research Fund Inc. can be sent to First Vermont Bank, Rutland, Vt. 05701.

Ceil Meloling delivered news of tragedy and hope. Two of her children, Sean and Colleen required bone marrow transplants because of FA. Sean died in Seattle at age 14 in 1989, after a mismatched marrow transplant from his father was not successful.

The Milford, Connecticut Mirror carried a beautiful tribute to Sean's courage, and to the outpouring of community support inspired by Sean and his family.

Ceil wrote us in September, 1990 of the positive outcome of daughter Colleen's marrow transplant in Paris. Brother Keith was her donor. The attached stories describe a family full of optimism and inspiration for us all.

Home for good

Life almost normal for Colleen Satterlee

By AIMEE SUHIE
Associate Editor

Colleen Satterlee received the best news of her life last week: Doctors told her her blood count was normal for the first time since she was diagnosed with Fanconis anemia seven years ago.

When a visitor sees this tiny 11-year-old bundled up on the couch of her 33 Knollwood Road home, it is easy to imagine the harrowing four months she's just spent in a strange country — undergoing chemotherapy and a bone marrow transplant and enduring the stares of strangers gawking at her bald head and face mask.

But the minute she opens her mouth, and that pixie voice starts to answer questions and comments on everything — throwing in words in perfectly accented French — her spunk and wit shine through.

"I'm fine, and I'm going back to school Dec. 2," she says with such assurance her mother, Ceil Meloling, cringes a little.

"The doctor in Paris said she could resume a normal life six months after the transplant," Meloling says. "But her doctor here suggests she not go back to school until March."

The Central Grammar School sixth-grader is being tutored at home since she returned from Paris two weeks ago, where she and her mother and various devoted relatives rotated staying with Colleen and her mother since May. She underwent the transplant May 31 with her brother, Keith Satterlee, 19, of West Haven, serving as her bone marrow donor.

Because it was a perfect sibling match, doctors predicted the smooth progress of Colleen's recovery. The graft "came in" eight days after the transplant, she returned home on schedule — and now the news of the normal blood count.

Her mother speaks sadly of the circumstances which were so different in the case of Colleen's brother, Sean, who died last year at the age of 14 of the same disease. Sean's father, Bruce Satterlee of West Haven, was not a perfect match when he donated his marrow to his son at a Seattle hospital.

Both children needed marrow to generate new white and red blood cells as well as platelets which the rare disease destroys.

And as far as Colleen is concerned, Paris and pain and 20 pills a day are a thing of the past. Although she must stay away from salt, hot dogs and cold cuts because she is on prednisone, should eat only fresh foods and must still take eight pills a day, she says she is ready to resume her life.

She hops on her bike to ride down to

Chucky's Country Store on New Haven Avenue when the mood strikes and is back in dance class at Danceworks, 354 New Haven Ave.

But what she really wants is to go to the mall with her friends on a Friday evening.

"We're still working on that," Meloling said. "We hope she can go to the mall and be around people soon without wearing her mask."

For the time being, Colleen can only have friends in a few at a time and must wear the mask if she goes anywhere indoors with a lot of people.

She also must have all the immunizations she got as a baby again, because the chemotherapy that wiped out her bone marrow also destroyed all the protection she'd gotten against such diseases as diphtheria and polio.

"She can never get live vaccinations, however," Meloling said. "That means she can't be immunized against measles, mumps and rubella. But the doctors feel that since everyone else has these immunizations, she should be pretty safe."

Meloling was also amazed to discover the $51,000 fund which the Milford community had raised for Colleen still has about $16,000 left. Although their first apartment in Paris cost $100 per day, food was exorbitant, and the trip home on the Concorde was a necessary expense, the fund will still pay for some medical visits and medication.

"Whatever is left, we would like to donate to Fanconis anemia research," Meloling said. "That's what we did with Sean's fund, too, in his memory. But that was right before we knew Colleen was going for the transplant. We always knew her transplant would happen some day, but we thought we would have years. It was extremely upsetting to have to go so soon after the experience in Seattle with Sean. If we had known ... but I'm still glad we donated the money in his memory, because the people raised it for him.

