Fanconi anemia and its diagnosis:

Fanconi anemia (FA), named for Swiss pediatrician, Guido Fanconi, is one of the inherited anemias that leads to bone marrow failure (aplastic anemia). It is a recessive disorder: if both parents carry a defect (mutation) in the same FA gene, each of their children has a 25% chance of inheriting the defective gene from both parents. When this happens, the child will have FA.

There are at least 13 FA genes [A, B, C, D1 (BRCA2), D2, E, F, G, I, J, L, M and N]. These 13 account for the majority of the cases of Fanconi anemia. Mutations in FA-A and FA-C account for FA in 76% of patients worldwide.

FA occurs equally in males and females. It is found in all ethnic groups. Though considered primarily a blood disease, it may affect all systems of the body. Most patients develop bone marrow failure, necessitating a bone marrow transplant. Many patients eventually develop acute myelogenous leukemia (AML). Patients who live into adulthood are extremely likely to develop such cancers as head and neck, gynecological, and/or gastrointestinal and at a much earlier age than in the general population. Patients who have had a successful bone marrow transplant and, thus, are cured of the blood problem associated with FA still must have regular examinations to watch for signs of cancer. Many patients do not reach adulthood.

Fanconi anemia patients are usually smaller than average. FA usually reveals itself before children are 12 years old, but in rare cases no symptoms are present until adulthood. Patients may feel extreme fatigue and have frequent infections. Nosebleeds or easy bruising may be a first sign. Blood tests may reveal a low white, red cell or platelet count or other abnormalities. Sometimes myelodysplasia or AML is the first sign of FA.

FA sometimes is evident at birth through a variety of physical defects. These may include any of the following:

* Thumb and arm anomalies: an extra or misshapen or missing thumbs and fingers or an incompletely developed or missing radius (one of the forearm bones).
* Skeletal anomalies of the hips, spine or ribs.
* Kidney problems.
* Skin discoloration (café-au-lait spots); portions of the body may have a suntanned look.
* Small head or eyes.
* Mental retardation or learning disabilities.
* Low birth weight.
* Gastrointestinal difficulties.
* Small reproductive organs in males.
* Defects in tissues separating chambers of the heart.

The definitive test for FA at the present time is a chromosome breakage test: some of the patient's blood cells are treated, in a test tube, with a chemical that crosslinks DNA. Normal cells are able to correct most of the damage and are not severely affected whereas FA cells show marked chromosome breakage. There are two chemicals commonly used for this test: DEB (diepoxybutane) and MMC (mitomycin C). These tests can be performed prenatally on cells from chorionic villi or from the amniotic fluid.

Many cases of FA are not diagnosed at all or are not diagnosed in a timely manner. FA should be suspected and tested for in any infant born with the thumb and arm abnormalities described previously. Anyone developing aplastic anemia at any age should be tested for FA, even if no other defects are present. Any patient who develops squamous cell carcinoma of the head and neck, gastrointestinal or gynecological system
at an early age and without a history of tobacco or alcohol use, should be tested for FA. Many FA patients show no other abnormalities. It is absolutely essential to test for FA before contemplating bone marrow transplantation for aplastic anemia or treatment for cancer. FA patients respond extremely poorly to standard chemotherapy and radiation protocols.

While the total number of FA patients is not documented worldwide, scientists estimate that the carrier frequency (carriers are people carrying a defect in an FA gene, whose matching FA gene is normal) for FA is somewhere between 1 in 600 and 1 in 100.

**The Fanconi Anemia Research Fund, Inc:**

Lynn and Dave Frohnmayer started the Fanconi Anemia Research Fund, Inc., in 1989, to fund research into this disease and to provide support to affected families worldwide by medical referral, education, publications, and annual family meetings. To this end, over $18 million has been raised since the Fund’s inception.

In the area of research, donors to the Fund have seen their gifts multiply manyfold. 35 laboratories have received support from the Fund for over 132 research projects to study FA. Many of these researchers have gone on to receive major grants for FA research from the National Institutes of Health and other governmental and nationwide agencies. Grants from private foundations have helped us move FA science faster than ever thought possible.

In addition, the Fanconi Anemia Research Fund, Inc., publishes *Fanconi Anemia: A Handbook for Families and Their Physicians; Fanconi Anemia: Standards for Clinical Care;* the FA Family Newsletter, the Science Letter, the Fanconi Anemia International Directory, and the FA Courier, a publication to encourage families to contribute research materials, such as tumor samples, for FA research. These publications are sent worldwide to thousands of researchers, physicians, and families.

The Fund also convenes an annual International Fanconi Anemia Scientific Symposium at which researchers from around the world present the results of their research. The Symposium in 2006 was held in Bethesda, MD, and 114 researchers presented their research to over 226 participants from 15 countries. The Fund also convened a bone marrow transplant conference in April 2001, at a meeting in Chicago to allow transplanters the opportunity to share their transplant protocols for FA patients and to collaborate with one another. In April 2002 and, most recently, in April 2006, the Fund sponsored a meeting of leading cancer experts to discuss the solid tumors that affect FA patients. In March 2003, the Fund held the Standards for Clinical Care Conference to update the *Fanconi Anemia: Standards for Clinical Care* handbook. In June 2004, the Fund held a Fanconi Anemia Cytogenetics Conference attended by 27 diagnosticians, researchers and physicians from 9 countries.

For families, the Fund convenes the Annual FA Family Meeting, which is also a recreational camp for parents and children. Besides the networking and recreation aspects of the family meeting, physicians and researchers present research and treatment updates to parents during a three and one-half day conference. This meeting is invaluable to youngsters who can meet with other FA youngsters in a fun and activity-filled environment, for parents who can relax with other FA parents and have an opportunity to talk directly with FA experts, and for those experts to have an opportunity to talk with FA families. In addition, the Fund holds smaller regional meetings throughout the year, bringing together FA families with physicians and researchers to hear about treatment and research updates and to have an opportunity to network with one another.

Finally, in addition to the Annual Family Meeting, the Fund also provides ongoing telephone, letter, and e-mail support to FA families worldwide.

**To contact the Fanconi Anemia Research Fund, Inc:**

Fanconi Anemia Research Fund, Inc.
1801 Willamette Street, Suite 200, Eugene, Oregon 97401
Telephone: 1-541-687-4658
Fax: 1-541-687-0548
E-mail: info@fanconi.org