"Sean would have wanted to find a cure for the disease that killed him."

Community Forum

Sean, a role model for Milford youth

By DON DeFORGE

Sean Satterlee is a role model for the youth of Milford. His battle with Fanconis Anemia is what most people will remember about Sean. His blood disorder is only a small part of his story. I was given the opportunity to meet him in one small frame of a 14-year picture of his life. But in that opportunity to meet him, he touched me in a very special way. The way in which he touched me is the way in which he will continue to touch all who knew him while he was here with us.

Sean's death is not the end but the beginning of life. A life that each and every youth in the city of Milford can make use of and learn from or simply allow to go to waste.

Sean's life stood for things that we talk about but fail to practice. He stood for things that we want to believe in but do not have the courage to face. Most importantly, his life exemplified a faith that we casually claim but never truly realize.

I met Sean a few days before he was transferred from Yale-New Haven Hospital to the Fred Hutchinson

In those few days he showed to me the courage of a man, not that of 14-year-old boy.

With constant worry and doubt in his mind, his faith allowed him to continue to try to do what was expected. He would fight and not complain. As Sean continues to live on in us, he would expect us to be less troubled by life. His message would be to stop complaining and to start acting.

There always will be family disagreements, problems in school, and general emotional unrest in our lives. Sean would ask that we challenge these problems and do the best with them that we can do.

Sean was given the ability to look beyond. He was allowed that special privilege of stepping outside of himself and being concerned about others.

When we spoke we spoke about his family. He was concerned about his mother and father, sister and brother, and his grandparents whom he loved dearly. The one thing he avoided discussing was his illness. He did not look for sympathy but tried to comfort

My main remembrance of Sean will be one enveloping love of others.

Sean was a gift to this world. Gifts are not to be ignored, or hidden away. Gifts are to be used, savored, and shared. Sean's message to me was clear. We must always care about each other. We must always share with one another. With this caring and sharing comes the greatest gift — LOVE for one another.

Role models and heroes don't all come from Hollywood, the world of sports or the political arena. Many of these giants are best described as real people. As Sean lives in us he will always be a giant, a role model, and a hero to the youth of Milford.

Let us look to the future with joy and hope that in knowing our special friend we can approach life optimistically and in a spirit of understanding, an understanding of ourselves and those we meet each day.

Don DeForge , V.M.D., Youth Minister St. Gabriel Church and Office of Religious Ministry, Yale-

NEW FAMILIES TO ADD TO FA SUPPORT GROUP

1. Jean & Ken Atkinson
   6442 E. Jamisen Circle S.
   Englewood, CO 80112
   303-741-5854

2. Carol & Bob Baden
   2421 W. Warner
   Chicago, IL 60618
   312-539-3458

3. Marie-Pierre & Charles Bichet
   12. Allee Emile Zola
   91330 Yerres FRANCE

4. Mike & Bronwen Carr
   Millstones
   Kings' Lane
   Barrowden
   Ruckland LE 158EF
   United Kingdom
   57287 861

5. Richard & Dorothy Day
   P.O. Box 173
   N. Clarendon, VT 05759
   802-773-6666

6. Don & Jennine Dorman
   109 E. 2nd
   Waterford, PA 16441
   814-796-2212

7. Nancy E. Fena
   1575 Adrian Rd.
   Burlingame, CA 94010
   415-697-6020

8. Susan Ferrell
   4235 S. Four Mile Run
   Arlington, VA 22204
   703-521-9395

9. Diana Fitch & Darrell Blecher
   6470 Jackson St.
   Pittsburg, PA 15206
   412-441-8316

10. John & Brenda Gooch
    P.O. Box 844
    Adamston, PA 19501
    215-484-1278

11. Terry & Tino Huertaz
    3011 Sol De Vida NW
    Albuquerque, NM 87120
    505-831-2194

12. Joe & Lynn Linsenman
    7465 Miller Dr.
    Bath, PA 18014
    215-837-8374 (H)
    201-475-5567 (His work)
    215-954-4376 (Her work)

13. Michael & Pam McCoury
    1020 Laurel Dr.
    Louisville, GA 30434
    912-625-3477

14. Gene & Karen McDaniel
    204 B. Lexington Dr.
    Clarksville, TN 37042
    615-645-1048

15. Moshe Moskowitz
    c/o Mike Tauber
    1 Acer Ct.
    Monsey, NY 10952
    914-425-0252 (H)
    914-425-1288 (W)

15. Jan & Richard Turner
    63 Lakewood Dr.
    TAUPO NEW ZEALAND

CHANGES IN ADDRESS

1. Lynne Baervoets
   3057 Carroll
   Montreal, P.Q.
   Canada
   H4K 2G5

2. Diane & Michael Bradley
   52 Sandlewood Ct.
   Rochester Hills, MI 48307
   (313) 651-0921

3. Mr. & Mrs. Jimenez
   8731 Sotheby Ct
   Fair Oaks, CA 95628

4. Alice & Robert Nicholson
   8631 E. San Lucas Dr.
   Scottsdale, AZ 85258
   602-948-1509

5. Does anyone have an address for Vicki Ware?

APPENDIX 1: FA GROUPS FORMED: A GUIDE TO OUR ASSOCIATIONS

Many family and community efforts have begun since your editors first searched nearly 6 years ago for other FA families. To avoid confusion, to simplify how to seek support resources and to clarify funding sources for scientists, we list the following organizations devoted to FA families, FA medical research, or both.

1. USA: Fanconi Anemia Research Fund, Inc.
   66 Club Road, Suite 390, Eugene, OR 97401
   Coordinator, Linda Solin
   Phone: (503) 687-4658
   FAX (503) 484-0892

   Dave and Lynn Frohnmayer (your editors) are advisors to the Fund.
   2875 Baker Blvd, Eugene, OR 97403
   Phone: (503) 686-0434

The Fund publishes this semi-annual newsletter, provides family support services, raises funds nationally for research, supports worthy scientific research proposals worldwide, and conducts an annual international scientific workshop on FA.

The Fund is governed by an independent Board of Directors. Funding proposals are screened by independent scientific experts. The Fund is a 501(c)(3) non-profit corporation under the Internal Revenue Code. Contributions to the Fund are tax deductible to the donor under that law.

2. USA: The Fanconi Anemia Research Foundation
   Suite 300 / Linpro Centre
   900 East 8th Ave., King of Prussia, PA 19406
   Phone: (215) 768-8023; FAX (215) 337-9548
   Michael I. Greenberg, M.D., President
   Constance M. Gray, Executive Director

The Foundation collaborates closely with the Fund. Dr. Greenberg and his colleagues have provided generous financial support for the FA workshops and for numerous FA research projects. The Foundation and the Fund have jointly considered and shared funding responsibility for selected scientific research projects. We expect to continue this partnership in the future.

The Foundation is a non-profit entity organized under Pennsylvania law. It is governed by an independent Board of Directors and has access to scientific expertise to evaluate project funding requests. The Foundation is a 501 (c)(3) entity under the Internal Revenue Code. Contributions are tax deductible.

3. Italy: Associazione Italiana per la Ricerca sull' Anemia di Fanconi (A.I.R.F.A.)

   Via San Mandato
   50,.I-80136 Naples, ITALY
   Phone: (39) (81) 34.77.21 or (39) (81) 5493678
   Contact: Dr. Giovanni Pagano

Engages in family support with Italian families, pursues scientific research on FA, raises funds,

arranges meetings and collaborations with European FA families and scientific researchers.

4. Germany: Betroffenengemeinschaft "Fanconi-Anamie"

c/o Cornelia Sowa-Dietrich & Ralf Dietrich
Bockenweg 4
4750 Unna-Siddinghausen, Germany

Provides support for German and other European families. Has arranged meetings with West and East German FA families following reunification. Raises funds for FA research support. Helps generate FA research interest in scientific and medical centers in Germany and Europe. Publishes regular extended family support newsletters in German. Also has prepared family letter for The Netherlands, Spain and Czechoslovakia.

5. France: Association Française de la Maladie de Fanconi - AFMF

Contact: Alain Silverston
Work: 50, Route de la Reine
B.P. 85
92105 Boulogne Billancourt Cedex
France
Phone: (1) 46-84-36-81
Residence:
10 Rue Emile Zola
94400 VITRY FRANCE

Support group founded with the assistance of the Bichet family. Organized with approximately 15 FA families to further two major purposes: (1) develop mutual family assistance; and (2) help science by raising funds. The scientific Council of this organization includes Professor E. Gluckman, Professor Jean Bernard and Professor Jean Dausset (Nobel Prize).

6. United Kingdom: Fanconi Anemia Breakthrough: United Kingdom (F.A.B.U.K.)
c/o David Westmoreland
4 Pateley Rd.
Woodthorpe, Nottingham
England NC3-5GF
0602-269634

As is true of all listed organizations, we are gratified by the energy, close collaboration and deep commitment of these families and scientists. If we have overlooked other FA resources, please give us information for the next FA Family Newsletter.

APPENDIX 2: SECOND ANNUAL FANCONI ANEMIA SYMPOSIUM - A SUMMARY

Diagnostic Issues Noted

Scientists and treating physicians in attendance agreed that Fanconi anemia is significantly underdiagnosed or diagnosed belatedly. This problem poses significant problems for therapy, family planning and related issues.

Obviously, the wide variety of presenting symptoms of FA (clinical heterogeneity) contributes to the difficulty. However, scientists also noted that the DEB test or other chromosomal breakage tests are not routinely used when the presence of various physical manifestations or birth defects should suggest FA as a possible underlying diagnosis.

A number of scientists agreed to write articles for specialized medical journals such as radiology, urology, orthopedic and plastic surgery and hematology to help broaden the recognition of FA in related medical specialties.

Bone Marrow Transplantation

Updates were received from two major centers with significant experience in FA marrow transplantation. (A representative of the Paris group was invited, but unable to attend).

Dr. I. Dokal of the Hammersmith Hospital in London reported on the Hammersmith experience with FA from 1977 - 1990. Twenty-three patients with FA were transplanted during this period of time. Two, transplanted before 1980, received high dose cyclophophamide conditioning and both died. Subsequently 21 patients received conditioning with low dose cyclophophamide 5mg/kg/4 and total body irradiation 200 cGyx3. Eleven of 21 received HLA identical sibling marrow; seven out of this group (64%) survived.

Hammersmith Hospital transplanted five FA patients from partially matched relatives and five from matched unrelated donors (MUD). Only one patient is alive of the five (20%) who received marrow from a partially matched relative compared to two of the five (40%) transplanted from matched unrelated donors. Dr. Dokal wrote: "We conclude that allogenic BMT using a low dose cyclophosphamide protocol is a satisfactory treatment for FA patients who have a normal HLA identical sibling. MUD-BMT (matched unrelated donor bone marrow transplantation) should be considered in patients who lack an unaffected HLA identical sibling."

Dr. Fred Applebaum of the Fred Hutchinson Cancer Research Center reported on the Seattle experience in FA transplantation since 1973. Dr. Applebaum writes: "Twelve patients with Fanconi anemia have undergone marrow transplantation with a resulting cure in eight patients. The four patients who were not cured died because of complications of the transplant, principally graft-versus-host disease or renal failure. Results of marrow transplantation in patients with Fanconi anemia who have developed a subsequent leukemia were not as favorable. Only one of five such patients transplanted survived free of disease more than five years after the transplant. Thus, although we can cure two-thirds of patients with Fanconi anemia without leukemia, if transplant is delayed, results are considerably worse. In Seattle, we are working hard to try and improve upon results of marrow transplantation in patients with Fanconi anemia. Our research is directed towards decreasing the toxicities associated with the preparative regimen as well as decreasing the incidence of graft-versus-host disease. It is our view that these studies are extraordinarily important since there is no cure for Fanconi anemia other than marrow transplantation, and that with the development of the National Marrow Donor Program transplantation should soon become a real option for virtually any patient with this disorder."

Role of Oxygen Toxicity in FA Victims

Considerable discussion of both American and European researchers focussed on the oxygen-sensitive nature of FA cells.

1. Experiments with superoxide dismutase therapy

Dr. Johnson Liu of the National Institutes of Health authorized publication of the following "lay summary" for our Newsletter:

"As you know, Fanconi's anemia is a genetic disorder which causes low blood counts and bone

marrow failure. The basis of the disorder is felt to be damage to the DNA or genetic material of cells which cannot be repaired adequately. Furthermore, this damage seems to be increased from by-products of oxygen metabolism in the air we breathe. We are interested in the use of drugs which might decrease the amount of genetic damage in patients. We are currently testing a drug called superoxide dismutase. This is a normal human protein which protects cells from toxic oxygen by-products. It can be administered safely to patients and, hopefully, may decrease the amount of genetic damage. In future, we would like to develop drugs like this which might also increase the blood counts. If you have questions about our study, please contact the Fanconi Anemia Research Fund or Dr. Johnson Liu at the NIH (1-301-496-5093).

2. The Role of Oxygen Damage in FA Cell-Cycle Research

Dr. Hoehn's laboratory in the Department of Human Genetics at the University of Wurtzburg, Germany reported experiments designed to bring better understanding to cell cycle disturbances in the growth of FA victim cells. Dr. Hoehn reports: "FA cells are delayed or even completely arrested in the G2 phase compartment of the cell cycle; this particular cell cycle stage is thought to act as a kind of filter where genetic damage must be repaired before a cell is allowed to enter cell division. Several experimental approaches in our laboratory are currently directed at finding ways of how to mitigate the endogenous G2 phase cell cycle defect in Fanconi anemia cells. The single most important clue obtained from these studies to date is that fibroblast-like cells from Fanconi anemia patients tolerate atmospheric oxygen less well than cells from healthy donors."

3. Oxygen Free Radicals and Iron Levels in FA Victims

Giovanni Pagano, PhD from Naples, Italy reported on further research he and his colleagues have pursued on plasma haptoglobin levels and the clinical conditions of FA patients. These researchers suggest various inquiries to study whether "oxygen scavengers" can be used to correct the "wrong steps" in oxygen and/or in iron metabolism in FA subjects.

Growth Factors

Previous editions of the FA Family Newsletter have described the proposed trials with "growth factors" - cloned substances that may stimulate one or more lines of blood production. Dr. Blanche Alter of the Mount Sinai Hospital in New York reported on her experiments with EP (erythropoietin) to stimulate red cell production. Schedule conflicts prevented attendance by invited representatives of Children's Hospital in Boston. Consequently, workshop participants did not evaluate updates in the treatment of aplastic anemia, or FA victims by GMCSF.

Workshop participants expressed hope that combinations or "cocktails" of various growth factors - including GMCSF and Interleukin 3 - might generate significant future treatment experiments. A recently developed growth factor, the "steel factor" or "stem cell factor" was mentioned as a potentially valuable future therapy for FA patients. [Editors' note: following the workshop we learned that two laboratories are beginning *in vitro* FA studies of the steel factor in combination with other colony stimulating factors. Depending on FDA and drug company approvals, human trials may begin in approximately one year].

We caution explicitly that FDA and drug company approvals have not yet been obtained for many speculative growth factor treatments of FA victims. The effect of such treatments, while hopeful, is yet unknown, and the possibility that proposed therapies could hasten the development of leukemia is a risk that knowledgeable scientists continue to evaluate. Your treating physician should be consulted should you wish to participate with these major medical centers.

Gene Research

Reports of research in progress revealed several alternative approaches toward isolating the gene or genes responsible for FA. As was the case last year, researchers agreed that locating, cloning and study-

ing the molecular defect should be our highest priority. Among the approaches discussed at the workshop were the following:

A. Linkage Analysis

Previous editions of this newsletter have contained descriptions of the work of Arleen Auerbach, PhD of The Rockefeller University in attempting to map the FA gene(s) by linkage analysis using RFLP markers. Dr. Auerbach presented information with lod scores suggesting linkage between Fanconi anemia in some families and chromosome 20q. Dr. Auerbach's research data supporting this chromosome assignment has been accepted for publication.

The next steps are to narrow the map on the target chromosome location and then to examine candidate genes within that area.

B. Functional Complementation

Dr. Manuel Buchwald is attempting to isolate the FA genes by focusing on the extreme sensitivity of FA cells to chemicals that crosslink DNA, particularly mitomycin-C (MMC). FA patients have a profound defect in their ability to repair the damage caused by these chemicals. Dr. Buchwald introduces cDNA from normal cells into FA cells using vectors containing the Epstein-Barr virus replicon, and then treats the cells with MMC. Only those cells that have incorporated the normal gene can survive. Molecular genetic techniques are now being applied to isolate the FA gene from the surviving cells.

In addition to his attempts to secure the gene location, Dr. Buchwald has continued his pioneering work in identifying "complementation groups", a process which helps identify how many genes generate the FA defect.

C. Rodent Mitomycin C-Sensitive Mutants

It has been shown that rodent cell lines are a useful tool for the isolation of human genes. Recently, Dr. Margaret Zdzienicka of Leiden, The Netherlands, has isolated a mitomycin C-sensitive V-H4 mutant of Chinese hamster cells which has the same characteristics as cells derived from FA patients. DNA from normal human cells can complement or correct the defect in the V-H4 cells but DNA from FA-A (complementation group A) cells cannot, showing that the defective gene in the V-H4 cells is analogous to the FA-A gene.

Studies are currently being pursued to isolate the FA-A gene using this unique mutant. Human DNA can be isolated from the corrected V-H4 cells and characterized when the V-H4 cells take up the "proper" piece of human DNA. This correcting material can subsequently be isolated and characterized. Additional transfection is in progress. Once the FA-A gene is isolated and characterized, we will understand the precise molecular defect in FA-A.

D. FA Gene Isolation by Complementary Studies

Investigator Robb Moses reports as follows:

"The research on Fanconi anemia in this laboratory has two goals: identification of the biochemical defect in the cells of affected individuals and isolation of the gene. We are pursuing our first goal by introducing small DNA molecules which have been damaged by chemical links between the two strands of the molecules. It is known that Fanconi anemia cells show increased sensitivity to such damage. However, it has not been clearly shown that such damage is refractory to repair in Fanconi anemia cells. We have demonstrated that the repair of DNA chemical cross links is reduced markedly in Fanconi anemia cells. This gives us a basis for proceeding to identify the specific biochemical defect in the disease.

In complementary studies we are attempting to compensate for the cellular sensitivity to cross-linking damage by introduction of the normal gene. We are attempting to do this in tissue cultures of Fanconi anemia cells by use of two different DNA preparations or 'libraries'. So far we have encouraging results with cells which have been returned to normal resistance to cross-link damage, but we have not yet been able to recover the gene.

E. Selective Amplification Cloning Strategy

Jean-Michel Vos suggests that FA cells might be mutated in a function controlling tumor suppressor activity because of the recessive nature of this disease. The goal of his project is to isolate the

normal homologue of the defective FA gene and determine the molecular role of its gene product in the development of normal versus FA individuals.

Since selection is an optimal condition for gene amplification (duplication) and since FA cells are hypermutable, it is speculated that the partially defective FA genes can be amplified under selective pressure. DNA crosslinking will be achieved by a photochemotherapeutic drug, psoralen, in the presence of UV-A light (PUVA). As an alternative cloning strategy, Dr. Vos is using DNA mediated transfer technology to complement the PUVA sensitivity of FA cells; the principle will be to select PUVA resistant FA cells after their transfection with a human episomal vector carrying either an expressed cDNA or genomic library prepared from normal human lymphoblastoid cells.

Once identified and cloned, the FA gene and its normal homologue will be used with the dual purpose of disease prevention through genetic screening and disease treatment through the development of specific therapy. This study may offer a general approach for the molecular isolation and characterization of gene(s) that might be defective in other DNA damage sensitive recessive cancer-prone human syndromes.

F. Gene Cloning Through Analysis of the Drosophilia mus308 Gene

James B. Boyd is studying a potential analogue of Fanconi anemia in the model genetic organism Drosophila (fruit fly). The goal of this program is to isolate a Drosophila gene that can then be employed to recover the corresponding human gene. Cell cultures derived from Fanconi anemia patients exhibit four unique properties that are shared by the Drosophila mus308 mutant. The concurrent association of this unique set of properties with single genes in both organisms strongly suggest that the mus308 gene encodes the same function as one of the Fanconi genes. A nuclease isolated from FA-A cells has isoelectric point shifted from that of the nuclease of normal cells. The Drosophila mus308 nuclease shows the same shift in isoelectric point compared with that from normal Drosophila cells. This correlation has stimulated efforts to clone the mus308 gene by chromosomal walking. Cytogenetic information necessary for that effort has been accumulated during the past year. This study has localized the mus308 gene to a very precise chromosomal position. With that information it will soon be possible to recover the DNA sequences from that portion of the chromosome. Once those sequences are available, the position of the mus308 gene will be identified by using the available mutants. The mus308 gene sequences can then be used to recover the corresponding human gene sequences.

Gene Therapy

Tremendous progress has been made in recent years toward making gene therapy a reality for certain genetic illnesses. Scientists present at this symposium discussed progress to date, and problems still needing resolution before this therapy is available to FA patients.

Dr. Donald B. Kohn of the Children's Hospital in Los Angeles, summarizes the status of gene therapy as follows:

"Many human genetic diseases of blood cells (eg Fanconi's anemia, sickle cell anemia, 'bubble boy' disease) have been successfully treated using bone marrow transplantation. Currently, such transplants may only be done if the patient has a marrow donor with the same tissue type. New treatments are needed for the majority of children who do not have a suitable donor. Gene therapy techniques will attempt to correct these genetic diseases by putting normal copies of the responsible gene into the patient's cells. Each patient could then be transplanted using his own genetically corrected bone marrow.

The technical hurdles to implementation of gene therapy are the need to efficiently put the gene into a large number of bone marrow cells and to have the gene work properly in the blood cells which are made by the marrow. The field of gene therapy has made considerable progress in the past few years as new basic knowledge has been obtained by many scientists about the biology of genes, viruses and blood cells."

To All Fanconi Anemia Families:

Dr. Vicki Athens of our support group has offered to assume a leadership role in organizing a weekend symposium for Fanconi anemia families. She is asking that all families in our support group return the following questionnaire, indicating level of interest in this idea. Our deepest gratitude to Vicki for spearheading this exciting opportunity.

An interesting idea has come up for all of us. Below is a questionnaire directed to Fanconi anemia families, relatives, doctors, or interested persons. I would like to organize a Fanconi Anemia Family Symposium for a weekend (perhaps at a holidome type setting, etc.). This symposium would allow families to meet, discuss and learn more about Fanconi anemia. An agenda has not been made nor has a location been chosen. Please fill out the questionnaire below and return it to me. Dr. A. Auerbach has expressed an interest in being present for this symposium. Thanks, Vicki A. Athens.

_____ Yes, We are interested in a Fanconi anemia symposium.
_____ No, No interest in this meeting.

Western US _____
Midwest _____
East US _____
Southern US _____

Fall _____
Winter _____
Spring _____
Summer _____

Name: _____
Address: _____
Phone: (____) _____ - _____

Topics you would like to hear discussed:

1. _____ 2. _____
3. _____ 4. _____
5. _____ 6. _____

____ Yes, I would like to help organize.
____ I would like to help but I cannot.

Other recommendations:

Return to: Dr. Vicki A. Athens
29113 East River Road
Grosse Ile, MI 48138